An-Najah National University
Faculty of Graduate Studies

EFFECTS OF TWO DIFFERENT DOSE REGIMENS OF PROPOFOL ANESTHESIA ON SEIZURE ACTIVITY AND HEMODYNAMICS DURING ELECTROCONVULSIVE THERAPY FOR PSYCHIATRIC PATIENTS: A PROSPECTIVE, RANDOMIZED, OPEN-LABELED, AND CROSSOVER TRIAL

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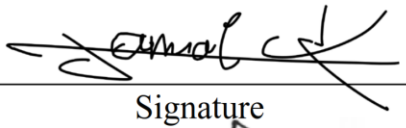
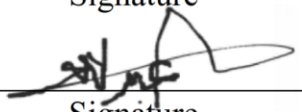
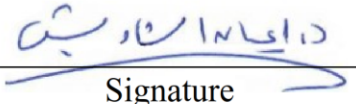
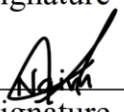
Dr. Jamal Qaddumi Supervisor	 Signature
Dr. Abdallah Alwawi External Examiner	 Signature
Dr. Eman Alshawish Internal Examiner	 Signature
Dr. Naim Kittana Internal Examiner	 Signature

Dedication

I dedicate this achievement to my lovely mother, who always be there for me, supporting me, and pushing me toward success

Acknowledgment

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Declaration

I, the undersigned, declare that I submitted the thesis entitled:

EFFECTS OF TWO DIFFERENT DOSE REGIMENS OF PROPOFOL ANESTHESIA ON SEIZURE ACTIVITY AND HEMODYNAMICS DURING ELECTROCONVULSIVE THERAPY FOR PSYCHIATRIC PATIENTS: A PROSPECTIVE, RANDOMIZED, OPEN-LABELED, AND CROSSOVER TRIAL

I declare that the work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

Student's Name: Mohammad Shaban Abdulrahman Al Haj

Signature: 

Date: **13/9/2023**

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Abstract

Background: Anesthesia is essential for the safety and efficiency of electroconvulsive therapy (ECT). While propofol is widely used as an anesthetic agent for ECT, there are concerns that it produces a dose-dependent reduction in seizure activity.

Objectives: the study aimed to determine a therapeutic propofol dose for optimal ECT outcome by comparing two propofol doses and assessing their effects on seizure activity, hemodynamics, and clinical impacts over ECT.

Methods: The researcher adopted a prospective randomized crossover design to evaluate 25 patients with different psychiatric disorders undergoing two sequential ECTs. Patients were randomly allocated to receive either 1 or 1.5 mg/kg of propofol on the first session of the study. In the subsequent session, the other dose was used. A total of 50 ECT sessions were divided into two groups. LP: low dose propofol (1 mg/kg) and HP: high dose propofol (1.5 mg/kg). Succinylcholine 0.6 mg/kg was given to all patients for neuromuscular blockade. Seizure duration (motor and electroencephalogram), hemodynamic parameters (systolic blood pressure, mean arterial pressure, and heart rate), recovery profile (return of spontaneous breathing, eye-opening, obeying verbal command and ambulation), adverse events, agitation, and patient satisfaction score, were recorded.

Results: LP was associated with a significantly longer motor ($P < 0.002$) and electroencephalogram seizure duration ($P < 0.001$) and a significant increase in the incidence of optimal seizure duration compared with HP. Systolic blood pressure and mean arterial pressure were recorded at 0, 2, and 5 minutes after the seizure ended and were higher following LP. Time to obey verbal commands and ambulation was significantly longer ($P < 0.05$) following LP. Headache was the most obvious adverse

effect following ECT, especially following LP. Agitation and satisfaction scores were comparable following the two administered doses.

Conclusions: Seizure activity and hemodynamics were optimized following LP. The duration of the ECT-induced seizure is the primary determinant of early recovery rather than the propofol dose. In conclusion, the researcher recommends using 1 mg/kg of propofol as it optimizes seizure activity. Further studies are recommended to investigate more anesthetic agents related to ECT practice with a larger sample and consider age-related dosing.

Keywords: Propofol, anesthesia, electroconvulsive therapy, Seizure.

Chapter One

Introduction and Theoretical Background

In the realm of the psychiatric field, the administration of anesthesia plays a crucial role in ensuring the safety and efficacy of Electroconvulsive Therapy (ECT), particularly the dose of anesthesia, which plays a pivotal role in shaping the delicate balance between electrophysiological variables and seizure parameters (1).

ECT is considered an international procedure used to treat patients with certain neuropsychiatric disorders by the inducement of a generalized seizure of the central nervous system (CNS) to produce adequate seizure activity (2). It is considered first-line therapy for major depressive disorder (MDD) when psychotic features and suicide tendencies are severe and rapid improvement is desired. It is used when it is not safe to wait until medications take effect as it is considered to have a more rapid therapeutic response than pharmacotherapy (3), it is also used in patients who have not responded to medication and cannot tolerate side effects (4). However, multiple sessions may be required. In the acute stage of illness, ECT is typically implemented twice weekly, up to 12 sessions (4,5). If the outcome is desirable, the clinical improvement starts to appear after three to five sessions (5). Long-term maintenance therapy may be required to prevent the incidence of relapses by gradually increasing the session interval from once a week to once a month (5).

A variety of theories was hypothesized regarding the mechanisms of action of ECT, which includes altering in the blood-brain barrier, cerebral blood flow, epigenetic processes, various changes in hormone levels such as pituitary or hypothalamic hormones, neurotransmitters (dopaminergic, serotonergic, and adrenergic), and neurotrophic factors, alterations of immune mechanisms and neuroplasticity (6).

The ECT has been used in psychiatric practice since the 1930s as an effective treatment for managing various psychiatric disorders. The most frequent indication of ECT is pharmacological-resistant major depression. At the same time, it is also an effective therapy for treating neuroleptic malignant syndrome, schizophrenia, bipolar, and obsessive-compulsive disorder (7). However, it is not a promising therapy in patients with psychoneuroses, substance abuse, or personality disorders (8).

ECT involves transmitting direct pulses of electrical energy to the patient's scalp by electrodes to generate a generalized tonic-clonic seizure, effectively reducing symptoms

(9,10). Furthermore, the effectiveness of ECT not only depends on the patient history of the therapy but is also influenced by the electrical stimulation's physical properties, which can affect the threshold of the potential seizure, such as electrode location, stimulus dose, pulse amplitude, pulse width, and seizure duration which represented the beneficial impact of the ECT (8,11).

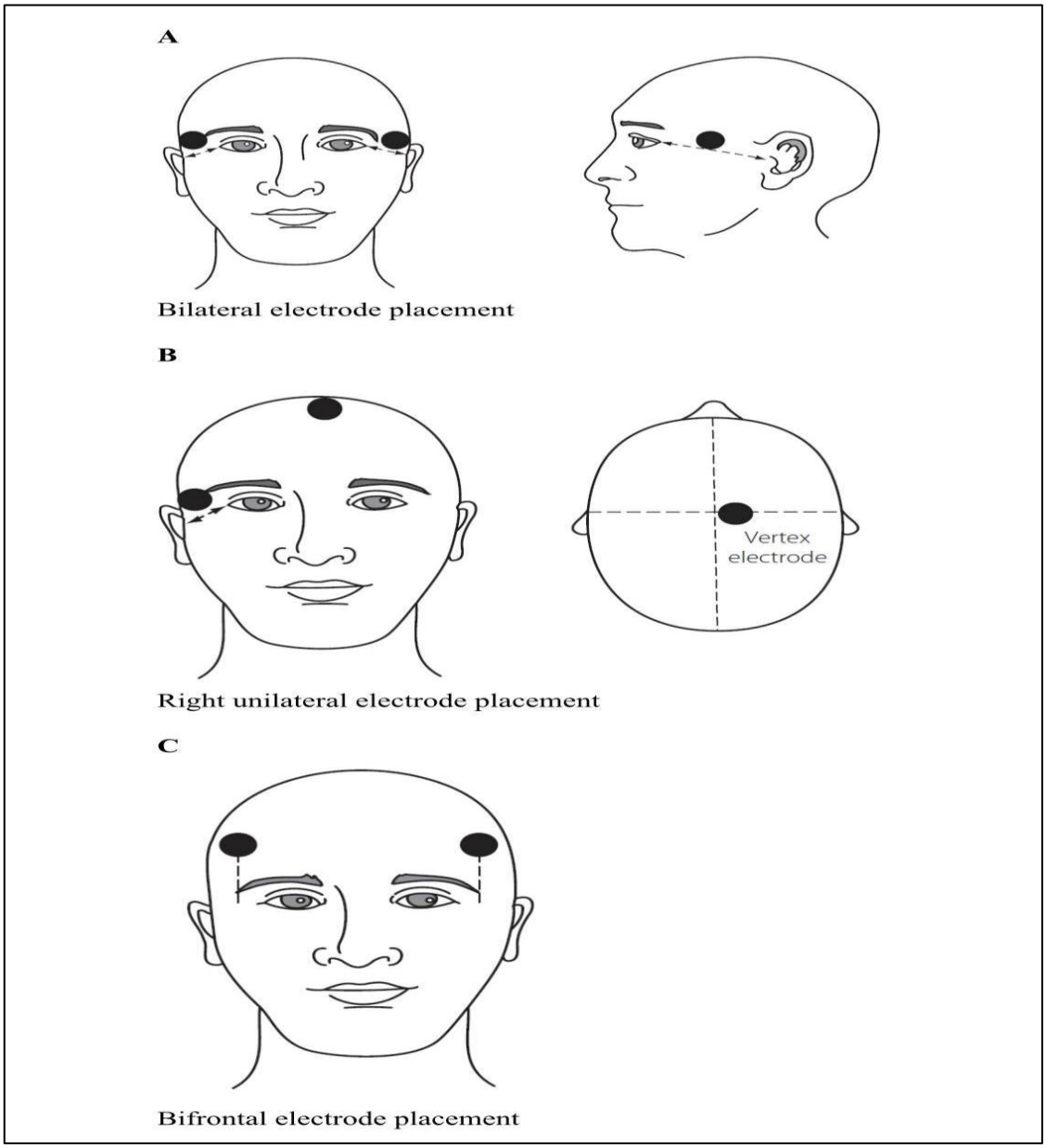
ECT is considered a safe procedure a treatment consideration may need to be taken in pregnant women when the pharmacologic treatment may put her or the developing fetus at risk. However, fetal exposure to anesthetic agents needs to be minimized (10). Regarding the pediatric population, ECT is considered a safe treatment for children; some of the most common psychiatric disorders that can be treated with ECT include autism, catatonia, schizophrenia, bipolar, refractory depression, and unresponsiveness to pharmacological therapy (12), regarding elderly patients, ECT is considered a favorable treatment in the elderly, when the pharmacological therapy may put them at risk. However, the response to ECT becomes slower with advanced age, and the therapeutic effect is limited (13).

Another consideration may be required for patients with cardiac devices or deep brain stimulators. Patients with cardiac devices such as pacemakers are considered safe during ECT, while the device is outside the range of electrical stimulus. However, ECG monitoring is initial. Interpersonal skills are required between the cardiologist and anesthesiologist to balance the risk of illness and the risk of anesthesia(10). A specialized physician regarding deep brain stimulation should be consulted, as it must be turned off to prevent electrical interference from occurring when a generalized seizure is induced (14).

There are three different sites of electrode placements that are commonly used in ECT practices: bilateral (BL), right unilateral (RUL), and bifrontal (BF) Figure 1 (15). Choosing electrode site placements is primarily based on the severity of illness and patient responses to treatment (11). In general unilateral ECT is considered less effective than bilateral and may require a higher stimulus dose for better outcomes. However, unilateral ECT may provide better protection against cognitive impairment following ECT (15). Patients may require multiple sessions depending on their response to treatment (11,15).

Figure 1

Location of electrodes Placement



(A) This site, also known as "bitemporal," or sometimes, "bifrontotemporal," electrodes are positioned symmetrically on the forehead just above the midpoint of a line that runs from the outer canthus on either side of the eye to the auditory meatus. The inferior edge of the circular metal will be about an inch above the line. (B) For the RUL, the right electrode is positioned in the same as for the bilateral. The left electrode is positioned on the left edge directly on a line, which runs from the middle of the skull to the back and is connected to the auditory canal's perpendicular line. While the left edge of the electrode disc is at the vertex position, the center of the disc will be an inch to the right of the vertex.

(C) For the BF, The electrodes are positioned on the forehead about 5 cm above the eye's outer canthus. Reproduced with modifications from Kellner CH et al. Handbook of ECT, American Psychiatric Press, Inc., 1997. (15).

ECT is associated with acute hemodynamics and physiology changes that are usually temporary and reversible, which cause profound autonomic nervous system (ANS) activity (3). At the time of electrical administration and the onset of the generalized seizure, a tonic phase begins, activating the parasympathetic response, resulting in hypotension and short-lived bradycardia lasting 10 to 15 seconds or even asystole (3). Followed by a sympathetic reaction which occurs during the clonic phase of the seizure, causes hypertension in which systolic blood pressure (SBP) increases by 30%-40%, tachycardia in which heart rate (HR) may increase up to 20%, and increase the index of myocardial oxygen demand due to the release of catecholamines in the body which may last from 5 to 10 minutes after the seizure (8). A summary of the physiological responses and adverse effects associated with ECT is shown in Table 1.

Table 1

Physiological responses and adverse effects associated with ECT

Body system	Response
Cardiovascular system (CVS)	Increase blood pressure, heart rate (HR), and Cardiac output (CO); cardiac arrhythmias (Bradydysrhythmias and Tachydysrhythmias)
Central nervous system (CNS)	Increase intracranial pressure, cerebral metabolism, and blood flow velocity; headache, dizziness, confusion, amnesia, and agitation.
Musculoskeletal system	Tonic-clonic seizure, muscle, and joint pain, bone dislocations/ fractures, myoclonic-toxic contractions
Miscellaneous responses	Hypersalivation, nausea, vomiting, oral cavity lacerations, and dental damage.

Note: (3,8,16).

A special consideration related to intracerebral aneurysms, intracranial masses, or retinal detachment may be required due to the high risk of not tolerating the increased intracranial or intraocular pressure from the sympathetic surge after seizure-induced, which can adversely affect the aneurysms and increase the incidence of rupture and altering in cerebral blood flow which leads to worsening patient condition if not treated

appropriately (3). In addition, patients with pheochromocytoma, bleeding disorders, or cardiovascular diseases such as ischemic heart disease, myocardial disease, hypertension, or cardiac arrhythmias may not be favorable for ECT for difficult tolerating the hemodynamic changes from the intensity of parasympathetic and sympathetic responses following the procedure (17). Therefore, for optimal patient care, several pharmacological treatments, such as anticholinergic, β-blockers, calcium channel blockers, α-two agonists, direct-acting vasodilators, local anesthetics, analgesics such as rapid, short-acting opioids, dexamethasone, and diuretics such as furosemide to decrease peritumoral edema have also been explored to reduce the stress response related to ECT (3,18).

During the parasympathetic surge, if the bradycardia is prolonged enough, it may raise the risk of myocardial ischemia. Anticholinergic medicine such as glycopyrrolate or atropine may be prescribed as an antisialagogue or to prevent asystole by blocking the parasympathetic response of bradycardia and hypersalivation. However, using anticholinergic drugs has the unfortunate consequence of causing prolonged tachycardia, which is aggravated during the sympathetic reaction. On the other hand, during sympathetic activation, prolonged hypertension and tachycardia may increase the risk of cardiovascular events resulting in increased myocardial oxygen consumption (10). In addition, the sympathetic responses cause an increase in cerebral hemodynamics, the cerebral metabolic rate of oxygen, cerebral blood flow, and intragastric, intracranial, and intraocular pressure. β-blockers such as esmolol can blunt the sympathetic response (1).

According to the American Psychiatric Association (APA), there are no absolute contraindications to ECT except for a known history of pheochromocytoma (11). There are specific medical conditions that might raise the risk of serious morbidity or mortality, such as vascular diseases, aneurysms, cerebral infarction, high intracranial pressure, and some pulmonary conditions such as (asthma, pneumonia, or severe chronic obstructive pulmonary disease), as well as patients status ranked as American Society of Anesthesiologists (ASA) level 4 and 5 (19).

Historically, prior to the introduction of anesthesia in ECT practice, the procedure had significant physical and psychological impacts on patients' health, resulting in injuries such as bitten tongues, dental and bone fractures, and spine injuries secondary to tonic-

clonic seizures due to electrical stimulation. Thus, it is a very excruciating and stressful procedure (4). In the 1950s, anesthesia was applied to ECT practice to produce ultra-brief general anesthesia combined with a skeletal muscle relaxant to decrease awareness and prevent musculoskeletal injury while minimizing the overall adverse events associated with the ECTs (4).

Appropriate anesthesia is a significant part of optimal ECT outcomes to control hemodynamic response and related complications. Administering intravenous (IV) anesthetics and neuromuscular-blocking agents provides amnesia and musculoskeletal relaxation, allowing effective patient treatment (10). It aims to provide an immediate loss of consciousness, prevent the likelihood of jerky movements, maintain hemodynamic stability, prompt the early recovery of consciousness and spontaneous ventilation, and consider early ambulation to decrease the length of stay in the hospital (18). Although the client feels pain-free, memory loss and confusion are common side effects of ECT. Also, It has been recommended to avoid deep anesthesia to avoid excessive suppression of the seizure activity, which is vital to the treatment (1,4). In the past, ECT was performed under general anesthesia, which may lead to excessive suppression of the seizure activity and decreased effectiveness. Nowadays, there are several options for providing appropriate anesthesia while avoiding general anesthesia (10). Specialists such as psychiatrists and anesthetists must be aware of the factors that affect the seizure activity and overall effectiveness of ECTs, such as hyperventilation, the type of the selection induction agent, the dose requirement, and pre-treatment with xanthine, or caffeine, which has been proven to increase CNS stimulation, resulting in improving seizure activity (1,20,21).

In general, several monitors are required during anesthesia, recommended by ASA, including HR, BP, temperature, oxygenation, ventilation status, and ECG, for observing fluctuating heart rhythm. In addition, specific ECT monitors are required for successful ECT attempts, such as an electroencephalogram (EEG) monitor peripheral nerve stimulator such as electromyography (EMG) to provide a reliable record of seizure activity during the ECT. It is also recommended to use capnography monitoring due to hypercarbia and hypoxia, which may adversely affect seizure duration (22).

Before an ECT attempt, reviewing the patient's medical history is essential, which significantly affects ECT's safety and efficacy (23). During the initial ECT consultation, a review of the patient's concurrent medication is required to taper, discontinue, or temporarily withhold before each ECT. In the past, most psychotropic drugs were tapered and discontinued before ECT. Nowadays, combining some psychotropic medications with ECT is much more permissive due to safety evidence of improved efficacy of ECT (15). A summary of the major categories of psychotropic drugs and their interaction with ECT is listed below:

1. Lithium is considered safe in combination with ECT. It may lower the seizure threshold and increase seizure intensity. Moreover, it delays succinylcholine's action and causes post-ECT delirium. Therefore, it is recommended to be held for at least 24 hours before ECT as it causes the blood-brain barrier to be more permeable following the procedure (3,15).
2. Antidepressant medications have important outcomes during ECT for preventing the incidence of relapse. The newer generation of antidepressant agents, selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), pose less cardiovascular effects compared with the older generation tricyclic antidepressants (TCAs) between the interactions of antidepressants and ECT or the anesthetic agents that used during the ECT course (15). In relation to monoamine oxidase inhibitors (MAOIs), some authors recommend safe conjunction with ECT (24). However, it causes a drug-drug interaction with ephedrine, possibly leading to a hypertensive crisis (3).
3. Benzodiazepines (BZP) can alter the seizure threshold and duration following ECT. Therefore, a taper and/or discontinuation before ECT is recommended (15).
4. Anticonvulsants raise the seizure threshold, which may negatively interfere with the efficacy of ECT. Therefore, a tapered and discontinued before beginning ECT or withholding only the previous day's dose is recommended (15).
5. Antipsychotic medications may lower the seizure threshold. Therefore, combining ECT with antipsychotic drugs may provide a better outcome than when used separately (15).

6. Atypical antipsychotics (AAP) or second-generation antipsychotic medication are recommended to combine with ECT as with first-generation drugs, as it is associated with additive benefits, especially for schizophrenia (15).

