An-Najah National University

Faculty of Graduate Studies

Effectiveness of Using Topical Insulin on Healing of Pressure Ulcers among Intensive Care Unit Patients, using Randomized Control Trial

By

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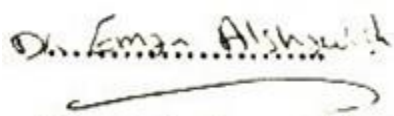
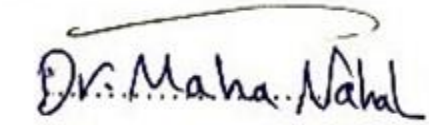
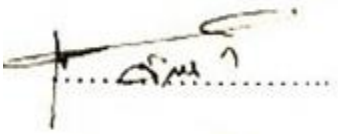
• **Dr. Eman Al shawish / Supervisor**	
• **Dr. Maha Nahal / External Examiner**	
• **Dr. Wael Sadaqa / Internal Examiner**	

Dedication

الى من وقفا بجانبي وذللا لي الصعاب ولهما الفضل بعد الله فيما انا فيه ابي وامي امد الله بعمرهما وقدرني على برهما

الى اخواتي واخواني الغالين

الى زوجي الغالي ابراهيم

الى ابنتي حفظها الله سوسن

الى عائلتي الكبيرة والغالية اخص بالذكر حماتي وحماي العزيزين

الى صديقتي الغالية اية

الى اختي التي لم تلدها امي مها

Acknowledgement

أود التقدم بالشكر والتقدير والاهداء...

الى استاذتي الدكتورة ايمان الشاويش على كل جهد ووقت بذلته معي والحمد لله ان يسرها لي وسهل بها امري

الى زوجي الغالي ابراهيم محمد غول الداعم الاساسي لي من بداية المشوار

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الى ادارة وطاقم مستشفى النجاح الوطني الجامعي

الى كل من ساعدني وقدم لي يد العون

الاقرار

أنا الموقع أدناه، مقدّم الرسالة التي تحمل العنوان:

Effectiveness of Using Topical Insulin on Healing of Pressure Ulcers among Intensive Care Unit Patients, using Randomized Control Trial

أقر بأن ما اشتملت عليه هذه الأطروحة إنما هو نتاج جهدي الخاص، باستثناء ما تمت الاشارة إليه حيثما ورد. وأن هذه الرسالة كاملة، أو اي جزء منها لم يقدم من قبل لنيل اي درجة او لقب علمي او بحثي لدى أي مؤسسة تعليمية أو بحثية أخرى.

Declaration

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: **اسم الطالب:** وفاء سميح قديس

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Date: **التاريخ:** 28.12.2021

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List of Abbreviations

ICU	intensive Care Unit
PUSH	Pressure ulcer score of healing
NPUAP	National Pressure Ulcer Advisory Panel
EPUAP	European Pressure Ulcer Advisory Panel
IU	International unit
Na Cl	Sodium chloride
IGF	insulin-like growth factor
PKB	Protein kinase B
NNUH	An-Najah National University hospital

Effectiveness of Using Topical Insulin on Healing of Pressure Ulcers among Intensive Care Unit Patients, using Randomized Control Trial

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Abstract

Background and Aims: Pressure ulcer one of the biggest challenges and most issues face health system in organizations, cause an undue burden on both the patients and the healthcare system, treatment of pressure ulcers are numerous and diverse and include many strategies, Therefore, the aim of this study was to investigate the efficacy of applying topical insulin therapy for improving pressure ulcers healing in the intensive Care Unit patients at An-Najah National University hospital.

Method: True experimental research design was conducted in Intensive care units (ICU) at NNUH. The sample of this study composed of 62 patients divided into two equal groups. study group who receive topical insulin dressing and control group who receive routine hospital dressing. Inclusion criteria for the two groups are patients 18-70 years old, both gender, pressure ulcers stage 2 and 3, wound size less than 10 cm2. And Exclusion criteria for the two groups are Patients under 18 years and over 70 years of age, pressure ulcers grade 1, 4 and unstageable, Patients who have insulin allergy, vascular disease (Arterial insufficiency, Buerger’sdisease), Immunodeficiency, pregnancy, osteomyelitis, varicose and burns ulcers, patient with hypotention, Patients with hemoglobin levels <12.0 g/dL.