This research was performed in Bethlehem Psychiatric Hospital in Palestine, as with every ECT procedure, informed consent needed to be obtained from a legal guardian of the patient. Relating to anesthesia care for ECT patients, a pre-ECT evaluation is essential for a successful ECT, focusing on the patient's medical diagnosis, psychiatric history, physical health, and the patient's current medication, type, dosage, and side effects are also considered. Physical and laboratory examinations, 12-lead electrocardiogram (ECG), chest radiography, serum creatine, and electrolytes are required to overview the patient's health status. Also, airway evaluation must be considered, especially for those complaining of obesity with sleep apnea syndrome, short necks, or a Mallampati Classification III or IV, as they are at higher risk for aspiration and prolonged ventilation. An airway device may be necessary as it maintains a patent airway. The anesthetic must be aware of any signs of airway deterioration and be able to act quickly during emergencies at any time during the procedure (8).

Patients should be instructed to fast for at least 6 hours for solids and 2 hours for liquids before ECT to prevent pulmonary aspiration. Their regular oral medications, such as bronchodilators, thyroid drugs, and cardiovascular agents, such as antihypertensives and anticoagulants, may need to be taken the morning of the procedure with only sips of water as they do not interfere with the seizure activity (10).

ECT is considered a low-risk procedure; special consideration should be taken in patients with acute or chronic hemodynamic abnormalities that put them at risk. Patients with severe hypertension or electrolyte imbalance must be corrected and well-controlled before the procedure (10). Therefore, carefully monitoring and preparing for cardiopulmonary resuscitation is required. Airway equipment includes supplement O2, nasal and oral airway, facemask, a positive pressure ambu-bag, suctioning equipment, laryngoscope, and endotracheal tube with appropriate size, as well as emergency resuscitation medications such as epinephrine, atropine, ephedrine, cortisone, diphenhydramine, and a bronchial dilator inhaler are significant to be standby during anesthesia for any potential life-threatening emergencies such as respiratory depression

or even a sudden cardiac arrest as a result from parasympathetic activation. Ensuring skilled team assistance and adequate resuscitation facilities is required (15).

After the electrode is applied to the chosen site, the proper waveform and stimulus level are selected. After anesthesia induction and loss of consciousness, a soft rubber bite block is placed in the oropharynx to protect the tooth, lip, and tongue from injury during the epileptic seizure (3), followed by positive pressure ventilation via an ambu-bag, and a facemask is continued until the return of spontaneous breathing (25). One of the most significant considerations during ECT is seizure duration. The length of convulsion during ECT is initial for representing the treatment's effectiveness. If necessary, a nerve stimulator and reversal neuromuscular blockade should be used; an EEG and motor seizure duration may be required to determine the seizure quality and effectiveness. A tourniquet technique method to an extremity may be used to prevent the muscle relaxer from affecting an extremity which can help to obtain a reliable record of motor seizure duration (10).

Although ECT is considered a safe treatment, it is associated with common adverse effects such as headache, confusion, myalgia, urinary incontinence, nausea, memory disturbance, cognitive impairment, and post-ECT agitation (26). In addition, pulmonary aspiration or respiratory failure must be considered potential complications due to the residual effect of neuromuscular agents. Premedications such as nonsteroidal anti-inflammatory drugs (NSAIDs) such as ketorolac, BZP such as midazolam, or dexmedetomidine may minimize these effects (8).

A close interprofessional colleague between the anesthetist, psychiatrist, and nursing staff is essential to provide optimal care before, during, and after the procedure (27). The anesthetist must know of the standard physiological alteration and adverse events associated with ECT, determine the patient's comorbidities, and understand the pharmacological actions of anesthetics and adjuvant drugs to promote patient safety. The psychiatrist determines the pattern, amplitude, electrode placement, and stimulus intensity to produce the desired seizure duration with minimal adverse effects, depending on the severity of the disorder. The nursing staff helps to coordinate, schedule the patients, position, monitor, and ensure all safety guidelines are met during the seizure (10,20,28).

This study aims to investigate in advance the anesthetic agents that are most commonly used in ECT anesthesia. However, since propofol is the most common agent used, further studies related to propofol are required.

1.1 Literature review

Several researchers have studied the impact of anesthetic agents on ECT practice. They compared several different anesthetic agents or doses of the same agent regarding seizure activity, hemodynamics stability, recovery time, adverse events, agitation, and patient satisfaction score.

Anesthesia is an essential part of ECT to provide amnesia to decrease the intensity of seizures, prevent anxiety and pain during the procedure, and allow the administration of the muscle relaxant. The induction agents have different anticonvulsant properties in the CNS, so they impact the induced seizure in the ECT setting differently. Since the optimal agent has to be rapid onset and recovery with short duration, maintaining hemodynamic stability, and having lesser adverse effects on seizure activity; therefore, different agents can be used depending on the patient's clinical characteristics (1,29).

When selecting an anesthetic dose for ECT, it is essential to ensure that the level of sedation is appropriate, as it varies depending on the patient's response to various drugs. Furthermore, too deep an anesthesia level raises the seizure threshold, and it may negatively interfere with the seizure quality and increase the incidence of short and missed seizures. In contrast, light sedation may be painful and stressful for all patients (30). Thus, it is recommended to maintain a balance between providing adequate anesthesia and avoiding deep anesthesia to avoid excessive suppression of seizure activity, which is a significant part of the treatment (31). Literature confirmed that the appropriate level of sedation during ECT is achieved when the absence of verbal commands and loss of eyelash reflex (32,33). This eyelash reflex test is usually used following propofol administration to confirm that the level of sedation is appropriate. The efferent limb of the eyelash reflex is mediated by the facial nerve (cranial nerve VII), whereas the afferent limb is via the trigeminal nerve (cranial nerve V). The eyelash reflex can be triggered by gently brushing a finger across the patient's eyelashes and observing for involuntary blinking of the orbicularis oculi in response to the stimulus (30). However, even with the use of modern devices in ECT to determine the level of anesthesia, such as the

bispectral index (BIS), it has been proven that it is not a reliable method for these patients due to the interictal changes that occur in the conscious patients following the ECT treatment (34).

1.1.1 Methohexital

Methohexital is an ultrashort-acting barbiturate that stimulates Gamma-aminobutyric acid (GABA) receptors, the brain's primary inhibitory receptors. It is considered the drug of choice for ECT as it has a lesser interference with the seizure threshold does not directly affect seizure quality, and maintains hemodynamic stability, which makes it the optimal drug for ECT except when there is a contraindication to a barbiturate, such as acute intermittent porphyria. In addition, it can also cause moderate cardiac depression, which counteracts the effect of the sympathetic responses following the seizure. The typical dose for ECT is around 1 to 1.5 mg/kg (8,35).

Since methohexital is the agent of choice in ECT, as mentioned in previous literature (36). It is not available in many countries. An appropriate replacement of methohexital is required. Different studies have recommended several anesthetic agents in ECT, such as thiopental, propofol, etomidate, and ketamine (4).

1.1.2 Thiopental

Thiopental is another barbiturate agent similar to methohexital; It promotes the action of GABA-A receptors in the brain and causes hypnosis. However, it produces an anticonvulsant effect. Therefore, it reduces seizure length and is associated with a longer recovery time than methohexital due to its longer duration. Also, compared to propofol, it has a higher incidence of arrhythmias, such as sinus bradycardia and premature contractions. It can increase cerebral blood flow and produce moderate hemodynamic changes, which makes it less favorable in ECT anesthesia. The typical dose is 2-4 mg/kg. (4,8).

1.1.3 Propofol

Propofol is a sedative-hypnotic agent, popular in anesthesia for induction and maintenance of general anesthesia, used in a wide range of settings for procedural sedation and prolonged sedation in intensive care units. It is an alkylphenol derivative, highly lipid-soluble. It also acts as a GABA agonist. It is a nonbarbiturate agent with

antihypertensive and antiemetic properties. It has a rapid onset and duration. It produces a temporary loss of consciousness up to 40 seconds following IV injection, lasting 8 minutes, depending on the dose. The typical dose is 1.0–1.5 mg/kg (4,8).

Propofol suppresses the effects of acute hemodynamic variations following ECT and depresses the cerebral cortex, leading to decreased vascular and systemic peripheral resistance and lower central venous pressure in a dose-dependent manner. The decline in preload and contractility lowers the stroke volume and leads to hypotension. Propofol significantly reduces vascular resistance, blood pressure, and stroke volume compared to thiopental. Additionally, it produces more significant respiratory depression (4). It is usually preferred over other agents in treating patients with chronic hypertension or for patients with hemodynamic instability (37). However, it has potent anticonvulsant properties, which may raise the seizure threshold and interfere with seizure quality (30). Therefore, it is usually preferred in patients with low seizure thresholds, such as adolescents, to prevent prolonged seizures (37).

Different authors have different recommendations regarding the use of propofol in ECT. Some believe it is a better alternative to methohexital as it can provide a rapid emergence and recovery, more hemodynamic stability, and is favorable for patients with cardiac disease (9,38–42). Additionally, propofol is usually indicated for patients with a low seizure threshold and a history of prolonged seizure duration >170 seconds, those with refractory post-ECT nausea and vomiting, and a history of severe postical agitation (22). Other authors advise against its routine use due to its anticonvulsant effect as it has a dose-depend adverse impact on the quality of seizure when compared with other anesthetic agents, which significantly decreases seizure duration (43,44) – hence, several seizures can be considered inefficient (42). However, kind of literature shows that using propofol may not necessarily affect ECT's efficiency when treating depression (38,45). Therefore, a further investigation of propofol anesthesia regarding ECT is required.

In a retrospective study by Vaidya et al. (36), reviewed in patients anesthetized with propofol or methohexital, propofol was found to be associated with lower-quality seizures, requiring restimulation for short seizures, and a higher stimulus dose may indicate. A randomized, non-crossover trial by Geretsegger et al. (40) compared propofol and methohexital in 50 patients by using age-based dosing, allowing comparison of the

anesthetic impact on cognitive functions throughout five timepoints of ECTs; before the beginning of the ECT sessions, after the third to fifth sessions, after the end of the last ECT session, and follow up at two weeks and eight weeks later after the last ECT session. Unfortunately, no conclusions were presented to compare the effects of methohexital and propofol at these timepoints. Instead, general results are presented. Investigating the significant reduction of seizure duration is limited due to the lack of data regarding stimulus dose. Although there were no differences in the anterograde memory function of subjects, those who were given propofol showed better cognitive performance. At the same time, propofol has been associated with altering seizure adequacy by raising the seizure threshold and reducing seizure duration. However, the difference is insignificant in this study; these results might be due to higher stimulus doses in the propofol group. Despite the reduction in seizure duration, the impact on seizure quality is minimal. Furthermore, it has been suggested that there is no relationship between seizure duration, seizure quality, and the overall clinical efficiency of ECT. Therefore, the study has proven propofol is a safe anesthetic agent for ECTs (40).

A group of 50 patients by Jarineshin et al. (41) compared the influence of propofol (1-1.5 mg/kg) and thiopental (2-3 mg/kg) on seizure duration and hemodynamics, which include SBP, diastolic blood pressure (DBP), and HR during ECT. Patients with a history of heart disease, kidney failure, neuromuscular disease, hypertension, and diabetes mellitus were excluded. The mean seizure duration of the propofol group was significantly lower (32±11.3 sec) than the thiopental group (40.3±16.6 sec) (P=0.001). No significant differences in the mean energy level were applied in both groups. Concerning hemodynamics SBP, DBP, and HR at 3 and 5 minutes were significantly lower in the propofol group than in the thiopental group. Propofol may provide better hemodynamic stability and is recommended over thiopental, especially for patients with cardiovascular disease. However, one study limitation is that the group did not have co-existing or underlying medical conditions, which may affect the results. Another research by Swaim et al. (43) established that propofol was associated with increased missed or short seizure incidence and required a higher electric stimulus dose than methohexital and thiopental. However, certain studies (39,46) have recommended propofol over thiopental as it has a superior effect on hemodynamic stability during ECT with earlier recovery parameters, including cognitive functioning.

1.1.3.1 Comparison of Propofol doses

A previous retrospective study by Aytukuk et al. (7) compared two different ranged doses of propofol sorted into two groups, group (low dose: $<$ 1 mg/kg) and group (high dose: $\geq$ 1mg/kg), and recorded their effect on seizure duration, energy requirement, and seizure threshold. Longer seizure duration was observed in the low-dose group. A higher electrical threshold was found in both groups. However, this rise was more evident in the high-dose group. Another author Sakamoto et al. (47) assessed the impact of three different propofol doses (1.0, 1.5, or 2.0 mg/kg) and thiamylal (4 mg/kg) on overall recovery, including cognitive functioning and their impact on seizure duration and hemodynamics. The study reports that thiamylal was associated with higher seizure activity compared with propofol in a dose-dependent manner, whereas a low propofol dose inhibits the early cognitive recovery time. The mean maximum increases of SBP above the baseline in propofol (1.5, 2.0) groups was significantly less than propofol (1.0) and thiamylal. However, The mean maximum increase of HR over the baseline was considerably less than with thiamylal. The recovery time of the four groups was not significantly different. The study summarized that the reduction of seizure durations due to propofol may not be associated with a reduction in the therapeutic efficacy compared with other anesthetic agents.

A study by Avramov et al. (35) utilized a crossover design to analyze the impact of three doses of three different anesthetic agents on seizure duration, hemodynamic stability, and cognitive recovery. Propofol, methohexital (0.75, 1.0, and 1.5 mg/kg), and etomidate (0.15, 0.2, and 0.3 mg/kg). Following ECT, The highest seizure duration (motor and EEG) was observed with etomidate induction and the lowest with propofol. Therefore, increasing propofol and methohexital doses resulted in reduced seizure duration compared to etomidate, whereas etomidate was not dose-dependent on seizure duration among the three doses. In addition, propofol significantly reduced hemodynamic response and decreased mean arterial pressure (MAP) in the patients. However, the effects of etomidate and methohexital were not significant. Regarding recovery time, they were similar regardless of the type of hypnotic agent or given dose. Moreover, cognitive recovery was delayed following a more extended seizure period.

1.1.4 Etomidate

Etomidate, another anesthetic drug, activates GABA receptors in the brain. It is recommended in patients with a history of shortness of seizure activity lasting less than 20 seconds. Literature has demonstrated that it promotes seizure activity compared to propofol, thiopental, or methohexital. (48). Additionally, As it is less likely to induce cardiac depression, the sympathetic responses are more prominent when used as a sole agent for ECT. Adjunctive agents, β-blockers such as esmolol, or short-acting opioids such as remifentanil may minimize the sympathetic response. Etomidate is associated with a higher incidence of delirium, confusion, nausea, and vomiting. It is contraindicated for patients with critical illness or adrenal insufficiency because prolonged use can cause adrenal suppression. The typical dose is 0.15 - 0.3 mg/kg, lasting up to 10 minutes (8,49,50).

A recent study by Shastry et al. (54) contained 80 patients divided into two equal groups to compare propofol 2 mg/kg and etomidate 0.3 mg/kg. Seizure duration and hemodynamics following ECT were recorded. Seizure duration following etomidate administration was significantly longer than propofol (P = 0.001). Regarding the hemodynamic response, both agents had similar profiles with no significant differences. Concluded that propofol was associated with a shortening of seizure activity, while with etomidate, there was a better quality of seizure. It recommended that propofol may have a near-favorable and ideal seizure duration compared to etomidate.

Gazdag et al. (48) conducted a randomized crossover study of 34 patients with schizophrenia aimed to assess the influence of propofol (1 mg/kg) and etomidate (0.2 mg/kg) on both EEG and EMG seizure duration and hemodynamics MAP and HR during ECT. The length of seizure duration, as measured by EEG and EMG, was significantly shorter with propofol than with etomidate (47.9 ± 21.3 s, 61.29 ± 22.4 s, P= 0.014) and (33.6 ± 15.9 s, 46.3 ± 23.8 s, P= 0.006) respectively. Meanwhile, no difference was observed between the two agents regarding the number of restimulations required for short seizure duration that lasted less than 20 seconds. Based on the study findings, etomidate is recommended if a total dose of propofol cannot produce an appropriate seizure duration lasting 20 seconds. This outcome may be explained by propofol reducing seizure duration to less than 20 seconds and may only affect seizure duration, not threshold. Relating to hemodynamics, following propofol administration, the rise in MAP

due to seizure was far less than when etomidate was administered. Therefore, propofol seems preferable for patients with a risk of cardiovascular complications; another research by the same authors (51) compares the influence of propofol (1 mg/kg) and etomidate (0.2 mg/kg) on seizure activity EEG and EMG and seizure threshold in a group of 30 patients with different types of schizophrenia. Both EEG and EMG seizure duration following propofol administration was less than etomidate (39.7 ± 19 s, 49.6 ± 23.1 s, P= 0.026) and (32.8 ± 17.6 s, 41.4 ± 22 s, P=0.16), respectively. However, there were no significant differences in the minimum energy for seizure-eliciting stimulation among both agents.

Rosa et al. (52) conducted a study containing 30 patients with depression to assess the impact of thiopental, propofol, and etomidate on the cardiovascular system by recording SBP, DBP, and HR variation during ECT before induction of the anesthetic agent and immediately after the seizure ends. The participants in the study were healthy, with no previous history of cardiovascular disease, and were not on any current therapy. There were no significant hemodynamic differences among the three anesthetic agents. Therefore, they concluded that these anesthetic agents may be appropriate for patients with a free medical history of heart disease. Another research by Rosa et al. (53) assesses the impact of the three anesthetics: thiopental, propofol, and etomidate, on recovery time following ECT. The recovery parameters were based on the Aldrete-Kroulik index. There were no significant differences among the three agents regarding recovery time. However, the propofol group provided the shortest recovery time, although this group was treated with the highest stimuli dose.

The inconsistent results between Rosa et al. and Gazdag et al. might be due to the research conducted by Rosa et al. was performed on healthy patients with no history of cardiac disease, and they were not on antihypertensive drugs, whereas these from the study conducted by Gazdag et al. concurrently receiving psychotropic medications (48,52).

A study by Erdil et al. (54) demonstrated that propofol controlled the hemodynamic response more effectively than etomidate and did not cause QT prolongation on ECG compared to etomidate. Hence, propofol might be a better choice for ECT with a lower incidence of arrhythmias. However, Stadtland et al. (55) demonstrated that the switch from propofol to etomidate who could not have an epileptic seizure lasting more than 30

seconds, even with a higher stimulus dose of electrical current, resulting in a significant prolongation of seizure activity lasting 18–43 seconds duration.

1.1.5 Ketamine

Another notable anesthetic agent in ECT practices is ketamine, an N-methyl-D-aspartate (NMDA) receptor antagonist with both hypnotic and analgesic effects. It has antidepressant properties so that it may speed the onset of the antidepressant effect of ECT, and it is effective for seizure-inducing results and lengthens short seizures. Therefore, it is recommended for patients with increased seizure thresholds (56). However, ketamine-based anesthesia has unfavorable adverse effects as it is associated with excitation of the cardiovascular system, sympathetic activation of the nervous system, and hypothalamic depression. Furthermore, it can also cause psychiatric adverse effects, such as hallucination, disorientation, and confusion, and increase the incidence of post-ECT nausea and vomiting; all these factors limit its routine use in ECT (57–59). However, Ketamine's antidepressant properties make it an ideal choice for treating patients with depression. The typical dose is 1–2 mg/kg for adequate anesthesia with optimal ECT outcome (8). Compared with the other anesthetic agents, ketamine recovery is the longest, followed by etomidate, methohexital, and propofol (10).

Hoyer et al. (59) examined 3932 ECT sessions retrospectively on four anesthetic agents: thiopental, propofol, etomidate, and ketamine, regarding their effect on the quality of seizure based on five parameters (seizure duration, central inhibition, amplitude, synchrony, and activation of ANS). Due to the lack of anticonvulsant properties of ketamine and etomidate, they were associated with higher seizure activity compared with thiopental and propofol. Ketamine was the most favorable agent regarding central inhibition. At the same time, The highest percentage of patients who had higher MAP with SBP over 200 mmHg was observed with ketamine (47.3%), followed by thiopental (29.2%), etomidate (23.2%), and propofol (7.1%).

1.1.6 Ketofol

Literature has recommended the use of a combination of propofol and ketamine (also known as ketofol) over ketamine alone to combine the advantage of both hypnotic agents, as it is well-proven that propofol can efficiently decreases ketamine's side effects in many clinical setting (32,33,58).

Erdogan Kayhan et al. (33) compared propofol 1 mg/kg and ketofol 1 mg/kg (propofol 0.5mg/kg plus ketamine 0.5 mg/kg) on seizure quality, hemodynamics parameters, recovery profiles, and adverse events. EEG and motor seizure duration were similar among the two groups, propofol (38±16 and 28±13 seconds, respectively) and ketofol (41±17 and 29±17 seconds, respectively). The Postictal suppression index (PSI) was lower in the propofol (79.74±14.6)($P < 0.05$) than in the ketofol (89.63±7.88). In the propofol group, hemodynamics MAP and HR were significantly lower than in the ketofol group at 0 and 5 minutes following the seizure. Obeying commands were prolonged in the ketofol group ($p<0.05$). The study concluded that ketofol could be an excellent alternative strategy to improve seizure quality and enhance the overall clinical efficiency of ECT.

1.1.7 Inhalational agents (sevoflurane and enflurane)

Most ECTs are performed outside the operating room, and IV anesthesia is generally preferred over inhalational agents. However, it is an appropriate technique to initiate anesthesia for an uncooperative awake patient with agitation, needle phobia, expected difficult airway management, and IV access is still not in place. When used for short periods, it has a rapid recovery time and can be a more potent agent to reduce acute hemodynamic changes following ECT. However, they have a slow induction compared to IV anesthetics and are considered a trigger agent for malignant hyperthermia (MH) (8,60). Sevoflurane and enflurane have been compared favorably with propofol (44,60). Studies conducted on sevoflurane revealed that it significantly decreased the activity of seizures compared to barbiturates, ketamine, and propofol (61). Adjective agents such as β-blockers or opioids are often used to maintain hemodynamic stability because they do not reduce sympathetic activation during ECT. However, it enhances muscular blockade compared to IV anesthetics (60).

Pekel et al. (60) have compared propofol 0.75 mg/kg and sevoflurane 5% with respect to seizure duration, PSI, BIS values, hemodynamics MAP and HR, recovery profiles (onset of spontaneous respiration, open-eyes, and following verbal commands) and adverse events. No significant differences were found between the two agents regarding induction time, PSI, stimuli dose, seizure activity, and recovery. Concerning hemodynamics, HR was significantly higher with propofol than with sevoflurane ($P= 0.001$) at 1 min

following ECT, and MAP was significantly lower with propofol than sevoflurane (P=0.048).

Another study by Wajima et al. (62) compared sevoflurane, propofol, and sevoflurane-propofol as combined during ECT relating to hemodynamics and seizure activity. Peak HR and MAP were highest in sevoflurane. Recovery time was the longest in sevoflurane-propofol. Regarding seizure activity, motor, and EEG seizure duration was significantly highest in the propofol group, followed by sevoflurane and sevoflurane-propofol. Therefore, anesthesia based on propofol is the most advantageous regarding seizure activity. Regarding hemodynamics, propofol-sevoflurane anesthesia is the most advantageous compared with propofol and sevoflurane. Thus, the study recommends that the routine use of sevoflurane induction is not an appropriate alternative anesthetic agent for ECT because it has no benefits on seizure activity and hemodynamics in ECT and should only be used when venous access is challenging due to dehydration, confusion, agitation, or when needle phobia is present.

In another study by Dogan et al. (44), propofol and enflurane were compared during general anesthesia regarding their effects on seizure duration and recovery time following ECT. Twenty patients were enrolled to receive either propofol 1.2 mg/kg or enflurane 5% in random turn by crossover design. No significant differences were found regarding seizure duration, whereas propofol recovery time was significantly higher. Therefore, they have concluded that sevoflurane and enflurane may provide an appropriate alternative induction agent to propofol for patients undergoing ECT. However, no additional benefits were revealed in reading to seizure activity compared to propofol (44,62).

A summary comparison of anesthetic agents related to seizure duration, threshold, hemodynamics, and recovery time following ECT is shown in Table 2.

Table 2

Comparisons of the anesthetic agents regarding seizure parameters, hemodynamics, and recovery time following ECT

Domains	Description	Anesthetic agents
Seizure Duration	Seizure duration increasing property in ascending order:	Propofol < Thiopental < Sevoflurane < Methohexital < Ketamine < Etomidate
Seizure Threshold	Seizure threshold increasing property in ascending order:	Etomidate < Ketamine < Methoheital < Sevoflurane < Thiopental < Propofol
Hemodynamics	HR increasing property in ascending order:	Propofol (decreased) < Etomidate (no effect) < Thiopental < Methohexital < Ketamine
	MAP increasing property in ascending order:	Propofol (decrease) < Thiopental < Methohexital < Etomidate (no effect) < Ketamine (increase)
Cerebral Hemodynamics	The cerebral metabolic rate of oxygen increasing property in ascending order:	Propofol < Sevoflurane < Methohexital and Thiopental < Etomidate < Ketamine
	Intracranial pressure and cerebral blood flow increasing property in ascending order:	Propofol < Methohexital and Thiopental < Etomidate < Ketamine
Recovery Time	Recovery time increasing property in ascending order:	Sevoflurane < Propofol < Barbiturates < Etomidate < Ketamine

Note: (1) HR; heart rate, MAP; mean arterial pressure.

1.1.8 Depolarizing neuromuscular blockade

The Primary aim of muscle relaxation during ECT is to protect the musculoskeletal system during the electrical stimulus from the massive tonic-clonic seizure that could lead to muscle and bone injuries, rhabdomyolysis, or hyperkalemia, as well as to obtain reliable evidence of seizure and improve airway management (63). Succinylcholine is an ultra-short-acting, depolarizing neuromuscular blocker. Therefore, it is considered the muscle relaxant of choice for ECT. The recommended dose in the clinical practice ranges between 0.5– 1 mg/kg for appropriate muscle relaxation. It typically lasts up to 8 minutes after induction, with independent reversibility (64). However, it is associated with several

adverse events, such as myalgia, which can be minimized by NSAIDs such as ketorolac. Also, it causes hyperkalemia by raising the serum potassium level by 0.5 meq/L following injection. Therefore, it should be avoided when there is a high plasma potassium level to prevent further lethal arrhythmias. Moreover, it is considered a trigger agent for MH, and it should be replaced with another muscle relaxant if the patient has a history of MH (8,65).

1.1.9 Nondepolarizing neuromuscular blockade

Conversely, nondepolarizing neuromuscular blocking agents do not affect serum potassium and do not cause hyperkalemia which are appropriate alternatives to succinylcholine when susceptible to MH or with contraindications to succinylcholine (66). While the most commonly used in ECT are vecuronium and rocuronium, which are as effective as succinylcholine, literature has shown that a dose of rocuronium 0.6 to 0.7 mg/kg would give a similar effect to succinylcholine (65). However, the long duration is the most significant disadvantage of these agents, whose effects persist for up to 25 minutes; the usage of appropriate reverses, such as sugammadex, could make these agents useful in ECT.

Sugammadex and Rocuronium, as combined, are proven to be an appropriate replacement for succinylcholine regarding seizure activity and overall clinical outcomes, as they are associated with rapid action and recovery (67). Anesthesiologists must be aware of antiepileptic medications or mood stabilizer agents such as lithium, which may adversely affect the activities of depolarizing and nondepolarizing neuromuscular blocking agents and larger doses may be required (10).

1.1.10 Adverse events

ECT is considered a low-risk procedure with minor adverse events that could be associated with the treatment itself or the induction agent (26). Patients may experience headaches, confusion, myalgia, and nausea. Headache and myalgia can be appropriately managed with paracetamol, aspirin, or NSAIDs such as ketorolac or ibuprofen. The stress and anxiety before the ECT attempt, the induction agent, the seizure itself, or air in the stomach from ventilation can all trigger nausea; therefore, It can be managed with agents such as metoclopramide or ondansetron (22,25). In relation to the induction agent, propofol is associated with several adverse effects, such as hypotension, bradycardia,

respiratory depression, burning on injection, and arrhythmias. Precaution must be taken in elderly patients with cardiac compromise, respiratory disease, hypotension, and increased intracranial pressure. A small dose of lidocaine 1% before induction or mixed with the same syringe may be appropriate to minimize the burning sensation during the injection. Also, it may be appropriate for patients at risk for postoperative nausea and vomiting (PONV) as it has antiemetic properties. However, it is contraindicated in patients with a history of seizures, as it has been shown to have convulsant and anticonvulsant effects (25).

The most popular adverse events following ECT are headaches and cognitive functioning impairment, especially following a prolonged seizure duration (68). A long seizure duration may occur frequently in adolescents and patients at their first ECT session (26). If unmanaged, this may increase post-ECT confusion and amnesia (69). Therefore, propofol or benzodiazepine may require to termination of a prolonged seizure (10). Other less common adverse events that may be minimized with appropriate anesthesia are bone and tissue injury, constant seizure duration, facial flush, changes in autonomic function, respiratory distress, and hypoxia (70,71). In addition, the impact of hemodynamics response following ECT, cardiovascular response, sequentially stimulating sympathetic and parasympathetic nervous systems, increases HR and BP, followed by bradycardia or asystole, which may cause transient ischemic changes, arrhythmias, and increased myocardial oxygen demand. Transient cardiac changes before ECT could be minimized with premedication such as anticholinergics, IV narcotics such as remifentanil, or local anesthetics such as lidocaine. Variations after ECT can be controlled by β-blockers such as labetalol or esmolol, antihypertensives such as nitroglycerin or nitroprusside, or calcium channel blockers such as nifedipine or verapamil (2).

During recovery, an evaluation by cardiology or neurology may be required due to the risk of developing acute neurological and cardiovascular variations such as myocardial infarction, hemorrhagic, or ischemic stroke. Patients also usually experience temporary memory and cognitive impairment (10). In the first type of cognitive impairment, the patient becomes briefly restless, confused, agitated, and postictal adverse effects such as paralysis or mania up to 30 minutes following the procedure. A second type that may be noticed later is anterograde amnesia, in which the patient cannot form new memories. It can be frightening to patients and usually subsides within days to a few weeks. A third

type is retrograde memory dysfunction, in which the patients fail to recall memories for several weeks to months. There is no evidence that ECT causes brain injury or leads to long-term cognitive impairment. Moreover, several factors may be involved, such as the number of ECT sessions the patient had, stimulus energy, electrode placement, and the type of anesthetic agent (25). Therefore, The common side effects of each anesthetic agent and their impact on ECT before and after electrical administration are summarized in Table 3.

Post-ECT agitation (restlessness, excitement, and panic) is the most common concern following the procedure. A recent study compared three different types of anesthetic agents during ECT, thiopental 3 mg/kg, Propofol 1 mg/kg, and ketofol 1 mg/kg (ketofol is a mixture of propofol 0.5 mg/kg plus ketamine 0.5 mg/kg) regarding their effects on seizure duration, hemodynamics, recovery parameters, and agitation score. Seizure duration was highest in thiopental (30.78 ± 12.80) compared to propofol (24.85 ± 10.72) and ketofol (25.88 ± 12.25); Therefore, the difference was not significant. The agitation score was significantly highest in thiopental (2.13 ± 0.57), compared to propofol (1.63 ± 0.49) and ketofol (1.77 ± 0.63). No significant differences were observed in recovery parameters or overall hemodynamics (72).

Dexmedetomidine has been recommended in ECT anesthesia as premedication, decreasing the acute hemodynamic responses that ECT may cause and reducing the intensity of post-ECT agitation with no adverse effect on seizure duration and quality and patient recovery profiles (8). A study containing 40 patients with depression aims to assess the impact of ketofol with and without dexmedetomidine when given as preadministration on agitation score and patient satisfaction following ECT. Agitation score > 2 was significantly higher in ketofol group (8.6%) than ketofol-dexmedetomidine group (1.4%). And the patient's satisfaction score was significantly lower in the ketofol group (1.53 ± 0.16) than ketofol-dexmedetomidine group (1.75 ± 44) (73).

Table 3

Effects of anesthetics on hemodynamics during ECT (before/after) electrical administration

Anesthetic drugs	Anticonvulsive properties	Seizure duration	Heart Rate	Blood Pressure	Cerebral Blood Flow	Common side effects
Methohexital	++	intermediate	→ / ↑	↓ / ↑↑	NE	Nausea, hypotension, and delayed awakening
Thiopental	++	short	↑ / ↑	↓ / ↑↑	↓ / ↑↑	Nausea, hypotension, Histamine release
Propofol	+++	short	↓/↑→	↓/↑	↓ / ↑	Injection pain, hypotension
Ketamine	-	long	↑ / ↑	↑/ ↑↑	↑ / ↑↑	Psychotic action, hypersalivation, PONV
Ketofol	++	intermediate	→ / ↑	→ / ↑	NE	Decreased ketaminergic side effects
Etomidate	+	long	→ / ↓	→ / ↑↑	NE	Adrenal suppression
Benzodiazepine	+++	short	→ / ↑	↓ / ↑	NE	Long Acting
Sevoflurane	+++	short	↑ / ↑	↓ / ↑	↑/ ↑↑	Slow induction, a trigger for MH
Enflurane	+++	Short	↓ / ↓	↓ / ↑	↑ / ↑↑	Slow induction, a trigger for MH

Note: (2,4,8,29,32,33,40,44,74,75) ECT: electroconvulsive therapy, NE: not evaluated, MH: malignant hyperthermia, PONV: postoperative nausea and vomiting.

1.2 Problem statement

The usage of ECT is increasing. Therefore, there are some weaknesses related to this therapy. A delayed or resistant effect of ECT has been reported. Adjunctive treatment with psychotropic drugs or different anesthetic agents may significantly alter ECT's beneficial outcome (58). Anesthesia is a significant aspect of the safety and efficiency of ECT (27). While under anesthesia, an external electrical device is attached to the patient's scalp to induce a seizure, resulting in a generalized seizure with a varied duration (10).

The ideal hypnotic agent provides amnesia with rapid onset and emergence, minimal interference with the seizure activity, and minimal physiological and physical responses.

However, since most short-acting anesthetic agents have anticonvulsant properties, they can adversely affect seizure activity by raising the seizure threshold and reducing the widespread of seizures and therapy efficacy (35). For ECT, anesthesia can be achieved with two agents, the induction agent, and the muscle relaxant, with the assistance of ventilation and oxygenation. Therefore, various induction agents and muscle relaxants are used (76). Choosing an induction agent is a balance to ensure adequate amnesia while minimizing its effects on the ECT's efficiency (21,44).

Methohexital is the agent of choice used worldwide for ECT due to its favorable characteristics, such as rapid onset and brief duration with minimal anticonvulsant properties. However, it is not available in Palestine territory. Therefore, several alternative agents may be applied in ECT anesthesia, such as thiopental, etomidate, ketamine, and propofol (27). Different characteristics of each anesthetic agent can affect ECT effectiveness and tolerability (29).

Similar to methohexital, thiopental is a barbiturate that can be used to treat various conditions. However, it has a longer recovery time with more incidence of cardiac arrhythmias, such as sinus bradycardia and premature contractions (27). Etomidate is a nonbarbiturate imidazole derivative; it seems the preferable agent regarding seizure activity compared with other induction agents due to the lack of anticonvulsant properties (1). It also provides cardiac stability as it is less likely to cause hypotension in patients with congestive cardiac failure (27,77). However, it has been reported as associated with myoclonus, angialgia, longer recovery time, and more incidence of post-ECT confusion (27,78). For the NMDA antagonist, ketamine has intrinsic antidepressant properties, and it may speed up the onset of the antidepressant response of ECT (1). However, several adverse effects have limited its application in ECT anesthesia, such as the excitement of the cardiovascular system, hallucinogenic activity, and PONV. Therefore, it is considered an appropriate alternative to enhance seizure activity when it fails to induce generalized seizure with barbiturates (58).

Propofol, another popular anesthetic agent, is fast-acting, nonbarbiturate, and has potent anticonvulsant and antihypertensive properties (27,58). It has become a common agent for ECT as it is associated with rapid onset and recovery and positively impacts overall hemodynamics. However, it produces a dose-dependent reduction in seizure activity due

to its anticonvulsant properties, which lead to decreased seizure duration (32,44). Even so, propofol's shortened seizure duration may not affect the quality of the seizure and ECT efficacy. It may be beneficial when prolonged seizures are present (1). In addition, it might be preferable for cardiac patients as it is associated with minor hemodynamic response, minimal post-ECT confusion, and PONV (77). However, propofol has Several challenges; it has no pharmacologic antagonist, a narrow therapeutic index, and can produce a profound hemodynamic and respiratory depression effect (2). Another common adverse effect of propofol is angialgia, which has a painful sensation on injection, which has been reported as the highest incidence of angialgia before propofol and methohexital induction (31).

Although a propofol dose ranging between 1 to 2 mg/kg is adequate for induction in most cases (7), using the lowest possible dose has been recommended to prevent seizure suppression (10). several factors might influence the propofol requirement, which can affect pharmacokinetics and pharmacodynamics, such as age, body mass index, degree of anxiety, cardiac output, speed of induction, and drug interaction (79,80). Therefore, a fixed dose may be required to define the therapeutic outcome of ECT. However, a fixed amount may have had different impacts on patients of various ages (81).

In summary, thiopental, an old barbiturate, was used in ECT as the first induction agent. However, it has a strong anticonvulsant effect on seizure activity, which limits its use in ECTs. Methohexital, a newer version of barbiturate, is considered the drug of choice for ECTs. However, it is not available. Etomidate and ketamine might be preferable in comparison with other agents due to the lack of their anticonvulsant properties. However, other factors, like drug safety, may require additional attention. Ketofol mixture or ketofol-dexmedetomidine combination can be used as an alternative induction agent to overwhelm the disadvantages of the main induction agents. Regarding inhalational agents, these agents may be appropriate for patients who are not cooperative with IV access; therefore, These agents rarely exist outside the operation room (1).

In the literature, the impact of propofol on seizure quality is controversial. There are several various findings on the effect of propofol on seizure activity with or without a history of seizure disorder; A study on propofol use revealed that lower doses tend to induce epileptic seizures. On the other hand, higher doses have anti-epileptic effects,

suggesting that propofol possesses proconvulsant and anticonvulsant properties in a dose-depended fashion. (82). Conversely, following propofol anesthesia, epileptic and non-epileptic patients have experienced seizure-like phenomena (SLP) (83). Various elements can influence the outcome of propofol on cerebral electrical activity, including the induction dose, speed of induction, time interval after administration, supplementary anesthetic and analgesic drugs, patient age, and co-existing disease state (51).

Several studies have revealed that propofol reduces seizure duration during ECT compared to methohexital. However, no significant differences were found regarding the overall clinical efficacy (39,40,84,85). Furthermore, it is well established that propofol raises seizure threshold dependent on dose based on animal studies (86). It is proven that patients sedative with propofol cannot experience a seizure longer than 30 seconds (55). Therefore, a higher electrical stimulus or another anesthetic agent (e.g., Etomidate) may be required to enhance the seizure duration length (55).

Regarding the study hospital, the hospital uses propofol as its primary induction agent for their ECTs. Also, the hospital policy does not allow the use of different anesthetic agents. Because of these challenges, propofol has become the only choice for this study, as it is a popular induction agent with low cost, wide accessibility, and advantages over other anesthetic agents.

Finally, ECT has been gradually increasing in treating psychiatric patients, but appropriate anesthesia is required to reduce anxiety and pain associated with seizures. However, an appropriate agent with a proper dose is required. Since propofol is the most available agent, it could be an appropriate choice for ECT with the lack of methohexital. But still, a suitable dose is required to adjust. Therefore, the current study aims to define an ideal propofol dose for optimal therapeutic response by comparing two fixed-dose regimens of propofol (low dose: 1 mg/kg, high dose 1.5 mg/kg) to improve the clinical effect of ECT by assessing its impact on seizure duration and hemodynamics.

1.3 Significance of the study

ECT involves applying an electrical stimulus through unilateral or bilateral cerebral hemispheres to induce a generalized seizure. Therefore, choosing the appropriate stimulus dose is one of the most significant in ECT for an adequate seizure, which is the therapeutic goal of ECT.

Seizure threshold determination is required to select an appropriate stimulus dose. It refers to the slightest electrical stimulus required to elicit a minimum of 25 seconds of seizure duration. A stimulus dose exceeding the seizure threshold several times may maintain the therapeutic ECT outcome. However, The induced dose may not be maximally therapeutic if it is very close to the seizure threshold. On the other hand, if the dose is far excessively from the seizure threshold, it may lead to excess cognitive impairment (15).

The initial threshold is known to vary among individuals. Elderly over 60 years old, currently on anticonvulsant therapy or frequent ECT sessions, may raise the seizure threshold. Unfortunately, no reliable method exists to estimate a patient threshold from clinical or demographic data. However, several strategies can be used to determine the initial dose level, such as titration-based, age-based, fixed-high, and based on patient characteristics (15,87,88).

Usually, on the first ECT attempt, the stimulus dose is determined by repeating the administration of electrical therapy until an appropriate fit is obtained. It has been recommended to exclude the first ECT attempt from research as it is also associated with longer seizure duration (89). ECT works by raising the threshold of seizures and reducing their duration due to the anticonvulsant effect that positively impacts the brain; therefore, an increase in electrical stimulus may be required after several sessions (25).