Results: a more significant improvement in Pressure ulcer healing for insulin group than control group with p value (< 0.05), no statically significant in Pressure Ulcer Scale for Healing (PUSH) score between diabetic and non- diabetic patients, no statically significant in push score between males and females, random blood sugar before insulin intake related to two hours after insulin intake were statistically not significant and the experimental group participant Pressure ulcer pictures was taken at day 1 before dressing and at day 7 after using topical insulin dressing that provided evidence for improvement in Pressure ulcer healing. **Conclusion:** use of topical insulin is safe and effective to accelerate Pressure ulcer healing.

Recommendations: we recommend using topical insulin dressing for patients with Pressure ulcer type 2 and 3, assess the patients' skin from the moment they enter the hospital using assessment tools and risk monitoring models, Increasing the awareness and knowledge of prevention of Pressure ulcer, to do further studies andto apply topical insulin dressing for pediatric patients with Pressure ulcer and large community.

Keywords: insulin, topical insulin, pressure ulcer, bed sore, decubitus ulcer, decubitus and chronic wound.

Chapter One
Introduction

1.1 Introduction

Insulin in topical form enhances the healing of wounds via regulating inflammatory responses and oxidative responses. it decreases reactive oxygen species' deleterious effects on lipids, proteins, Moreover, it increases the recruitment of neutrophils and anti-inflammatory effects in wounds by increasing the number of macrophages, phagocytosis, and secretion of inflammatory mediators to eliminate dead tissues. In addition, it increases epithelialization, and enhances fibroblastic reaction. maturation and deposition of collagen in burnt skin were observed, increases in the number of blood vessels in healing tissues while using topical insulin form. (Wang &Xu,2020).

Skin is an organ of the human body results from collection of many layers, any injury in its layers causes body to begin several operations to repair and restore skin integrity (Abdelkader, 2016). The injuries of skin resulted from prolong compression on one or more sites on the skin and neighbouring, this process is called 'pressure ulcer'. They involve some kind of shearing or friction to the skin, results from long-stay in the same position or when the patient is confined to bed, thispressure might leads to less perfusion of cells and consequently their death (Miller, 2016). Pressure ulcers are also called bedsores, pressure sore, or decubitus ulcer (Lewis, Pearson & Ward, 2003). Bedsores are explaining as an injury over bony prominence which

affecting the skin because of pressure, shear or both of them (European Pressure Ulcer Advisory Panel, 2009&National Pressure Ulcer Advisory Panel, 2009). Registered Nurses' Association of Ontario describes bedsores as any underlying tissue damage over bony prominence (Registered Nurses' Association of Ontario, 2005). Bedsores result in damage of skin or tissue caused by pressure which decreases blood supply to this area (National Institute for Health and Care Excellence, 2014).

The treatment of Pressure ulcers are too expensive financially (Defloor&Grypdonck, 2005) and cause a serious physical burden (Burdette-Taylor &Kass, 2002). Insulin used to treat other diseases rather than diabetes since early of 20th century, (King,1928). Systemic using of insulin treatment increases healing in skin wounds, and ulcers for animals (Gregory, 1965). Topical insulin acting through the insulin receptor-mediated phosphatidylinositol 3-kinase– Protein kinase B –Ras-related C3 botulinum toxin substrate 1 signal pathway will enhance the migration of keratinocytes and vascular endothelial cells, thus increase re-epithelialization and angiogenesis (Liu, 2009).In recent years, the National Pressure Ulcer Advisory Panel developed the Pressure Ulcer Scale for Healing (PUSH) to monitor the healing process over time (Black et al., 2011). This tool helps the health care providers to monitor surface area of the wound, wound exudate and type of wound tissue.