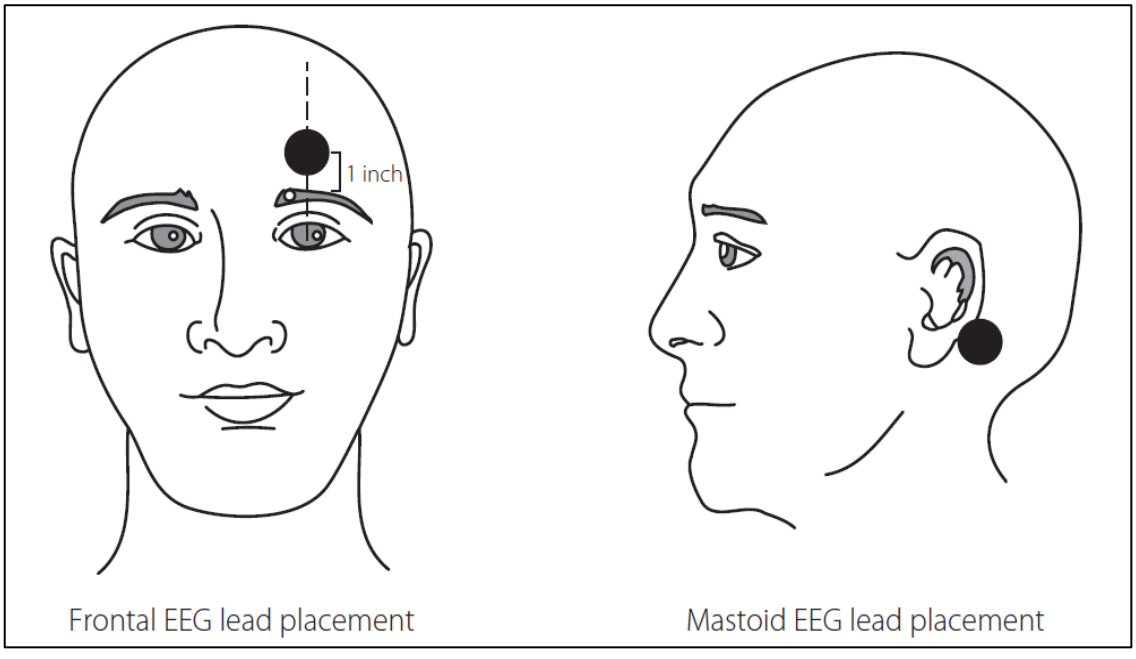
In the present study, The threshold determination will be determined by the resident psychiatrist based on patient characteristics dosing chart schedule by Braithwaite et al. containing factors that are known to be associated with the seizure threshold, such as the patient's age, sex, electrode placement, previous ECT attempt within at least a month ago, and on maintenance anticonvulsant therapy Appendix D.

One of the essential outcomes following ECT is to monitor the brain states during the seizure activity, which reflects the antidepressant effects. Two methods are used to

monitor seizure activity, including motor and EEG. Therefore, several techniques are used to monitor the seizure. For example, an EMG monitor is used to monitor the motor seizure activity by placing two electrodes into the isolated extremity and inflating a cuff pressure slightly above the SBP, so the muscle relaxant cannot reach the insolated extremity and observing tonic-clonic activity in that extremity—other techniques by using EEG seizure duration, EEG morphology, and Thymatron PSI. (74). An EEG contains four leads with a minimum of two channels; two leads are placed on the forehead 1 inch above the eyebrow in the mid-pupillary line of each side. The other two leads are placed behind the ear, at the mastoid bone, which allows better monitoring of seizure activity in both hemispheres Figure 2 (15). Moreover, several studies suggest that PSI correlates best with the clinical efficacy of ECT. Therefore, an increased PSI may increase effectiveness (90,91). The PSI is calculated by dividing the number of ECT sessions where the patient had postictal suppression by the total sessions received (92).

Figure 2

EEG electrode placement



EEG is considered to be more reliable regarding seizure activity in comparison with motor activity. Previous studies have shown that motor seizure duration is approximately 5 seconds slower than the EEG waveform under the same conditions (8). The optimal EEG seizure duration during ECT lasts 25 to 75 seconds for the best clinical outcome (5).

However, a motor seizure that lasts 25 to 50 seconds is considered optimal (8). Therefore, a period below 15 seconds is considered extremely short, while a period above 125 seconds is considered prolonged, which are inappropriate responses to ECT. The anesthetist needs to intervene for any untherapeutic seizure to improve or terminate the seizure by using several techniques as pharmacologic agents require. (5,28). Thus, knowing the pharmacological agents that may vary seizure threshold and duration is essential (93).

According to previous studies, The duration of seizure activity during ECT may be influenced by many factors, such as the electrode placement site, stimulus intensity dose, induction agent, the patient's present medication, time of ventilation and oxygenation, the first ECT session, as it has proven to produce a longer seizure duration, and the age, since the seizure threshold is increased with age (26,89,94,95) Therefore, using bilateral electrode placement instead of unilateral, higher intensity dose, or using addition pharmacological agent to improve the seizure activity such as caffeine or aminophylline, by stimulating the CNS (20). In addition, a recent study showed an improved seizure quality and clinical efficacy of ECT by extending the time interval between the hypnotic induction time and electrical stimulation of ECT to overcome the initial action of the anticonvulsant effect (96).

Propofol has become a popular and recommended anesthetic agent for several advantages; it is associated with less incidence of nausea and vomiting, faster emergence, rapid psychomotor and cognitive recovery, minimal hemodynamic response, and may be required to induce shorter seizure duration in patients with low seizure thresholds. However, it adversely affects seizure activity if not used appropriately (37). Also, it can cause vein irritation and painful injection sensations during induction (97). Unlike the BZP, there is no pharmacologic antagonist. Therefore, several studies have recommended using the local anesthetic agent lidocaine in several forms to prevent angialgia, such as injection into the IV line before the anesthetic with or without vein occlusion or mixing lidocaine with the anesthetic medication and injecting them simultaneously (31).

The degree of reduction in seizure duration during propofol anesthesia is dose-related (37). However, this reduction may not be associated with diminishing the clinical effect of ECT and may not alter PSI during propofol anesthesia (9,98).

Certain medications and techniques may be used to enhance seizure duration, such as hyperventilation for a few minutes, which allows minimum carbon dioxide levels and some redistribution of the propofol away from the brain, thus supplementing IV caffeine and aminophylline (given slowly), which results in longer seizure duration (38,99). Since propofol has potent anticonvulsant properties, previous studies suggest it is a suitable anesthetic agent for ECT as it does not reduce the overall clinical effectiveness. Even so, with the reduction of the seizure duration of propofol, the duration may still be within the optimal range. Therefore, an advanced exploration of propofol is required (40,85).

This research will focus on improving ECT outcomes by minimizing the unfavorable adverse effects of propofol on seizure duration as possible by comparing two different dose regimens of propofol. Low dose propofol 1 mg/kg (LP) and high dose propofol 1.5 mg/kg (HP) to define an optimal induction dose to achieve the desired sedation level with minimal interference on seizure activity and with minimal adverse events. Both motor and EEG will measure the seizure duration. However, unfortunately, the motor seizure duration will be observed without using the isolated extremity method due to the lack of an appropriate tourniquet in the study hospital.

1.4 Aims of the study

- To determine a therapeutic dose of propofol anesthesia for optimal ECT outcome for patients with psychiatric disorders in Bethlehem Psychiatric Hospital.
- To compare the effect of LP and HP administration on seizure activity of ECT for patients with psychiatric disorders in Bethlehem Psychiatric Hospital.
- To assess the hemodynamic variation following the two administered doses of propofol during ECT for patients with psychiatric disorders in Bethlehem Psychiatric Hospital.
- To compare the agitation score and patient satisfaction following the two doses of propofol for patients who underwent ECT in Bethlehem Psychiatric Hospital.

1.5 Research questions

- Are there differences in motor and EEG seizure duration following the two propofol doses during ECT?
- Is HP associated with a higher incidence of short seizure duration following the ECT course?
- Is LP associated with a higher incidence of optimal seizure duration following the ECT course?
- Is LP associated with a lower incidence of adverse events following ECT?
- Is HP associated with longer recovery time following ECT?
- Are there significant hemodynamics parameter variations following the two administered doses of propofol following the ECT course?
- Is there a significant difference in the agitation score and patient satisfaction following the recovery of the two propofol doses?

1.6 Hypothesis

1.6.1 The null hypothesis (H0)

There will be no significant differences at a level of ($\alpha \leq 0.05$) related to hemodynamics (SBP, MAP, and HR) following the two administered propofol doses among psychiatric patients during the timepoints of ECT.

There will be no significant differences at a level of ($\alpha \leq 0.05$) related to patient satisfaction scores following the recovery from the two propofol doses among psychiatric patients who underwent ECT.

There will be no significant differences at a level of ($\alpha \leq 0.05$) related to agitation scores following the recovery from the two propofol doses among psychiatric patients who underwent ECT.

1.6.2 The alternative hypothesis (H1)

There will be a significant difference at a level of ($\alpha \leq 0.05$) related to longer motor and EEG seizure duration following LP administration compared with HP throughout the ECT.

There will be a significant difference at a level of ($\alpha \leq 0.05$) related to a higher frequency of optimal seizure duration following LP compared to HP administration during the ECT.

There will be a significant difference at a level of ($\alpha \leq 0.05$) related to a higher frequency of short seizure duration following HP compared to LP administration during the ECT.

There will be a significant difference at a level of ($\alpha \leq 0.05$) related to a lower incidence of adverse events following LP administration compared to HP throughout the ECT.

There will be a significant difference at a level of ($\alpha \leq 0.05$) related to longer recovery time following HP compared to LP administration during the ECT.

1.7 Conceptual Definitions

Electroconvulsive therapy (ECT): It is a medical psychiatric procedure that induces a brief therapeutic seizure by delivering electrical currents to the brain via electrodes placed on the patient's scalp. It is particularly for major depressive disorder and other mood disorders when psychotic features and suicide tendencies are severe and rapid improvement is desired (19)

Electroencephalography (EEG): is a noninvasive diagnostic test that analyzes the amplitude and frequency of brain waves by inserting electrodes into the patient's scalp. The results are graphically shown (13).

The postictal suppression index (PSI) is dividing the number of ECT sessions where the patient had postictal suppression by the total sessions received (92).

Electromyography (EMG): A peripheral nerve stimulation device is commonly used in clinical practice to measure the transmission of neuromuscular signals. It can also be used to observe muscle contraction (99).

Seizure: an involuntary convulsion, spasm, or series of jerking movements of the face, trunk, arms, or legs as a result of the electrical stimulus of ECT (100).

Propofol: is an alkylphenol compound (2, 6-diisopropyl phenol) and is water insoluble. It is a hypnotic anesthetic drug used for general anesthesia induction and/or maintenance. It is also used as a sedative agent for monitoring anesthesia care; it has various settings. It

works as inhibitory neurotransmission mediated by the GABA receptor binding site. It has poor analgesia effect but with good antiemetic properties (3,99,101).

1.8 Operational DefinitionsMotor seizure duration

The interval between the end of the ECT stimulation to the end of tonic-clonic movement in the extremities (32).

EEG seizure duration: from initiating an amplitude waveform until return to baseline (102).

Seizure threshold: defined as the minimum electrical stimulus dose required to result in eliciting an appropriate seizure activity of at least 25 seconds on EEG and proven clinically (7,51).

Optimal seizure: a seizure duration motor lasts 25 to 50 seconds, and an EEG lasts 30 to 75 seconds (5,8,59).

Sub-optimal seizure: a seizure duration lasts longer than the optimal duration, up to 120 seconds (3).

Short seizure: a seizure duration of the motor lasts less than 25 seconds, and an EEG lasts less than 30 seconds (5,59).

A missed seizure: is when no motor activity develops following the stimulus's delivery (15).

A prolonged seizure: a seizure activity persists for more than 120 seconds (5,15).

Sedation level: when the patient no longer responds to verbal commands and loses eyelash reflex (32,33).

Agitation score: it is a score of five categories used to assess the level of agitation based on the clinical assessment, in which; “1 = sleeping”, “2 = awake and calm”, “3 = irritable and crying”, “4 = inconsolable crying”, “5 = severe restlessness and disorientation” (73).

Satisfaction score: it is a score of four categories used to evaluate patient satisfaction based on patient clinical assessment, in which “1 = pleased and calm patient”, “2 = no

complaint" (not bad satisfaction), "3 = some complaints" (neutral satisfaction), and "4 = complained" (treatment was unpleasant, and the patient does not want to undergo the same experience again) (73).

Early recovery criteria: is the time from succinylcholine administered until the return of (spontaneous breathing, eye-opening, obeying a simple verbal command, and ambulation) (32,33).

Post-ECT adverse events: headache, angialgia, myalgia, nausea, vomiting, delirium, hallucination, agitation, fear, hypertension, hypotension, tachycardia, bradycardia, and respiratory depression (32,58).

Headache or confusion: feeling dizziness and unable to walk (58).

Delirium: reduces awareness of the environment (58).

Hallucination: A profound distortion in a person's perception of reality (103).

Nausea: The urge to vomit (103).

Vomiting: Expulsion of stomach contents (103).

Angialgia is a painful sensation at the injection site during propofol induction (97).

Myalgia: is a common side effect of succinylcholine that involves muscle aches and pain, including the soft tissues and ligaments that connect bones (104).

Bradycardia: HR less than 50 beats/min (32).

Tachycardia: HR more than 100 beats/min (32).

Hypotension: MAP less than 60 mmHg (32).

Hypertension: MAP more than 120 mmHg (32).

Hypoxemia: peripheral oxygen saturation (SPO2) of 90% or less (32).

Respiratory depression: respiratory rate less than 10 breaths/min for longer than 10 seconds in duration or apnea longer than 6 seconds without respiratory effort (32,103).

Chapter Two
Methodology

This section of the study will introduce the methodology that is applied. It includes design, setting and period, population, inclusion and exclusion criteria, sample size, sampling technique, ethical consideration, instrument checklist, data collection method, and analysis plan.

2.1 Study design

A prospective, randomized, open-labeled, crossover trial. The reason for choosing a crossover design is the higher degree of variability between participants in response to the anesthetic agent and response to ECT. Having participants serve as their control decreases the chance of interpatient variability, enhancing the power of the study, and allowing smaller sample sizes.

2.2 Study setting and period

This study was conducted in the ECT room at Psychiatric Hospital in the West Bank, Bethlehem, Palestine. The study was conducted from November 2022 - January 2023.

2.3 Study population

Inpatients or outpatients with different psychiatric disorders who were scheduled to undergo several ECT sessions with BF electrode placement two times a week and fulfilled inclusion criteria were included during the study period at Bethlehem Psychiatric Hospital.

2.4 Inclusion criteria

Acute cases of inpatients or outpatients with different psychiatric disorders ranging between 18 to 60 years old with ASA grade I & II status as defined in Appendix C, who underwent two or more ECT sessions and have completed their first ECT session in Bethlehem Psychiatric Hospital.

2.5 Exclusion criteria

The exclusion criteria for this study were (1) first ECT session; (2) advanced age > 60 or young age < 18 years old; (3) ASA grade III –V; (4) chronic diseases in cardiovascular,

cerebrovascular, or intracranial hypertension or any respiratory tract diseases; (5) history of substance misuse; (6) history of allergy-related to propofol anesthesia; (7) pregnancy; (8) maintenance ECT session; (9) hypothyroidism and hyperthyroidism; (10) legal guardian of the patient refuse to signature; (11) severely agitate patients and uncooperative (12) requiring to increase seizure threshold dose; (13) special patients undergoing ECT without anesthesia; (14) require additional dose; (15) loss of follow up.

2.6 Study variables

2.6.1 Dependent variables

Seizure duration (motor and EEG), hemodynamic profiles, adverse events, recovery time, agitation score, and patient satisfaction.

2.6.2 Independent variables

Age, sex, weight, ASA status, propofol dose, stimulus dose, current medication, and the number of previous ECTs.

2.7 Sample size determination

The sample size was calculated based on previous study findings with the same comparison characteristics. According to Avramov et al. (35), the mean and standard deviation of the motor seizure duration of propofol 1 mg/kg and 1.5 mg/kg were obtained from the study. Using the G*Power version 3.1.9.4 sample size software calculator to reach a power of 0.95 at a significant level of 0.05, using a one-sample, two-sided nonparametric test, Each group was required to have at least 17 as shown in Appendix F. Accordingly, we included 25 participants with 50 ECT sessions to provide adequate power for our clinical outcome parameters. Flow charts of the patient's progress through the trial's phases are shown in Appendix G.

2.8 Sampling and data collection technique

On each day of ECT sessions (Sunday and Wednesday), one patient from the scheduled list was selected randomly by computer-generated random numbers to receive either 1 or 1.5 mg/kg of propofol for the first session of the study. On the next day of the ECT session, the patient was crossed over to the other dose, respectively (1:1) until the required sample was obtained.

A structured observations checklist was prepared in English, which includes three parts; the first part is the pre-ECT phase, which contains demographic and anesthesia data. The second part is the actual ECT phase, which contains seizure parameters and the monitoring of intra-procedure hemodynamic changes (SBP, MAP, and HR). The 3rd part is the post-ECT phase, which includes recovery parameters, adverse events, agitation, and patient satisfaction scores. Luckily, Due to the hypnotic and seizure effects, the patients were unaware they were observed. Therefore, the data were obtained by the author after becoming familiar with the checklist Appendix B.

2.9 Statistical analysis and interpretation

Data were analyzed using a Statistical Package for Social Sciences (SPSS), Chicago, IL, USA version 28 package. The data were validated and corrected by the investigator. The data distribution's normality was checked using Shapiro-Wilk tests, which showed that data was not normally distributed. The Mann-Whitney U test was used for non-parametric data, whereas the descriptive data were presented through their frequency, percentages, mean score, and stander deviation. A chi-square test was used for the categorical data. A value of ($\alpha \leq 0.05$) was considered significant.

2.10 Anesthesia and ECT administration

In Bethlehem Psychiatric Hospital, ECT was scheduled twice a week (Sunday and Wednesday) early in the morning. There are two types of patients, inpatients and outpatients. The inpatients are those patients who are residents in the hospital in the acute ward. However, the outpatients are those patients who are outside the hospital and were prescribed an ECT treatment multiple times by the outside clinic. The patient who planned for ECT had to fast for 6 hours for solids and 2 hours for liquids. Necessary drugs, such as bronchodilators, antihypertensive, anticoagulants, and thyroid medications, may be allowed to be taken with a sip of water early in the morning of the procedure day. Patients currently on maintenance therapy of oral anticonvulsant medication or a high dose of psychotropic drugs/ mood stabilizers such as lithium are instructed to be held for 24 hours before the procedure. The study was conducted as a prospective open technique with a crossover design. After selecting a random patient from the scheduled list by computer-generated simple random sample, a printed informed consent Appendix A and information sheet were provided to a legal guardian of the

chosen patient in both English and Arabic language as shown in Appendix H and I. After obtaining the signature of the patient legal guardian, the patient was officially included in our study. The crossover effect was three to four days, the patient who was selected for the Sunday session, will be carried over next Wednesday. Also, the patient who was selected for the Wednesday session will be carried over to next Sunday.

The patient was encouraged to go to the toilet to empty their bladder, as urinary incontinence is expected after the procedure. Initial vital signs were taken by applying a non-invasive sphygmomanometer to the left upper limb for blood pressure monitoring; HR and SPO2 were obtained by a pulse oximeter sensor which was fixed on the patient's right side. An IV access was established without giving any premedication for all patients. Thymatron EEG monitoring (Thymatron™ DGx, Somatics Inc, Lake Bluff, IL, USA) was applied to the patient's scalp as shown in Figure 2.

The patient was pre-oxygenated using 10 L/min O2 via a facemask. After a randomized selection of one of the two propofol doses (1 mg/kg, 1.5 mg/kg), a lidocaine of 10 mg at a concentration of 1%, was mixed with the propofol in the same syringe to avoid venous irritation. The induction agent was injected over 5 seconds. Loss of awareness was defined as the loss of response to simple verbal commands and the eyelash reflex. Muscle relaxation was achieved by succinylcholine 0.6 mg/kg to prevent convulsion-induced musculoskeletal injuries. Within 60 seconds after induction, an additional dose is administered if the patient is still responsive to verbal commands, the eyelash reflex has not been lost, or whatever propofol 1 mg/kg or 1.5 mg/kg failed to induce unconsciousness. therefore, the patient will be dropped out of the study.