The NPUAP 2014and EPUAP 2014 classified pressure ulcers as following: Stage I: site of sore is closed, red, warm, soft and painful but no breaks or tears are present. It can be felt firmer or softer than the area around it. Stage

II: partial thickness, open ulcer and loss of dermis. Stage III: Full thickness, appeared subcutaneous fat and loss of dermis. Stage IV: Full thickness tissue loss, bone is exposed, tendon or muscle may be present. Unstageable: Full thickness tissue lost, depth of the ulcer hided by slough or eschar in the site of pressure ulcer. (NPUAP, 2014&EPUAP, 2014).

There are two types of wound; acute wounds, such as burn, and chronic wounds such as pressure ulcers.Themain reason for chronic wounds is Diabetes mellitus. (Senet al., 2009). Although stem cells and growth factors promoting wound healing (Hassanet al.,2014). but it's too expensive and their safety still ambiguous. Therefore, we need a safer and cheaper therapy to improve wound healing. Insulin plays an important role in wound healing (Oryan et al., 2017). It is a growth factor and peptide hormone that can improve healing (Wang et al., 2019). In addition, it is cheap and safe to use to treat wounds (Zhao et al., 2017). Topical insulin increases cutaneous wound healing in insulin resistant cases (Yu et al., 2017). Other research in diabetic patients conducted on human being after surgical procedures found that systemic insulin decreases infections and enhances healing of Pressure ulcers; (Vatankhah et al., 2017). However, hypoglycemia and hypokalemia are side effects of using insulin systemically.Incontrast, topical insulin enhances wound healing without dropping of blood sugar levels in both diabetic and non-diabetic clients (Sridharan et al., 2017). And it is effective in burn wounds. (Hrynyk et al., 2014). Other systemic review study was conducted in 2020 on human beings and animals to assess topical insulin effect on wounds, they summarize that application of topical insulin is

effective, safe and without adverse effect systemically or topically (Wang &Xu,2020).Although many studies about systemic insulin use on wounds, but few have targeting to assess topical insulin application wounds. Therefore, this study aimed to assess the effectiveness of using topical insulin on healing of pressure ulcers.

1 .2 Background/Definition

Theoretical definitions:

Skin Injury: skin is an organ of a human being that results from a collection of many tissue layers, any injury in its layer's result causes the body to begin several operations to repair and restore skin integrity (Abdelkader,2016).

Wounds: a breakdown in the skin leading to loss of continuity of epithelium layer (Sen et al., 2009).

pressure ulcers: also called Bedsores, pressure sore, or decubitus (Lewis, Pearson & Ward, 2003). it is an injury over bony prominence which affects the skin because of pressure, shear, or both of them (EPUAP, 2009&NPAUP, 2009).

Insulin: it is a growth factor and peptide hormone that can improve healing (Wang et al., 2019). insulin used to treat other diseases rather than diabetes since the early 20th century, (King,1928). systemic use of insulin treatment increases healing in skin wounds, and ulcers for animals (Gregory, 1965).

Wound healing: dynamic process consisting of four continuous phases. haemostasis then mesenchymal cell differentiation, proliferation, and migration then suitable angiogenesis then proper synthesis, cross-linking, and alignment of collagen. (Guo, &DiPietro,2010).

Operational Definition:

pressure ulcers: Result in damage of skin or tissue caused by pressure decrease blood supply to this area its happen in person bedridden by illness and this result named 'pressure ulcers', or 'pressure sores'(National Institute for Health and Care Excellence, 2014), pressure ulcers classified as follow: Stage I: site of sore close, red, warm, soft, painful but no breaks or tears. And the stage 1 sore can feel either firmer or softer than the area around it. Stage II: partial thickness, open ulcer and loss of dermis. Stage III: Full thickness, appeared subcutaneous fat and loss of dermis. Stage IV: Full thickness tissue loss, bone exposed, tendon or muscle may be present. Unstageable: Full thickness tissue lost, depth of the ulcer hided by slough or eschar in the site of Pressure ulcer. (NPUAP, 2014&EPUAP, 2014).