After the loss of consciousness, positive pressure ventilation was applied using an ambu-bag balloon, and a facemask on 10 L/min oxygen was placed and continued until the return of spontaneous breathing. The ventilation was paused during the electrical stimulus delivery and resumed immediately after the end of the fit to prevent any interruption of the motor seizure duration and EEG waveform.

Prior to the application of electrical stimulation, a bite block was applied to protect teeth, lips, and tongue to prevent injuries and tongue laceration; the electrical impulse was applied 1 minute after succinylcholine injection via BF electrode placement, using a Thymatron system (Thymatron™ DGx, Somatics Inc, Lake Bluff, IL, USA) for all

patients. The psychiatrist determined the seizure threshold stimulus dose according to the dosing schedule Appendix D and maintained the same amount for each patient for both sessions to improve the interpretation of the relevance of the shortening in seizure duration.

The effectiveness of the ECT was verified by the length of the generalized tonic–clonic seizure that appeared on the patient's body and the duration of the EEG waveform until it returned to baseline. The psychiatrist confirmed these data every time.

For each patient, the following data were collected: patient gender, age and weight, ASA physical status, medical diagnosis, current medication, number of the current ECT, propofol dose either (1 mg/kg or 1.5 mg/kg), stimuli dose, seizure duration (motor and EEG), hemodynamics response (SBP, MAP, and HR), recovery parameters, adverse events, agitation score, and patient satisfaction.

Hemodynamic parameters (SBP, MAP, and HR) were subsequently monitored with pulse oximetry and sphygmomanometer, before the seizure (T-baseline), immediately after the seizure (T0), and following two (T2), five (T5), and ten (T10) minutes after the seizure ends.

The recovery measurement time was recorded from the end of succinylcholine administration until the return of spontaneous breathing, eye-opening, obeying a simple verbal command, and ambulation. The patients were assessed for adverse events such as headache, angialgia, myalgia, nausea, vomiting, delirium, hallucinations, hypertension, hypotension, tachycardia, bradycardia, sense of fear or agitation, and signs of respiratory distress.

After full recovery, agitation score and patient satisfaction were evaluated based on Shams and El-Masry research (73); the agitation score was assessed by an emergency agitation score in which “1 = sleeping”, “2 = awake and calm”, “3 = irritable and crying”, “4 = inconsolable crying”, “5 = severe restlessness, and disorientation”. Patient satisfaction score was evaluated by a satisfaction scale, in which “1 = pleased and calm patient”, “2 = no complaint” (satisfaction is not bad), “3 = some complaints” (neutral satisfaction), and “4 = complained” (the procedure was unpleasant, and the patient does not want to undergo the same experience again).

2.11 Ethical consideration

The Institutional Review Board (IRB) approved the study at An-Najah National University Appendix E. The investigator obtained approval from the Ethics Committee of the Ministry of Health (MOH), and permission from Bethlehem Psychiatric Hospital was obtained. A signature consent form was obtained from the patient's legal guardian before participation in the study Appendix A. Each patient and patient's legal guardian who participated in the study received a verbal and written information sheet and a full explanation about the purpose of the study before deciding to participate in both languages, English and Arabic as shown in Appendix H and I. The advantages and disadvantages of the study doses were explained.

The research followed the World Health Organization's (WHO) declaration on Helsinki's ethical principles for medical research on humans. Patients and their legal guardians were informed that participating in the study is voluntary, and they are free to withdraw from the study at any time without giving any excuse. All data were kept anonymous and under the investigator's use only. Integrity, respect, privacy, anonymity, and confidentiality were considered. All data was filled into SPSS and then discharged. No one has the authority to access any information except the investigator himself.

Chapter Three

Results

In this section of the study, the author includes the main results and highlights the signification outcomes of propofol (1.0 and 1.5 mg/kg) as an induction agent for ECT concerning seizure activity, hemodynamic parameters, recovery profile, agitation, and patient satisfaction score among the patients undergoing ECT.

3.1 Demographic and clinical characteristics

As shown in Table 4, the categories variables are expressed in frequencies and percentages, out of the 25 patients who participated in the study, 17 were male (68%), and eight were female (32%). with 19 ASA I (76%) and 6 ASA II (24%). Eight patients (32%) were on their 2^{nd} - 3^{rd} session, eight patients (32%) were on their 3^{rd} – 4^{th} session, five patients (20%) were on their 4^{th} – 5^{th} session and four patients (16%) were on their 5^{th} – 6^{th} session. The majority of patients receiving ECT were diagnosed with MDD (52%), followed by schizophrenia (20%), bipolar mood disorder (16%), schizoaffective disorder (8%) psychotic disorders (4%) Figure 3. At the same time, the majority of current medications were antidepressant therapy (76%), followed by AAP (68%), anticonvulsant drugs (52%), BZP (32%), and Lithium (20%) Figure 4.

The scale variables were expressed as (mean ± SD) and range, age was (37.48 ± 12.021) [21 – 60]. At the same time, the mean weight was (81.16 ± 11.862) [60 – 106]. Succinylcholine 0.6 mg/kg was given to all patients as the neuromuscular blockade agent, the mean of succinylcholine dose (48.84 ± 7.145) [36 – 64], LP (81.16 ± 11.862) [60 – 106], HP (121.72 ± 17.784) [90 – 159]. The psychiatrist determined the voltage value millicoulomb (mC) according to the dosing schedule as shown in Appendix D. The mean score of the voltage value is (27.20 ± 7.916) [15 – 45].

Table 4

Baseline Characteristics of the study group (n=25)

Variable	n	%
Gender		
Male	17	68.0%
Female	8	32.0%
ASA Status		
ASA I	19	76.0%
ASA II	6	24.0%
Sessions No. during the two periods		
(2nd – 3th)	8	32%
(3th – 4th)	8	32%
(4th – 5th)	5	20%
(5th – 6th)	4	16%
Diagnoses		
Major depressive disorder (MDD)	13	52.0%
Bipolar Mood Disorder	4	16.0%
Schizophrenia	5	20.0%
Psychotic Disorders	1	4.0%
Schizoaffective Disorder	2	8.0%
Current Medications		
Antidepressants	19	76.0%
Lithium	5	20.0%
Benzodiazepines (BZP)	8	32.0%
Atypical Antipsychotic (AAP)	17	68.0%
Anticonvulsants drugs	13	52.0%

Variable	Mean	SD	Min	Max
Age (years)	37.24	11.476	21	60
Weight (kg)	81.16	11.862	60	106
Succinylcholine dose (mg/kg)	48.84	7.145	36	64
LP (mg/kg)	81.16	11.862	60	106
HP (mg/kg)	121.72	17.784	90	159
Voltage value (mC)	27.20	7.916	15	45

Figure 3

Distribution of mental health disorders

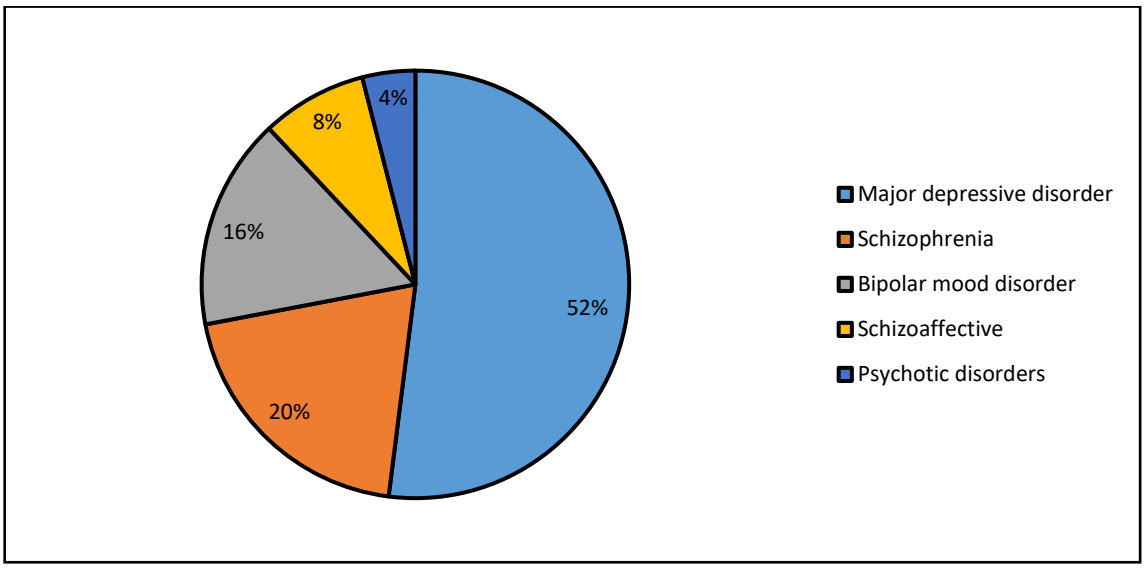
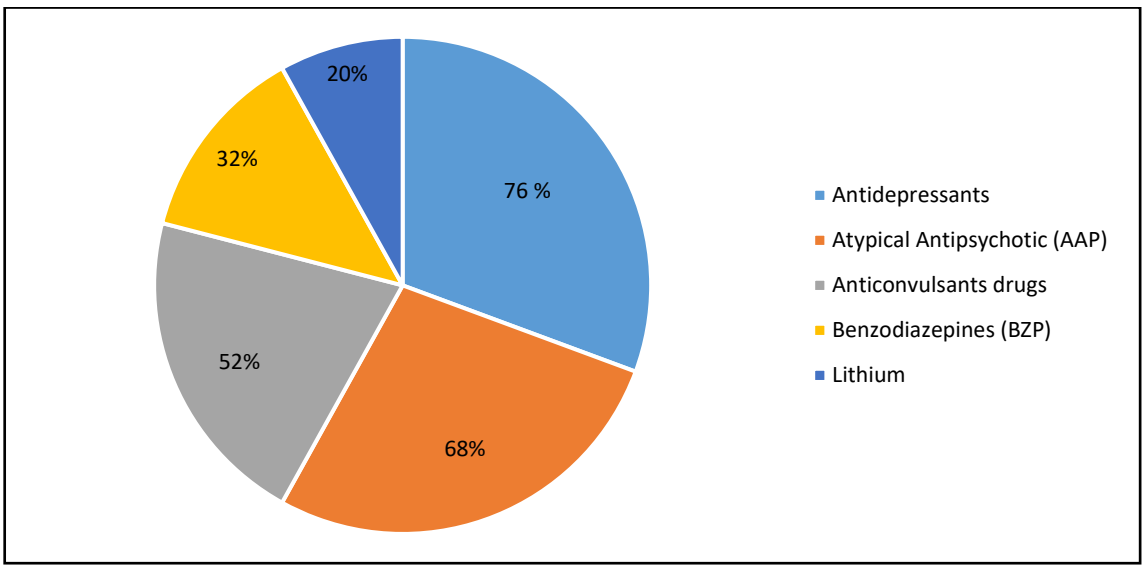


Figure 4

Current medication distribution among the subjects



3.2 Seizure parameters

As shown in Table 5 a significant dose-related difference in EEG (U=143, p=.001) and motor (U=154, p=.002) following LP and HP administration. A Mann-Whitney U test presented that patients following LP administration have a higher rank score than HP in EEG and motor seizure duration (32.28, 31.84) and (18.72, 19.16), respectively.

Table 5

Seizure activity parameters

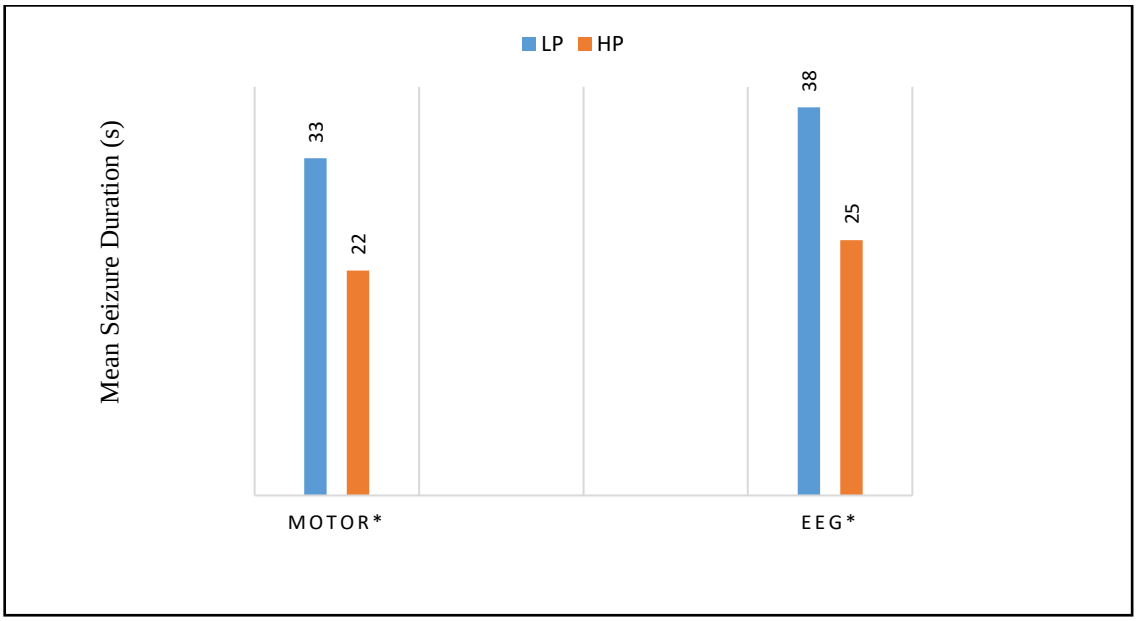
Variables	Propofol dose	n	Mean Rank	Sum of Rank	Statistical values	P-value
EEG duration (sec)	LP	25	32.28	807	U=143 Z=-3.293	<.001*
	HP	25	18.72	468		
Motor duration (sec)	LP	25	31.84	796	U=154 Z=-3.079	.002*
	HP	25	19.16	479		

Note: Mann Whitney U test.

*Significant at p=<0.05.

Figure 5

mean score of seizure activity during the ECT



Note: Mann Whitney U test.

*Significant at p=<0.05**.**

Figure 5 The duration of motor and EEG seizures following LP and HP administration. Blue bars = 1 mg/kg doses; Orange bars = 1.5 mg/kg doses. *significant differences (P < 0.05).

As shown in Table 6, seizure activity was sorted into five categories (missed, short, optimal, sub-optimal, and prolonged). No 'missed', 'sub-optimal', or 'prolonged' seizure was observed in either group. The optimal seizure duration measured by EEG and motor following LP and HP administration was [18/25 (72%), 11/25 (44%)] and [16/25 (64%),

8/25 (32%)], respectively. At the same time, the short seizure duration measured by EEG and motor following LP and HP administration was [7/25 (28%), 14/25 (56%)] and [9/25 (36%),17 (68%)], respectively. Therefore, the Chi-Square test indicates there is a significant difference between LP and HP related to the number of optimal and short seizure activities measured by both EEG (X2=4.023, p=0.045) and motor (X2=5.128, p=0.024).

Table 6

Seizure Activity Classification

Seizure activity domains	Seizure activity classification	LP		HP		Pearson Chi-square	P-Value
		n=25	%	n=25	%		
EEG	Optimal	18	72%	11	44%	4.023	.045*
	Short	7	28%	14	56%		
Motor	Optimal	16	64%	8	32%	5.128	.024*
	Short	9	36%	17	68%		

Note: Pearson Chi-Square test.

*Significant at p=<0.05.

Figure 6

Motor and EEG seizure duration classification

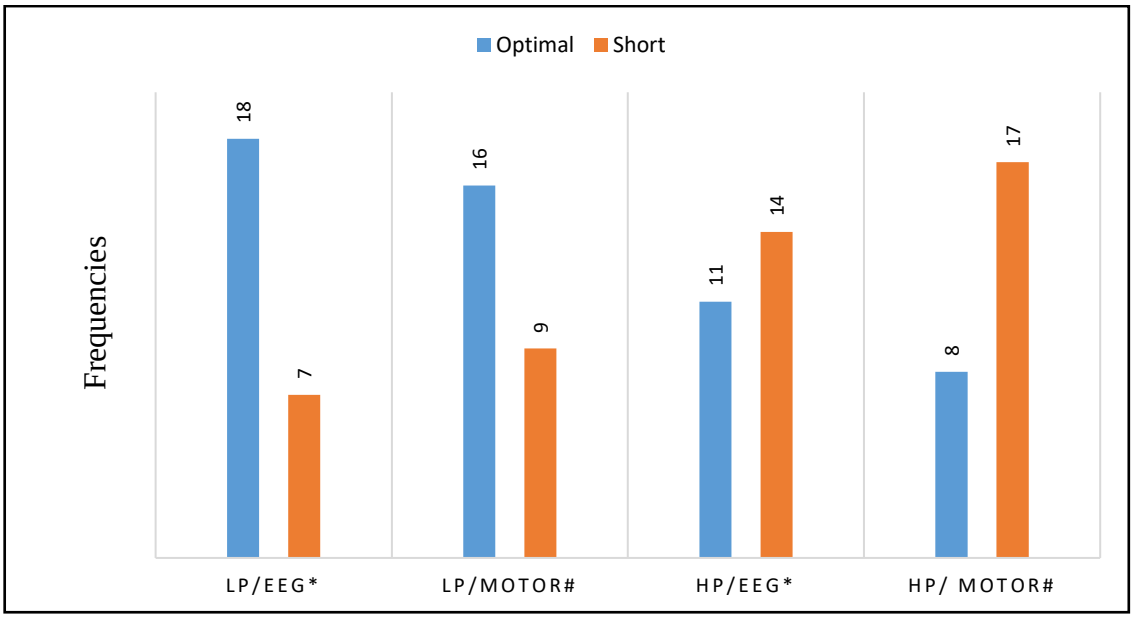


Figure 6 The frequencies of optimal and short seizure duration with motor and EEG following LP and HP administration. Blue bars = optimal seizure duration; Orange bars = short seizure duration. *significant differences (P < 0.05) between LP/EEG and HP/EEG. #significant differences (P <0.05) between LP/motor and HP/motor.

3.3 Hemodynamic variables

As shown in Table 7, A Mann-Whitney U test was used to assess the differences in the hemodynamic parameter changes (SBP, MAP, and HR) over the time points of ECT, following LP and HP administration.

There was a significant dose-related difference (p=<0.05) in a rank score of SBP following LP and HP administration compared with baseline values at T0 (U=101, p= .001), T2 (U=96, p=.001), T5 (U=143.5, p=.001). However, there are no significant differences in SBP following the two doses at T10 following the seizure (U=240.5, p=.162). The rank score of SBP following LP administration was higher than HP at T0, T2, and T5 of the ECT.

There was a significant dose-related difference (p=<0.05) in a rank score of MAP following LP and HP administration compared with baseline values at T0 (U=122, p= .001), T2 (U=10.8.5, p=.001), T5 (U=159.5, p=.003). However, there is no significant difference in MAP following the two doses at T10 following the seizure (U=217.5, p=.065). The rank score of MAP following LP administration was higher than HP at T0, T2, and T5 of the ECT.

There were no significant dose-related differences (p>0.05) in a rank score of HR following LP and HP administration compared to baseline values at T0 (U=307, p= .915), T2 (U=252.5, p=.244), T5 (U=239, p=.705) and T10 (U=290.5, p=.669). The rank scores of HR following LP and HP administration were similar at all the timepoints of ECT.

Table 7

Hemodynamic variables

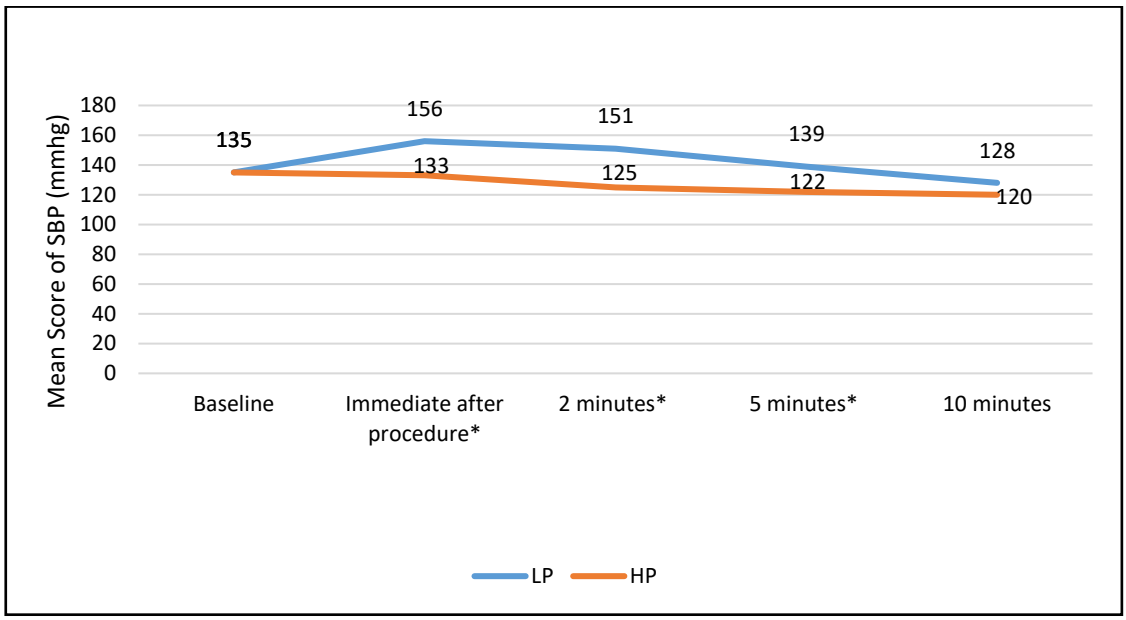
ECT period	Hemodynamics parameters	Propofol dose	n	Mean Rank	Sum of Rank	Statistical values	P-value
Before the seizure	SBP	LP	25	25.78	644.50	U=305.5 Z=-.136	0.892
		HP	25	25.22	630.50		
	MAP	LP	25	26.90	672.50	U=277.5 Z=-.679	0.497
		HP	25	24.10	602.50		
	HR	LP	25	27.10	677.50	U=272.5 Z=-.777	0.437
		HP	25	23.90	597.50		
Immediately after the seizure	SBP	LP	25	33.96	849.00	U=101 Z=-4.106	0.001*
		HP	25	17.04	426.00		
	MAP	LP	25	33.12	828.00	U=122 Z=-3.698	0.001*
		HP	25	17.88	447.00		
	HR	LP	25	25.28	632.00	U=307 Z=-.107	0.915
		HP	25	25.72	643.00		
2 minutes after the seizure	SBP	LP	25	34.16	854.00	U=96 Z=-4.203	0.001*
		HP	25	16.84	421.00		
	MAP	LP	25	33.66	841.50	U=108.5 Z=-3.960	0.001*
		HP	25	17.34	433.50		
	HR	LP	25	27.90	697.50	U=252.5 Z=-1.165	0.244
		HP	25	23.10	577.50		
5 minutes after the seizure	SBP	LP	25	32.26	806.50	U=143.5 Z=-3.283	0.001*
		HP	25	18.74	468.50		
	MAP	LP	25	31.62	790.50	U=159.5 Z=-2.970	0.003*
		HP	25	19.38	484.50		
	HR	LP	25	26.28	657.00	U=293 Z=-.379	0.705
		HP	25	24.72	618.00		
10 minutes after the seizure	SBP	LP	25	25.38	709.50	U=240.5 Z=-1.398	0.162
		HP	25	22.62	565.50		
	MAP	LP	25	29.30	732.50	U=217.5 Z=-1.845	0.065
		HP	25	21.70	542.50		
	HR	LP	25	24.62	615.50	U=290.5 Z=-.427	0.669
		HP	25	26.38	659.50		

Note: Mann Whitney U test.

*Significant at p=<0.05.

Figure 7

Mean score of the SBP during the timepoints of ECT

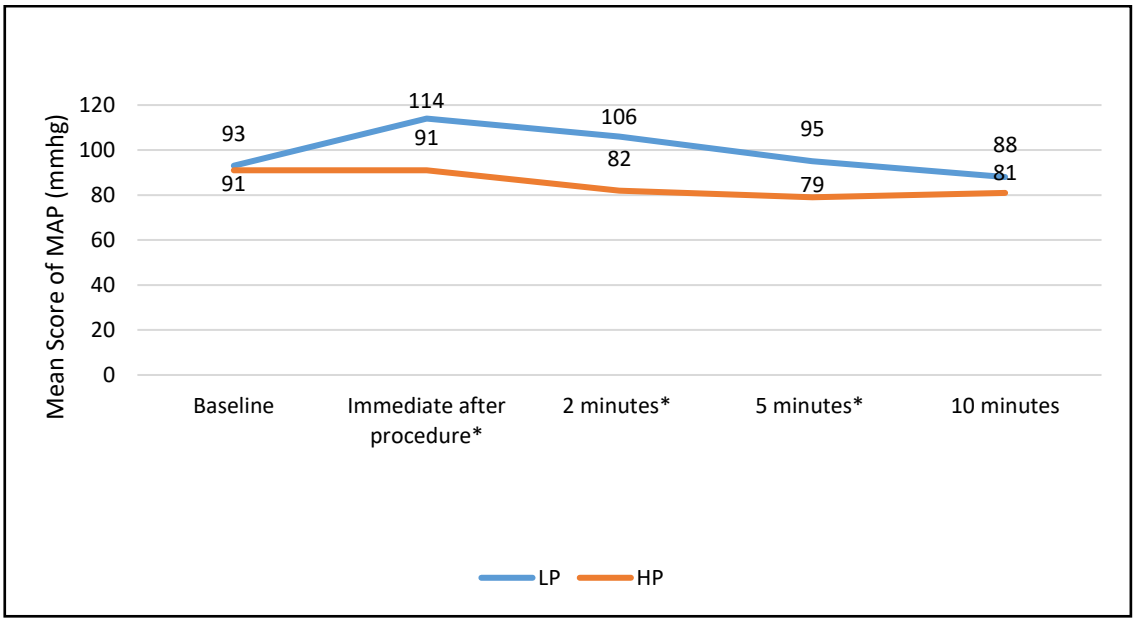


*Note: *Significant at p=<0.05.*

Figure 7 The changes of SBP in the different dose regimens (1 and 1.5 mg/kg) of propofol are presented over the timepoints of ECT. Blue line = LP; Orange line = HP. *significant differences (P < 0.05) following the two administered doses.

Figure 8

Mean Score of the MAP during the timepoints of ECT

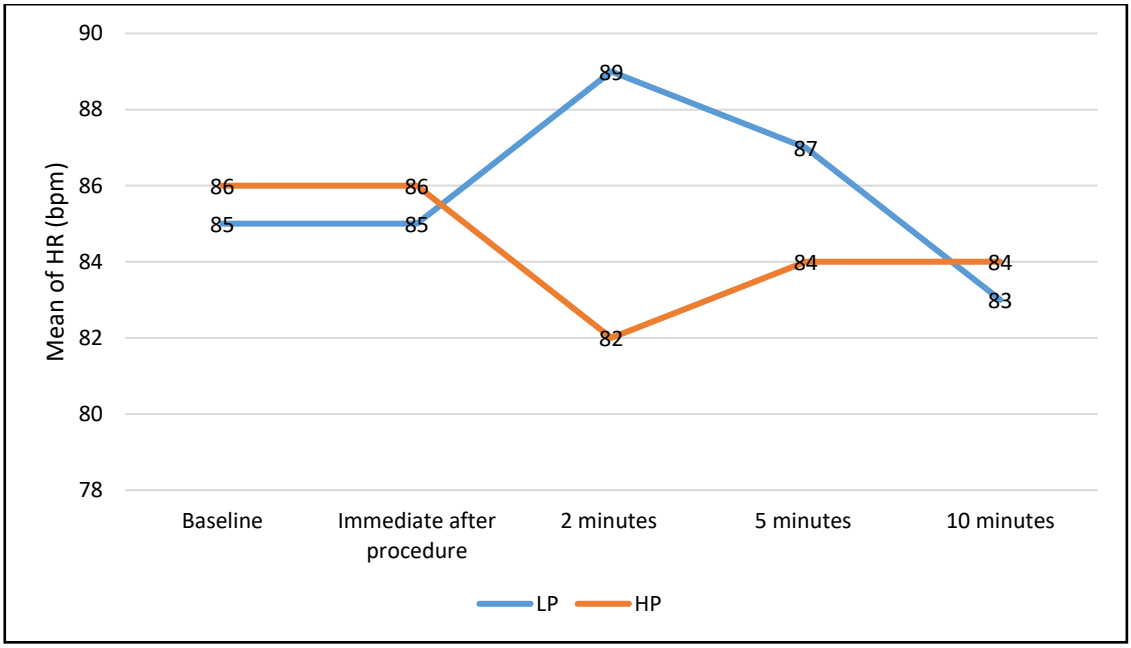


Note: *Significant at p=<0.05.

Figure 8 The changes of MAP in the different dose regimens (1 and 1.5 mg/kg) of propofol are presented over the timepoints of ECT. Blue line = LP; Orange line = HP. *significant differences (P < 0.05) following the two administered doses.

Figure 9

Mean Score of the HR during the timepoints of ECT



Significant at p=<0.05.

Figure 9 The changes of HR in the different dose regimens (1 and 1.5 mg/kg) of propofol are presented over the timepoints of ECT. Blue line = LP; Orange line = HP. *significant differences (P < 0.05) following the two administered doses.

3.4 Recovery profile

As shown in Table 8, according to the Mann-Whitney U test, the emergence time was similar regardless of the administered dose following the return of spontaneous breathing (U= 263, p=0.337) and eye-opening time (U= 271.5, p=0.426). However, a higher rank score was observed after LP administration than HP following the time to obey verbal commands (U= 176.5, p=.008) and ambulation (U= 128.5, p=.000). 30.94, 32.86, and 20.06, 18.14, respectively. It exhibited a negative dose-response relationship with LP administration.

Table 8

Recovery parameters

Recovery parameters	Propofol dose	n	Mean Rank	Sum of Rank	Statistical values	P-value
Spontaneous Breathing (min)	LP	25	23.52	588.00	U=263 Z=-.961	0.337
	HP	25	27.48	687.00		
Eye-opening (min)	LP	25	23.86	596.50	U=271.5 Z=-.796	0.426
	HP	25	27.14	678.50		
Obey Verbal Commands (min)	LP	25	30.94	773.50	U=176.5 Z=-2.640	0.008*
	HP	25	20.06	501.50		
Ambulation (min)	LP	25	32.86	821.50	U=128.5 Z=-3.571	0.000*
	HP	25	18.14	453.50		

Note: Mann Whitney U test.

*Significant at p=<0.05.

3.5 Adverse events

As shown in Table 9, the adverse events following LP and HP administration were headache (68% vs. 28%), angialgia (12% vs. 20%), myalgia (40% vs. 52%), nausea or vomiting (0% vs. 4%), delirium or hallucination (16% vs. 16%), hypertension (24% vs. 12%), hypotension (8% vs. 24%), tachycardia (8% vs. 8%), bradycardia (0% vs. 4%), fear upon awakening (12% vs. 16%). A Chi-Square test indicated a significant dose related to headache (X2=2.922, p=0.005), which was obvious following the LP administration. However, there were no serious adverse effects, such as respiratory depression or hypoxemia, in either group.

Table 9

Adverse events

Adverse events	LP		HP		Pearson Chi-Square	P-value
	n=25	%	n=25	%		
Headache	17	68%	7	28%	2.922	0.005*
Angialgia	3	12%	5	20%	0.595	0.702
Myalgia	10	40%	13	52%	.725	0.571
Nausea or vomiting	0	0%	1	4%	1.020	0.312
Delirium or hallucination	4	16%	4	16%	.000	1.000
Hypertension	6	24%	3	12%	1.220	0.269
Hypotension	2	8%	6	24%	2.381	0.123
Tachycardia	2	8%	2	8%	.000	1.000
Bradycardia	0	0%	1	4%	1.020	0.312
Fear upon awakening	3	12%	4	16%	.166	0.684
Respiratory depression or hypoxemia	0	0%	0	0%	-	-

Note: Pearson Chi-Square test.

**Significant at p=<0.05*.

3.6 Agitation and satisfaction score

As shown in Table 10 the chi-square test regarding patient agitation and satisfaction scores following ECT treatment indicates that there is no statistically significant difference between the two propofol doses concerning the patient's agitation (p=0.224) and satisfaction score (p=0.834).

Table 10

Patient agitation score and satisfaction score

Variables		LP		HP		Pearson Chi-Square	P-value
		n=25	%	n=25	%		
Agitation	(1) Sleeping	2	8%	6	24%	2.993	0.224
	(2) Awake and clam	16	64%	11	44%		
	(3) Irritable and crying	7	28%	8	32%		
	(4) inconsolable crying	0	0%	0	0%		
	severe restlessness and disorientation						
Satisfaction	(1) Pleased and clam	4	16%	3	12%	0.362	0.834
	(2) No complaint (not bad satisfaction)	10	40%	9	36%		
	(3) Some complaints (neutral satisfaction)	11	44%	13	52%		
	(4) Complained (the procedure was unpleasant, and the patient does not want to undergo the same experience again)	0	0%	0	0%		

Note: Pearson Chi-Square test

**Significant at p=<0.05.*

Chapter Four
Discussions and Conclusions

ECT is a proven therapy for many different psychiatric disorders, and using anesthetic agents during ECT has been widely researched. The key components of anesthesia during ECT are to provide a rapid loss of consciousness, muscle relaxation, maintain hemodynamic stability, minimal interference with seizure activity, and rapidly restore consciousness with spontaneous oxygenation and ventilation (105). The primary adverse effect of anesthesia is depressing the CNS, which diminishes seizure quality (106). Many studies examined the impact of anesthesia on seizure quality during ECT. Although thiopental and methohexital were the most commonly used agents for ECT, they have been widely replaced by propofol due to their availability is limited; regardless of its negative effect on seizure activity, it has a favorable impact on hemodynamics and it is wider availability. (41,106).

Regarding etomidate and ketamine, they have pro-convulsant properties, providing a higher seizure quality (107,108). However, they are associated with several adverse events, such as hallucinations, sympathetic stimulation, and depression of the hypothalamic, which lead to limited usage during ECT (59). Several studies demonstrated a poor correlation between seizure duration and the therapeutic efficacy of ECT. It is unclear if it is related to seizure duration or the amount of the current passed (47).

Limited studies have compared the effects of different propofol doses for ECT (7,35,51). Therefore, The impact of the induction dose can vary regarding the patient's age (81). However, Gazdag et al. (51) have shown no relationship was found regarding age-dependent dosing of the anesthetics. Based on these results, the present study aimed to compare two fixed doses of propofol regarding their impact on seizure activity duration, hemodynamics parameters, recovery profile, adverse events, agitation, and patient satisfaction score. Thus, the study aims to define a therapeutic propofol dose for ECT that produces adequate deep sleep and allows a sufficient seizure duration with more hemodynamic stability, early recovery time, minimal adverse events, and more patient satisfaction.

In contrast to Avramov et al. and Pekel et al. (35,60), our pilot study failed to induce reliable anesthesia with propofol 0.75 mg/kg as the lowest dose. Therefore, we managed to induce a successful deep sleep with 1 mg/kg, which supports the assumption of Gazdag et al. (51). The inconsistent results of the lowest dose to induce adequate anesthesia can be described as the different clinical characteristics of the patient's between the studies.

The clinical characteristics of patients in the present study showed that the (mean ± SD) age is (37.48 ± 12) years, and weight is (81.16 ± 11.86) kg. The total succinylcholine dose was administered (48.84 ± 7.14) mg/kg. The voltage value of both groups is (27.20 ± 7.9), maintaining the same voltage level in each patient for both sessions for better comparison over the propofol doses. Out of the 25 patients who participated in the study, 17 were male, and 8 were female, showing that males had higher representation compared to females requiring ECT. Whereas, 19 patients were graded as ASA I and 6 patients were graded as ASA II.

In Figures 3 and 4 of the present study, the majority of patients receiving ECT were diagnosed with MDD. Therefore, the most maintenance pharmacological therapy was antidepressants, followed by AAP and anticonvulsants.

Regarding seizure activity, there was a significant difference in the mean rank of seizure duration between the two doses. Shows that HP was associated with lower seizure duration, which has similar findings to (7,35,47) that propofol has a dose-depend effect on seizure activity, larger doses of propofol were associated with significantly shortened seizure duration and an increased seizure intensity may require; therefore, the H1 related to longer motor and EEG following LP administration was supported. However, proper motor and EEG seizure duration was recorded to achieve a clinical response to the therapy during the ECT course. Conventionally, an adequate motor seizure is considered to have a minimum duration of 25 seconds, and an EEG lasts 30 seconds (5,8,57,59). In the present study, EEG had a better indicator for observing the number of optimal and short seizure duration in comparison with the motor. LP was significantly sufficient to maintain an optimal range of motor and EEG seizure duration in comparison with HP. A higher frequency of optimal seizure duration was observed following LP administration whereas, a higher frequency of short seizure duration was observed following HP administration.; therefore, the H1 were supported.

Regarding hemodynamic characteristics variation (SBP, MAP, and HR) during the timepoints of the seizure, SBP and MAP decreased significantly following HP administration compared to LP; immediately, at 2 and 5 minutes after the seizure. However, at 10 minutes, no significant differences between the two doses were observed. These findings were comparable to Avramov et al. and Sakamoto et al. (35,47), that higher propofol doses were associated with lower SBP and MAP, and maximum variation in hemodynamic parameters was between 1–3min following the ECT and returned to baseline values at 5–10 min after ECT (47). These results confirm that HP provides the best protection against unpleasant hypertensive responses to ECT, while LP was less effective in blunting the hyperdynamic response.

Relating to HR, no significant differences between the two doses were observed at all timepoints of the ECT. These findings were comparable to Wojadacz et al. and Hoger et al. (4,59), as propofol, has the smallest increase in HR compared with the other standard anesthetics and has no direct effect on HR; therefore, the H0 was rejected regarding hemodynamics following the two propofol doses during the timepoints of ECTs.

The present study evaluated recovery time through four criteria: spontaneous breathing, eye-opening, obeying verbal commands, and ambulation. Usually, the effect of the hypnotic agents on recovery time is dose-dependent. However, this relation was not observed. In fact, there was an opposite relationship between the dose and recovery time. No significant differences were observed following the two administered doses regarding the return of spontaneous breathing and eye-opening. Time to obey verbal commands and ambulation were significantly longer following the LP administration; therefore, the H1 regarding longer recovery time following HP administration was not supported. These findings were similar to Avramov et al. (35), that an opposite relationship was observed between the dose and the recovery time. They measured the return of cognitive functioning using a simple questionnaire to 10 outpatients with MDD receiving maintained ECT sessions by comparing three doses of three induction agents (propofol, methohexital, etomidate). They concluded that all groups had a shorter recovery time after a short seizure duration.

In conclusion, These recovery characteristics may be affected more by the electrical shock dose or the length of seizure duration rather than the differences in propofol doses. The

apparent differences in the predicted course of early recovery can be due to the characteristic of the seizure itself (i.e., a higher propofol dose leads to shorter seizure duration and is associated with a rapid recovery time). Hence, Instead of the propofol dose, the critical factor affecting recovery time is the seizure duration.

During the procedure, ECT is associated with some adverse effects. Up to 45% of patients receiving ECTs develop headache. Other common side effects are confusion, amnesia, and agitation (16,109). Saricicek et al. (104) reported that headache and myalgia is a common side effect of succinylcholine at 1 mg/kg. Li et al. (97) reported that angialgia is a common side effect of propofol injection in up to 90% of patients. In the present study, the headache was the only apparent adverse event, especially following LP administration. Whittaker et al. (69) suggested that longer seizure duration is associated with an increase in the incidence of post-ECT confusion and amnesia. Therefore, the headache was much more relevant following LP administration due to the longer seizure duration; therefore, the H1 related to a lower incidence of adverse events following LP administration was not supported. In relation to myalgia, it was mildly observed in our group at a succinylcholine dose of 0.6 mg/kg, which was a sufficient dose for appropriate muscle relaxation with a lower incidence of myalgia. About angialgia, it was controlled in our study by mixing 1 mg of lidocaine with the propofol doses, which effectively resulted in significant shallow pain scores during the injection. No significant differences between the two doses regarding the number of hypertension/hypotension occur during the procedure, as the induced seizure may blunt the hypotension effect of propofol.

Agitation scores and patient satisfaction are significant and challenging to manage during recovery. Some patients may require physical restraint or sedation with a benzodiazepine or an antipsychotic medication such as haloperidol to control agitation (10). propofol is considered the most favorable anesthetic agent that is least likely to cause post-ECT agitation (72). Shams and El-Masry (2014) (73) showed that premedication with low-dose IV dexmedetomidine would improve patient agitation and satisfaction scores and reduce the propofol requirement, which has a better impact on seizure activity and ensures a rapid recovery with a better effect on patient agitation and satisfaction scores. In the present study, there was no altering of the patient's agitation and satisfaction scores following ECT, the potential reason for these resuts, is that propofol as a sole agent for ECT may not be enough to tolerate patient agitation score since it considers as a weak

analgesic agent. therefore, an agent with a better analgesic effect may be required to lower agitiation score and improve patient satisfaction scores; therefore, we cannot reject H0 regarding patient satisfaction and agitation scores.

4.1 Strength of study

The study's Prospective nature allows for the collection of high-quality, real-time data, and can help reduce inter-individual variability, making it easier to detect treatment effects. It also minimizes the impact of confounding variables, which can enhance the internal validity of the study. Also, this design is often considered more reliable than retrospective studies where data is collected after the fact. By employing a crossover design, the study can achieve a large number of ECT sessions with relatively few patients. This is cost-effective and maximizes the use of available resources. The consistent use of one type of anesthetic agent across all sessions and maintaining consistent parameters for each patient across the two study periods enhances the study's internal validity and could reduce the external validity of the study, this level of standardization can minimize variability in treatment administration and data collection, improving the study's reliability.

4.2 Limitations of the study

The potential limitation of the presented study is the measurement of motor seizure duration was based on observing tonic-clonic activity without using an isolated extremity technique or EMG waveform as these advanced techniques are known to provide a more accurate measurement of seizure duration. Without them, the study might not capture the full extent of motor seizure activity, potentially affecting the reliability of the results. The study did not evaluate cognitive function during recovery, as it is a significant side effect that may accumulate over frequent ECT sessions and persist beyond the ECT course (110). The lack of an ECG monitor in the ECT room to monitor the fluctuating rhythm during the sympathetic and parasympathetic activation; therefore, we couldn't detect any potential cardiac arrhythmias. Although the crossover design maximizes resource utilization, it can lead to a relatively small and homogeneous sample. This may limit the ability to generalize the findings to a broader population, particularly if the study population does not represent the diversity of patients who undergo ECT. Finally, two fixed doses of propofol were administered to all patients regardless of age, as there may

have been an age-related difference in the minimal dose required to induce loss of consciousness (81,111).

4.3 Conclusion

An appropriate propofol dose is a critical part of successful ECT. This study attempted to research an optimal dose of propofol for ECT anesthesia by comparing two propofol doses, 1 mg/kg and 1.5 mg/kg. The present study showed a shorter seizure duration with the increased propofol dose. A dose of 1.5 mg/kg may negatively affect seizure activity and require a higher stimulus charge to maintain the therapeutic range of ECT. Although a propofol dose of 1 mg/kg may maintain an optimal seizure duration. However, it was associated with a higher incidence of post-ECT headache. An opposite relationship was observed between the propofol dose and recovery time. The recovery time was shorter following HP administration after ECT treatment due to the short seizure duration. In conclusion, we recommend using 1 mg/kg of propofol as it has the optimal effect on seizure activity. Further studies are recommended to investigate more anesthetic agents related to ECT practice with a larger sample size, considering age-related dosing and taking into consideration the evaluation of cognitive functioning during recovery.

List of Abbreviations

Abbreviation	Meaning
AAP	Atypical Antipsychotic
ANS	Autonomic Nervous System
APA	American Psychiatric Association
ASA	American Society of Anesthesiology
BF	Bifrontal
BIS	Bispectral Index
BL	Bilateral
BZP	Benzodiazepines
CNS	Central Nervous System
CO	Cardiac output
DBP	Diastolic Blood Pressure
ECG	Electrocardiogram
ECT	Electroconvulsive therapy
EEG	Electroencephalogram
EMG	Electromyography
GABA	Gamma-aminobutyric acid
H1	Alternative hypothesis
H0	Null hypothesis
HP	High-dose Propofol (1.5 mg/kg)
HR	Heart Rate
IRB	Institutional Review Board
IV	Intravenous
Kg	Kilogram
LP	Low-dose Propofol (1mg/kg)
MAOIs	monoamine oxidase inhibitors
MAP	Mean Arterial Pressure
mC	millicoulomb
MDD	Major Depressive Disorder
MH	Malignant Hyperthermia
mmHg	millimetre of mercury
MOH	Ministry of Health
NMDA	N-methyl-D-aspartate

Abbreviation	Meaning
NSAID	Nonsteroidal anti-inflammatory drugs
PONV	Postoperative Nausea and Vomiting
PSI	Postictal suppression index
SBP	Systolic Blood Pressure
SPO2	Peripheral Oxygen Saturation
SLP	seizure-like phenomena
SNRIs	norepinephrine reuptake inhibitors
SPSS	Statistical Package for Social Sciences
SSRIs	Selective serotonin reuptake inhibitors
TCA	Tricyclic antidepressants
T0	Immediately after the seizure ends
T2	2 minutes after the seizure ends
T5	5 minutes after the seizure ends
T10	10 minutes after the seizure ends
RUL	right unilateral
WHO	World Health Organization

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Appendices

Appendix A

Consent Form

موافقة الاشتراك في البحث العلمي

اسم الباحث: محمد شعبان الحاج – طالب ماجستير تمريض التخدير – جامعة النجاح الوطنية – نابلس

المشرفون على البحث العلمي: -

د. جمال قدومي – عضو هيئه تدريسية في دائرة التمريض والقبالة – جامعة النجاح الوطنية – نابلس

<u>عنوان البحث</u>

دراسة أثر جرعتين مختلفتين من تخدير البربوفول على المدة الزمنية للنوبة وعلى الدورة الدموية للمريض خلال العلاج بالتحفيز الكهربائي للمرضى النفسيين: تجربة مستقبلية، عشوائية، مفتوحة التسمية، ومتقاطع

انا الموقع ادناه .....

اقر انه تم شرح طلب المشاركة في مشروع البحث العلمي (**دراسة أثر جرعتين مختلفتين من تخدير البروبوفول على المريض خلال العلاج بالتحفيز الكهربائي للمرضى الذين تم وصف جلسات علاجية لهم من قبل اخصائي الطبيب النفسي في مستشفى بيت لحم لطب النفسي)**

توقيع المشترك: .....

التاريخ: .....

Appendix B

Checklist

Pre-ECT phase

Demographic data	Anesthedisa data
Patient initials:	Succinylcholine (0.6mg /kg):
Period of the study:	Propofol dose:
1	1 mg/kg
2	1.5mg/kg
Sex:	The total dose given (mg):
M	
F	
Age:	History of allergies from any anesthetic agents:
Weight (kg):	No. of current ECT:
Medical diagnosis:	ASA status:
History of any complications from previous ECT sessions:	Current medication: Antidepressants – Benzodiazepines (BZU) – Atypical Antipsychotic (AAP) – Lithium – Anticonvulsants –

Actual-ECT phase

Seizure duration:

Stimulus dose (%):	
Motor duration (s):	
EEG duration (s):	

Hemodynamic changes:

	HR	BP	MAP	SPO2
Baseline				
T0				
T2				
T5				
T10				

Post-ECT phase

Recovery parameters:

Spontaneous breathing time (min)	
Open eyes time (min)	
Obey commands time (min)	
Ambulation time (min)	

Adverse Events:

Headache	
Nausea and vomiting	
Delirium or hallucinations	
Hypertension	
Hypotension	
Tachycardia	
Bradycardia	
Sense of fear upon awakening	
Behavioural agitation	
Respiratory depression	

After full recovery

Agitation Score

Score	Response
1	Sleeping
2	Awake and calm
3	Irritable and crying
4	Inconsolable crying
5	Severe restlessness and disorientation

Patient Satisfaction

Score	Response
1	Pleased and calm patient
2	No complaint (not bad satisfaction)
3	Some complaints (neutral satisfaction)
4	Complained (treatment was unpleasant, and the patient does not want to undergo the same experience again)

Appendix C

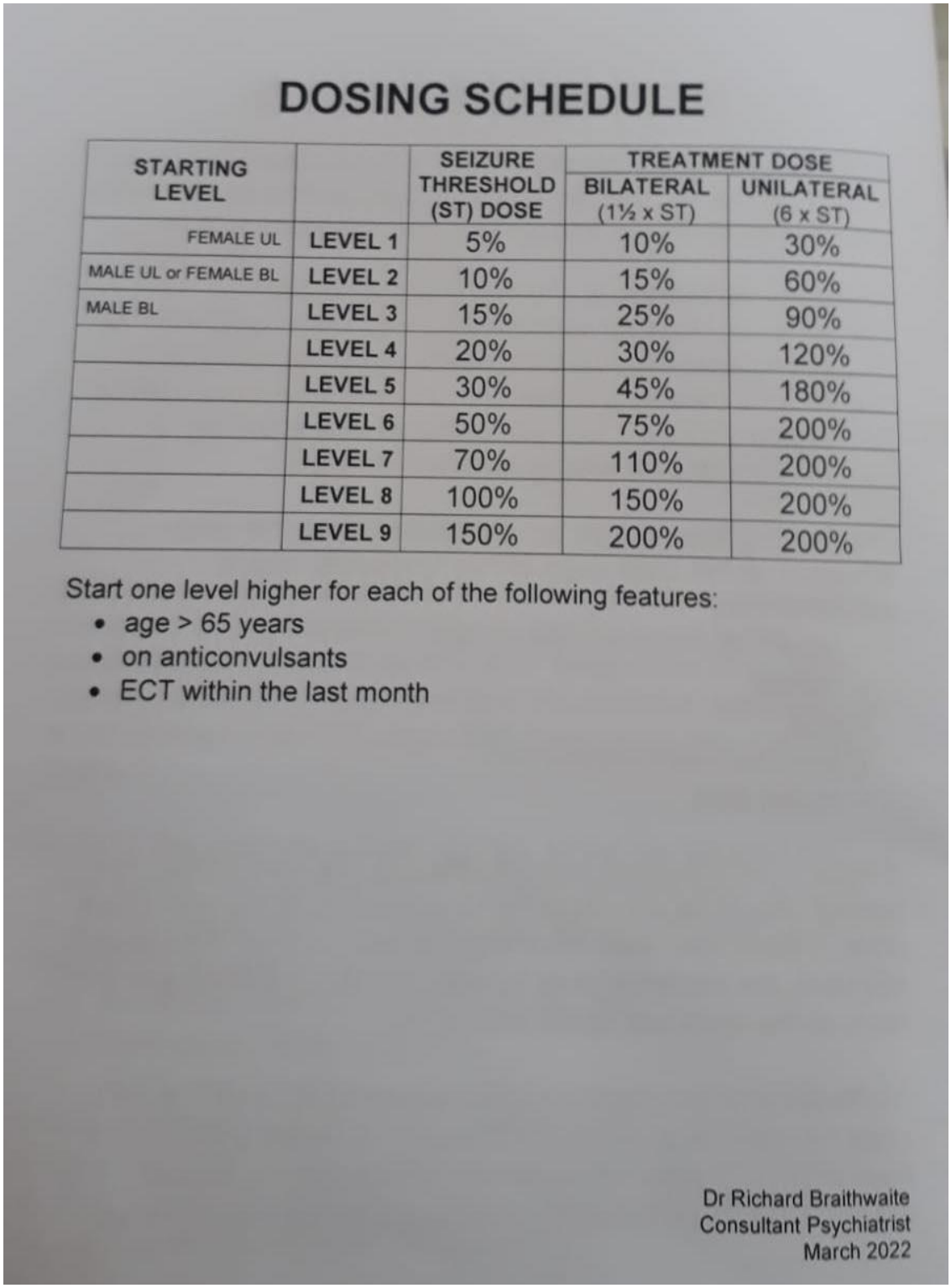
ASA Physical Status Classification System

ASA PS Classification	Definition
ASA I	A normal healthy patient
ASA II	A patient with mild systemic disease
ASA III	A patient with severe systemic disease
ASA IV	A patient with severe systemic disease that is a constant threat to life
ASA V	A moribund patient who is not expected to survive without the operation
ASA VI	A declared braindead patient whose organs are being removed for donor purposes

(112)

Appendix D

Dosing Schedule – Seizure Threshold Determination



DOSING SCHEDULE

STARTING LEVEL		SEIZURE THRESHOLD (ST) DOSE	TREATMENT DOSE	
			BILATERAL (1½ x ST)	UNILATERAL (6 x ST)
FEMALE UL	LEVEL 1	5%	10%	30%
MALE UL or FEMALE BL	LEVEL 2	10%	15%	60%
MALE BL	LEVEL 3	15%	25%	90%
	LEVEL 4	20%	30%	120%
	LEVEL 5	30%	45%	180%
	LEVEL 6	50%	75%	200%
	LEVEL 7	70%	110%	200%
	LEVEL 8	100%	150%	200%
	LEVEL 9	150%	200%	200%

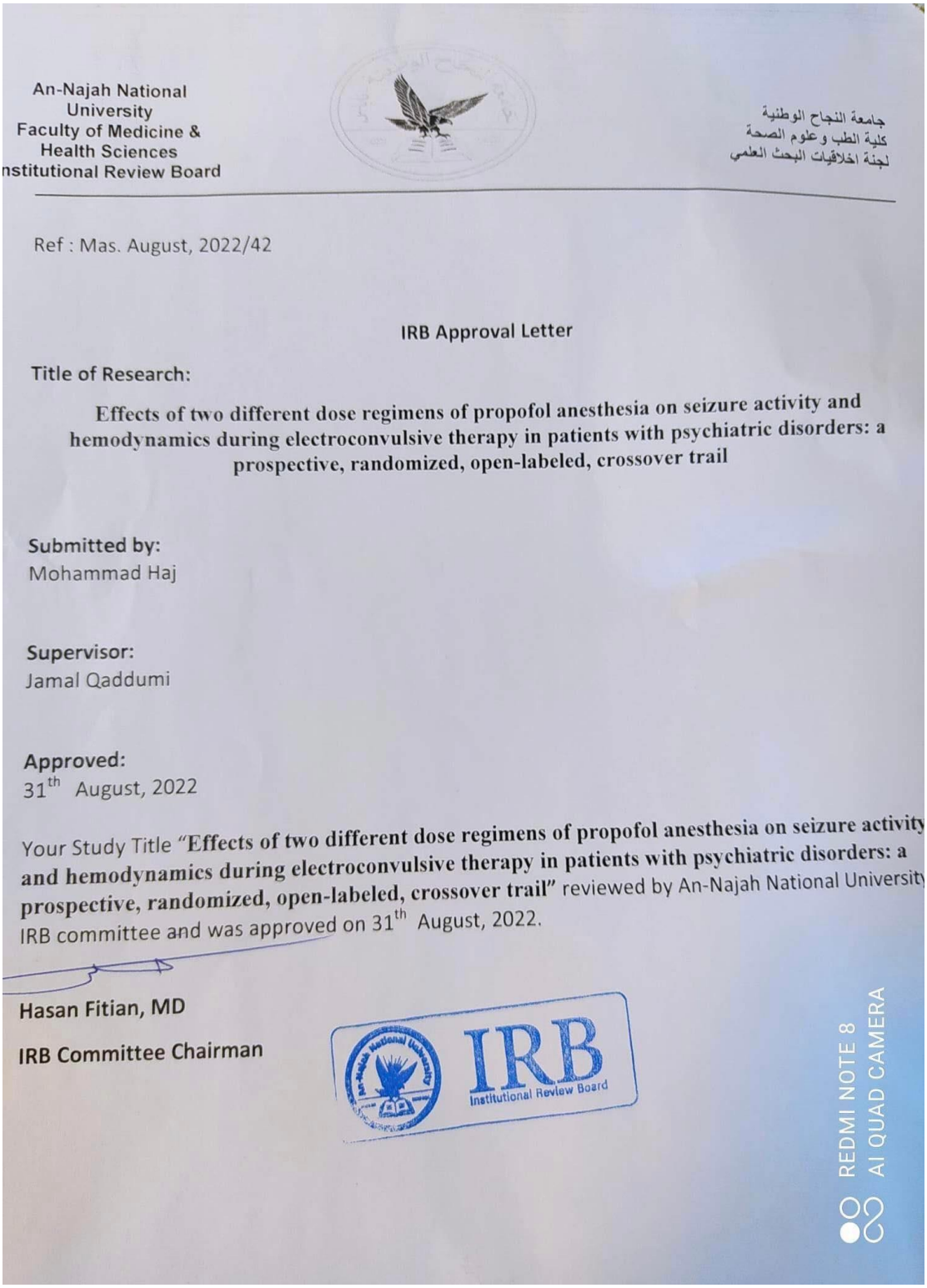
Start one level higher for each of the following features:

- age > 65 years
- on anticonvulsants
- ECT within the last month

Dr Richard Braithwaite
Consultant Psychiatrist
March 2022

Appendix E

IRB Approval



An-Najah National
University
Faculty of Medicine &
Health Sciences
nstitutional Review Board

جامعة النجاح الوطنية
كلية الطب وعلوم الصحة
لجنة اخلاقيات البحث العلمي

Ref : Mas. August, 2022/42

IRB Approval Letter

Title of Research:

Effects of two different dose regimens of propofol anesthesia on seizure activity and hemodynamics during electroconvulsive therapy in patients with psychiatric disorders: a prospective, randomized, open-labeled, crossover trail

Submitted by:
Mohammad Haj

Supervisor:
Jamal Qaddumi

Approved:
31th August, 2022

Your Study Title "**Effects of two different dose regimens of propofol anesthesia on seizure activity and hemodynamics during electroconvulsive therapy in patients with psychiatric disorders: a prospective, randomized, open-labeled, crossover trail**" reviewed by An-Najah National University IRB committee and was approved on 31th August, 2022.

Hasan Fitian, MD

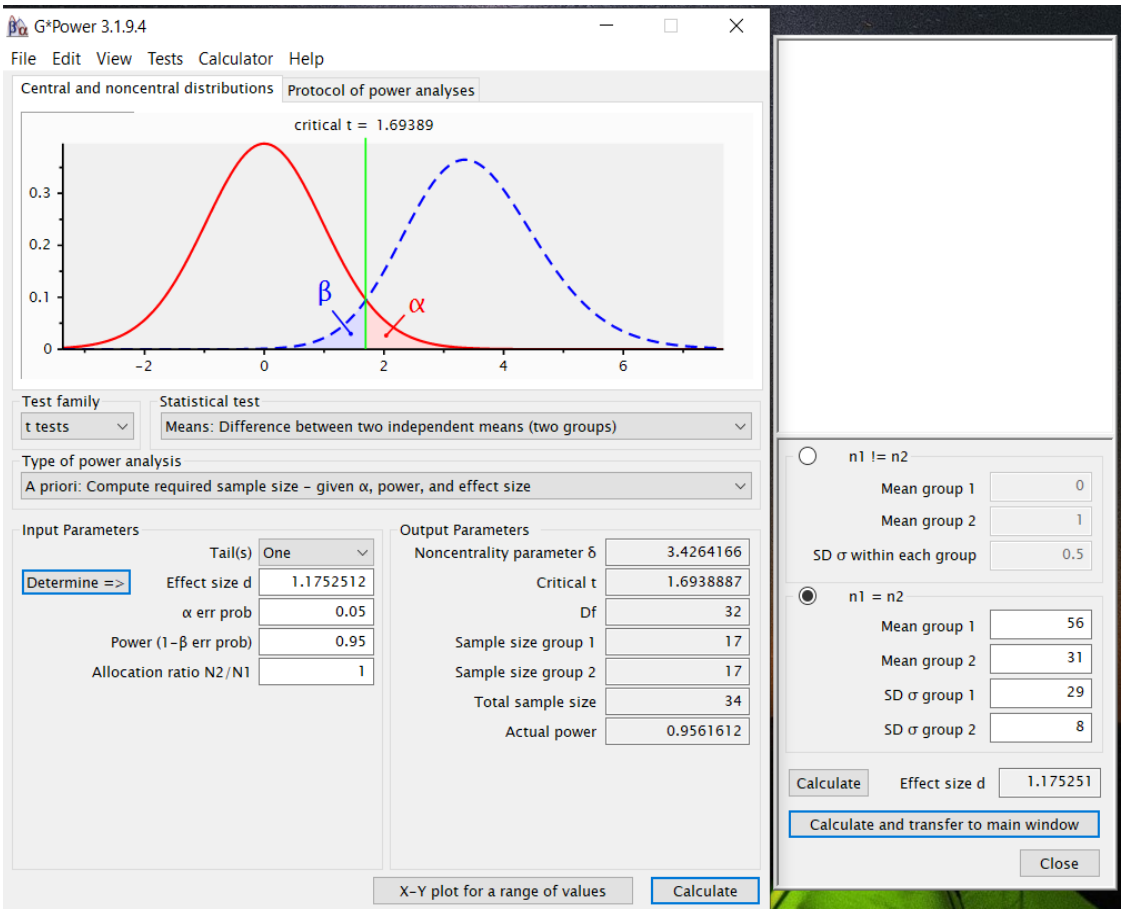
IRB Committee Chairman

IRB
Institutional Review Board

REDMI NOTE 8
AI QUAD CAMERA

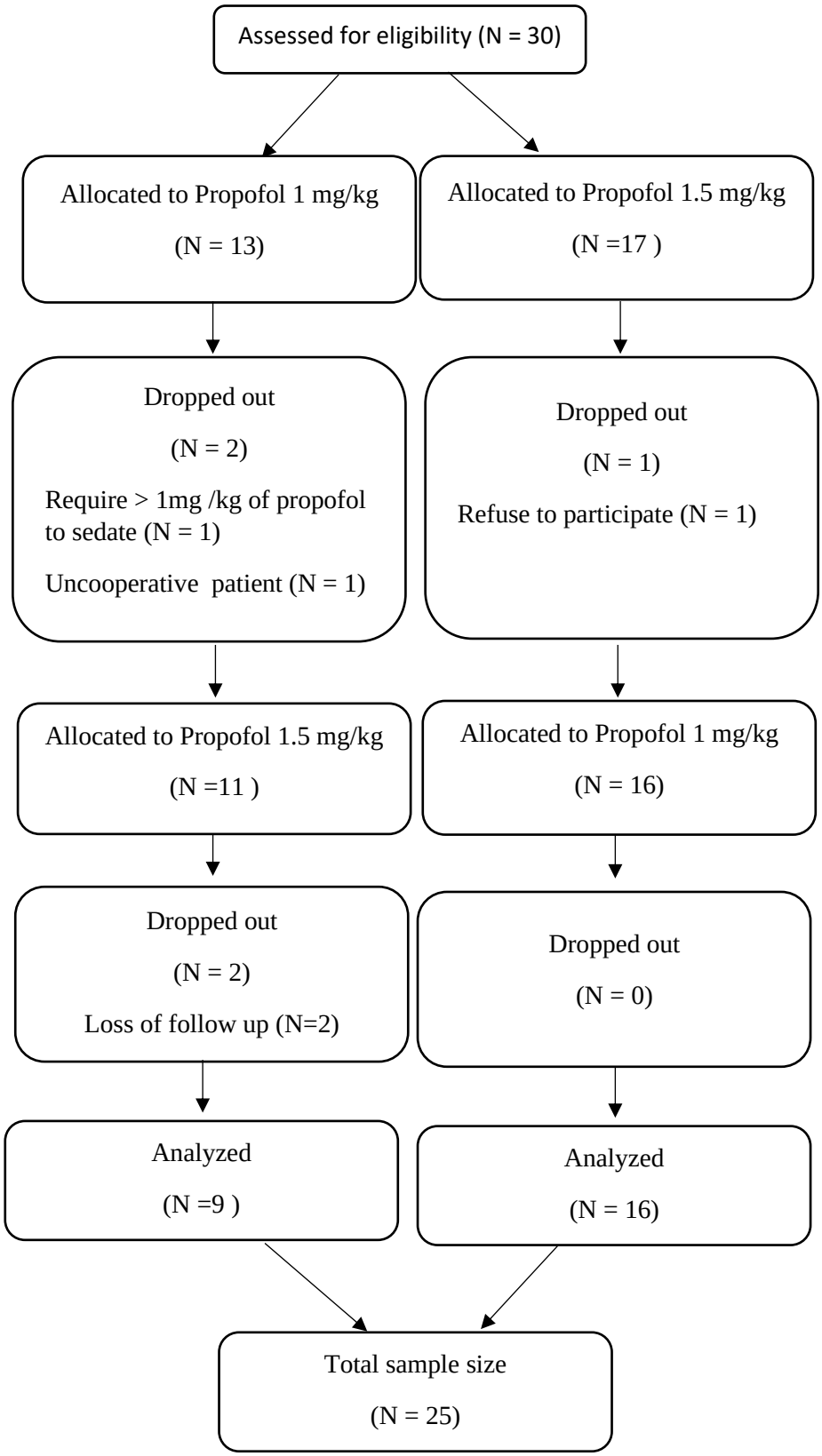
Appendix F

Sample Size Calculation Window



Appendix G

Flow Chart of The Patient's Progress Through the Trial's Phases



Appendix H

Information Sheet for Participation in English

Title of study

Effects of Two Different Dose Regimens of Propofol Anesthesia on Seizure Activity and Hemodynamics During Electroconvulsive Therapy for Psychiatric Patients: A Prospective, Randomized, Open-Labeled, Crossover Trial

Invitation paragraph

My name is Mohammad Alhaj, a master's student registered nurse in anesthesia, and this study forms part of my master's research at An-najah National University. I would like to invite your client to participate in this research project, but before you agree to do so, it is important that you understand the purpose and nature of the research and what your client's participation will involve if you agree. Please read the following information carefully, and please do ask if anything is not clear, or if you want more information.

Contact details are given at the end of this information sheet.

What is the purpose of the study?

The purpose of this study is to determine a therapeutic dose of propofol anesthesia for optimal ECT outcome with minimal interference with the induced seizure during the procedure, by comparing two different propofol doses (low dose: 1mg/kg, high dose 1.5mg/kg) during two sequential ECT over two ECT sessions, and assess their effects on seizure activity, hemodynamics and clinical impacts over ECT.

Why I have been chosen?

You have been chosen to take part in this study randomly by computer picking up random numbers as I aim to recruit 25 clients with different psychiatric disorders who were scheduled to undergo multiple ECT sessions and fulfilled inclusion criteria at Bethlehem Psychiatric Hospital from November 2022 to January 2023.

- **Inclusion criteria** are described as acute cases of inpatients or outpatients with different psychiatric disorders ranging between 18 to 60 years old with ASA grade I and II status, who underwent two or more ECT sessions and have completed their first ECT session in Bethlehem Psychiatric Hospital.

Do I have to take part?

Participation is completely voluntary. If you do decide to enroll your client into this study, you will be given this information sheet to keep and be asked to sign a consent form if applicable. You can withdraw your client from participation at any time during the procedure without giving a reason and without affecting any benefits that your client is entitled to.

What will happen to my client if he enrolls?

If you decide to enroll your client in this study, your client will be sedated with propofol agent during ECT with two different doses (1, 1.5 mg/kg) in two separate ECT sessions and your client will be under close observation during and after the procedure to determine the best dose in clinical outcome.

A piece of basic information about each client will be required such as age, gender, weight, number of current ECTs, current medication, and medical diagnosis. (Vital signs will be recorded multiple times during the procedure. In addition, recovery time, adverse event, and agitation score will be recorded) after the full recovery of each session, the patient's satisfaction score will be to each client to evaluate the impact of the two ECT sessions separately.

What are the possible disadvantages and risks of taking part?

There are no significant risks to taking part in this study. If you or your client find the observational method of the data collection distressing or upsetting for any reason you will be able to withdraw your participation. In addition, if your client does not sedate with the study doses, an additional dose will be given regardless of study requirements.

What are the possible benefits of taking part?

The benefit of the study is to improve the quality of ECT anesthesia by determining a therapeutic dose.

I will provide you with a summary of the final report describing the main findings, but there are no direct benefits to the participant from taking part.

It will be kept confidential?

Yes. Your client's involvement in this study will not disclosed to anyone other than me, all the information that we will collect about your client is information related to ECT

and ECT anesthesia, and it will be kept strictly confidential. Your client will not be able to be identified in any ensuing reports or publications.

What will happen to the results of the study?

The result of the study will be filled in my master's thesis, which will be accessible in print and online. Results may also be disseminated in discussion defense presentations at An-anjah National University and published articles. Your client's participation will not be identified in any report or publication.

Who is organizing and funding the research?

The study was conducted independently of any institutional influence and was not funded. There were no conflicts of interest.

Contact for further information

if you have any questions or require more information about this study, please contact me or my supervisor using the following contact details:

RN. Mohammad Alhaj, Student Registered Nurse Anesthesia, Beitunia, West Bank, Palestine

Telephone: 00972 59-759-2413

E-mail: muc.mohammadhaj@gmail.com

Supervisor of the research:

Dr. Jamal Qaddumi, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, West Bank, Palestine

Telephone: 00970 59-987-7617

E-mail: jamal9877@najah.edu

Thank you for reading this information sheet and for considering taking part in this research.

Appendix I

Information Sheet for Participation in Arabic

عنوان الدراسة

دراسة أثر جرعتين مختلفتين من تخدير البربوفول على المدة الزمنية للنوبة وعلى الدورة الدموية للمريض خلال العلاج بالتحفيز الكهربائي للمرضى النفسيين: تجربة مستقبلية، عشوائية، مفتوحة التسمية، ومتقاطعة

الدعوه الى الاشتراك في مشروع بحثي

انا الباحث محمد الحج، طالب ماجستير في تمريض التخدير، جامعة النجاح الوطنية – نابلس، وهذا المشروع البحثي هو متطلب من متطلبات الماجستير، وأود أن ادعو موكلك للمشاركة في هذا المشروع البحثي، ولكن قبل أن توافق على القيام بذالك، من المهم ان تفهم الغرض من البحث و طبيعته و ما ستضمنه مشاركة موكلك في حال تمت الموافقة. يرجى من حضرتكم التركم في قراءة المعلومات التالية بعناية، و يرجى الاستفسار إذا كان هناك أي شيء غير واضح أو اذا كنت تريد المزيد من المعلومات. تتوفر تفاصيل الاتصال في نهاية الورقة.

ما الهدف من الدراسة؟

الغرض من هذه الدراسة هو تحديد جرعة علاجية من تخدير البروبوفول للحصول على أفضل نتيجة بالعلاج بالتحفيز الكهربائي، من خلال مقارنة جرعتين مختلفتين من البروبوفول (جرعة مخفضة 1 ملغرام لكل كيلوغرام و جرعة مرفعة 1.5 ملغرام لكل كيلوغرام) خلال جلستين متتاليتين، وتقييم آثرها على المدة الزمنية لنوبة و على الدورة الدموية للمريض والأثر السريري الناتج عنهما خلال العلاج بالتحفيز الكهربائي.

لماذا تم اختياري؟

لقد تم اختيار موكلك للمشاركة في هذه الدرسة بشكل عشوائي عن طريق التقاط الحاسوب لأرقام عشوائية، حيث هدفت الدراسلة الي التقاط 25 مريضا يعانون من اضطرابات نفسية مختلفة و الذين استوفو معايير شروط الدخول في الدراسة و الذين سيخضعون لجلسات علاجية بالتحفيز الكهربائي في مستشفى بيت لحم لطب النفسي، من نوفمبر 2022 إلى يناير 2023.

معايير الدخول في الدراسلة:

على انها حالات حادة غير مزمنة من أمراض نفسية مختلفة، تتراوح أعمارهم بين 18 و 60 عامًا و الذين سيخضعون لجلستين علاجيتين او أكثرو قد انهو اول جلسة علاجية بالتحفيز الكهربائي من غير أثار جانبية خطيرة في مستشفى بيت لحم لطب النفسي.

هل يجب علي أن أشارك؟

المشاركة طوعية تماما، إذا وافقت على تسجيل موكلك في هذه الدراسة، فسيتم إعطاؤك ورقة المعلومات هذه للاحتفاظ بها وسيُطلب منك التوقيع على نموذج موافقة الاشتراك في البحث العلمي. يمكنك سحب موكلك من المشاركة في أي وقت خلال الدراسة، دون إبداء الأسباب و دون التأثير على أي من المزايا التي يحق لموكلك الحصول عليها.

ماذا سيحدث إذا وافقت على تسجيل موكلي؟

إذا وافقت على تسجيل موكلك في هذه الدراسة، فسيتم تخديره بجرعتين محتلفتين من تخدير البروبوفول 1 و 1.5 ملغرام لكل كيلوغرام خلال جلستين متتاليتين من التحفيز الكهربائي، وسيكون موكلك تحت رعايه ومراقبة متواصلة أثناء وبعد العلاج بتحفيز الكهربائي وذالك لتقييم النتائج السريريه ولتحديد الجرعة الأفضل.

ستكون هناك حاجة إلى معلومات أساسية عن كل مريض مثل العمر، الجنس، الوزن، رقم الجلسة، الأدويه الحالية، والتشخيص الطبي. خلال الجلسة سيتم مراقبة وتسجيل العلامات الحيوية في أوقات مختلفة خلال الجلسة. بالإضافة إلى ذالك، سيتم تسجيل وقت التعافي، والاعراض الجانبية ودرجة الانفعالات. وبعد التعافي التام من الجلسة، سيتم تحديد مستوى الرضا للمريض وذلك لتقييم الجلستين بشكل منفصل؟

ما هي العيوب و المخاطر المحتملة عند المشاركة؟

لا توجد مخاطر كبيرة مترتبة عند المشاركة في الدراسة. إذا شعرت بأن طريقة جمع المعلومات مزعجة لأي سبب من الأسباب، فيمكنك من سحب مشاركتك. بالإضافة إلى ذالك، إذا كانت جرعة التخدير المعطاه غير كافية، فسيتم أعطاؤه جرعة أضافية بغض النظر عن متطلبات الدراسة.

ما في الفوائد المرجوه من المشاركة؟

الفائدة المروجة من الدراسة هي تحسين جودة تخدير خلال العلاج بالتحفيز الكهربائي، عن طريق تحديد الجرعة الأنسب. يمكنك الحصول على التقرير النهائي الخاص بالدراسة مع وصف النتائج الرئيسية عند الانتهاء من الدراسة. ولكن لا توجد فؤائد مباشرى للأشخاص المشاركين.

هل سيتم الحفاظ على خصوصية المريض؟

نعم، لن يتم الكشف عن مشاركة المريض لأي شخص آخر غيري، حيث ان المعلومات التي ستجمع عن كل مريض هي معلومات اساسية متعلقة بالتخدير و العلاج بلتحفيز الكهربائي. لن يتمكن آحد من التعرف على المريض في أي تقرير لاحق يتعلق بالدراسة.

ماذا سيحدث لنتائج الدراسة؟

سيتم كتابة نتائج الدراسة في رسالتي الماجستير والتي ستكون متاحة عبر الأنترنت لاحقا، وسيتم مناقشة النتائج مع المشرفين عن الدراسة في جامعة النجاح الوطنية. ومن غير الممكن ان يتم تحديد أي من المشاركين في الدراسة.

من يقوم بتنظيم و تمويل البحث؟

أجريت هذه الدراسة بشكل مستقل وبتمويل شخصي بعيده عن أي تاثير مؤسسي، ولا يوجد أي تضارب في المصالح.

للمزيد من المعلومات او الأستفسارات يرجى التواصل مع مشرفي الدراسة عبر بيانات الاتصال التالية:

الباحث: محمد الحج، ممرض تخدير، بيتونيا، الضفة الغربية، فلسطين

00972 59-759-2413:Telephone

muc.mohammadhaj@gmail.com: Email

مشرف الدراسة: د.جمال قدومي، كلية الطب و العلوم الصحية، جامعة النجاح الوظنية، نابلس،الضفة الغربية، فلسطين

Telephone: 00970 59-987-7617

E-mail: jamal9877@najah.edu

نشكرك على قراءة هذه الورقة لتعريفية عن البحث وعلى التفكير في الممشاركة

Appendix J

Certificate of English Proofreading and Editing

Certificate of English Proofreading and Editing

This certificate confirms that the thesis mentioned below was proofread and edited by Dr. Islam A. Ismail, an expert in academic English.

The following issues were corrected: grammar, punctuation, sentence structure, and phrasing.

The Faculty of Graduate Studies at the concerned University can contact us for a copy of the edited document that the author submitted.

Thesis Title

Effects of Two Different Dose Regimens of Propofol Anesthesia on Seizure Activity and Hemodynamics during Electroconvulsive Therapy in Patients with Psychiatric Disorders: A Prospective, Randomized, Open-Labeled, Crossover Trial

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جـامعـــة النجاح الوطنية
كليـــة الدراســـات العليـــا

دراسة أثر جرعتين مختلفتين من تخدير البربوفول على المدة الزمنية للنوبة وعلى الدورة الدموية للمريض خلال العلاج بالتحفيز الكهربائي للمرضى النفسيين: تجربة مستقبلية، عشوائية، مفتوحة التسمية، ومتقاطعة

إعداد
محمد شعبان عبد الرحمن الحج

إشراف
د. جمال قدومي

قدمت هذه الرسالة استكمالا لمتطلبات الحصول على درجه الماجستير في تمريض التخدير، من كلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس– فلسطين.

2023

دراسة أثر جرعتين مختلفتين من تخدير البربوفول على المدة الزمنية للنوبة وعلى الدورة الدموية للمريض خلال العلاج بالتحفيز الكهربائي للمرضى النفسيين: تجربة مستقبلية، عشوائية، مفتوحة التسمية، ومتقاطعة

إعداد

محمد شعبان عبد الرحمن الحج

إشراف

د. جمال قدومي

الملخص

الهدف: التخدير هو جانب أساسي لضمان كفاءة العلاج بالتحفيز الكهربائي، بينما البربوفول هو الأكثر استخداما، الا انه هناك مخاوف من أنه ينتج عنه تقليل من نشاط النوبة اعتمادا على الجرعة المستخدمة. وبتالي هدفت هذه الدراسة الى تحديد جرعة مناسبة من تخدير البربوفول للحصول على أفضل نتيجة بالتحفيز الكهربائي، من خلال مقارنة جرعتين مختلفتين من البربوفول وتقييم أثرهما على المدة الزمنية للنوبة وعلى الدورة الدموية للمريض والأثار السريرية الناتج عنهما.

المنهجية: أجريت الدراسة اعتمادا على تصميمً عشوائيً التقاطع لتقييم 25 مريضاً يعانون من أمراض نفسية مختلفة، والذين لديهم جلستين علاجيتين متتاليتين من التحفيز الكهربائي، حيث سيتم تخديرهم بـ(1 ملغم/كغم) أو (1.5 ملغم/كغم) من البروبوفول بشكل عشوائي في الفترة الأولى من الدراسة وفي الجلسة المقبلة سيتم استخدام الجرعة الأخرى. تم تقييم 50 جلسة علاجية وتقسيمها الى مجموعتين: مجموعة جرعة منخفضة (1 ملغم/كغم) و مجموعة جرعة مرتفعة (1.5 ملغم/كغم). تم إعطاء السكسينيل كولين (0.6 ملغم/كغم) لجميع المرضى خلال التخدير لارتخاء العضلات. تم تسجيل كل من: مدة نشاط النوبة (الحركية وتخطيط الدماغي)، معايير الدورة الدموية (ضغط الدم الانقباضي، ضغط الشرياني الوسطي وسرعة ضربات القلب) ومتغيرات التعافي (التنفس التلقائي، فتح العين، إطاعة الأوامر اللفظية والمشي)، الاثار الجانبية، ودرجة انفعال المرضى ومستوى الرضى.

النتائج: ارتبطت الجرعة المنخفضة بمدة نشاط نوبة (الحركي والتخطيط الدماغي) أطول مع ارتفاع ملحوظ في عدد نشاط النوبات المثالية مقارنة مع الجرعة المرتفعة. فيما يخص معايير الدورة الدموية، كان معدل كل من ضغط الدم الانقباضي وضغط الشرياني الوسطي عند الدقيقة 0 و 2 و 5 من بعد انتهاء النوبة أعلى عند استخدام الجرعة المنخفضة. كان وقت إطاعة الأوامر اللفظية والمشي أبطئ بشكل ملحوظ بعد استخدام الجرعة المنخفضة. كان الصداع الأثر الجانبي الشائع بعد العلاج بالتحفيز الكهربائي وخاصه بعد الجرعة المنخفضة. بعد الاستيقاظ التام، كان لدى كلتا المجموعتين درجات متشابهة من الانفعالات والرضى.

الخلاصة: ارتبطت الجرعة المنخفضة بمدة نشاط نوبة ودورة دموية أفضل من الجرعة المرتفعة. تم الوصول الى إن مدة نشاط النوبة هي المحدد الرئيسي لوقت التعافي المبكر وليس جرعة البروبوفول المختارة. في الختام، نوصي باستخدام (1 ملغم/كغم) من البروبوفول لأنه لها التأثير الأمثل على نشاط النوبة والدورة الدموية للمريض. توصي الدراسة بإجراء دراسات تتعلق بأنواع أخرى من التخدير مع زيادة في حجم العينة، مع مراعاة الجرعات المرتبطة بالعمر.

الكلمات المفتاحية: البربوفول، التخدير، علاج بالصدمات الكهربائية، النوبة.