PUSH Tool: A Patient will be assessed two times before the beginning of topical insulin dressing and after seven days of dressing ended, Tool that was developed in 1997 consists of three parameters: length (cm) times width (cm) (length x width) scored from zero to ten, exudate amount (none, light, moderate, and heavy) scored from 0 to 3, and tissue type (necrotic tissue, slough, granulation tissue, epithelial tissue, and closed) scored from

0 to 4. the sum of the three parameters is a total score of wound status. (Thomas et al., 1997).

Braden scale: A Patient will be assessed daily for 8 days before initiation of dressing, The Braden Scale is a tool that was used for Predicting Pressure ulcer Risk, in 1998 they did a multi-site study to assess the validity of the tool then it was approved. Braden Scale consists of six subcategories as shown in Annex 4, (Bergstrom & Braden 1998)

Topical insulin: gauze soaked with insulin act rapid, the skin was left to dry and then covered with a sterile dressing, concentration of topical insulin that is 1 International unit of human soluble insulin (actrapid)in 10 ml) and amount of solution depends on wound size. (Wilson et al., 2008 ؛El-said et al., 2017).

1.3 Problem statement

There were no studies in Palestine about insulin effectiveness in the management of pressure ulcer,it is considered as a global problem and one of the most common health care problems in Palestine. (Jamal &Omar 2018), that affects people with different health illnesses and affects different age groups, i.e., young, adult, and elderly.people with mobility impairment have a higher risk of Pressure ulcer development. Pressure ulcers are considered as a big challenge to health care organizations worldwide (Anders et al. 2010). pressure ulcershave different stages or grades of development and the quality of the care depends on grade of the Pressure ulcer. For example, stage 1 will heal faster than stage 3 or 4

(NPUAP & EPUAP 2014). The treatment of Pressure ulcers is too expensive and takes a long time to heal completely (Vanderweeet al. 2007). A Pressure ulcersare an injury over a bony prominence that affects the skin because of pressure, shear, or both of them (NPUAP &EPUAP 2014). Pressure ulcers are one of the most common health care problems in Palestine and worldwide. (Jamal &Omar 2018) pressure ulcers are affecting both hospitalized people and non-hospitalized people (Coleman et al. 2014). There are an intrinsic and extrinsic risk factors for Pressure ulcers, Intrinsic factors like malnutrition, dehydration, immobility, circulation, and respiration problems, predispose many diseases (García-Fernández et al. 2014), age, weight, and inactivity (Petzold et al. 2014).In contrast, extrinsic factors like substances individuals exposed, humidification, environment temperature, the surface of furniture for sitting or lying, moisture in bony prominence area, friction (García-Fernández et al. 2014), and treatment with certain drugs like analgesics or hypnotics that increase sleeping time (Petzold et al. 2014). The consequences of Pressure ulcer is the cost of treatment and quality of life. The treatment of Pressure ulcer is expensive and it cause serious impact upon the individual, society and health care system (Herbergeret al. 2012). Starting from a patient's inability to work and family or society burden to the high cost of bedsore treatment and care (Bennett et al. 2004). Nurse and healthcare assistant time accounts for ninety percent of the cost for treating Pressure ulcer (Bennett et al. 2004). As identified in the systematic review study the Pressure ulcers affect negatively patients’ quality of life (Gorecki et al.

2009). Regarding patients' inability to work their emotional status will be more isolated and have low self-esteem (Spilsbury et al. 2007).

1.4 Significance of study

In intensive care units, many negative factors affect the care of skin integrity for the patients, these negative factors like critical illness, workload over nurses, effective devices, and dependence on technological support, (Coyer&Tayyib 2017). In the complexity of the ICU environment which cause adverse effect upon the clinical practices of skin care management, it is important to get the attention of the health care providers and hospital administrators to try other therapeutic measures that might facilitate the healing process of Pressure ulcer as the use of insulin, the present study was conducted in Intensive care unit patients, the study aimed to assess the effectiveness of topical insulin on the healing of Pressure ulcer. This study is important because it is the first study of its kind to assess the effectiveness of topical insulin on the healing of Pressure ulcer, we use as possible the best available evidence to improve ICU patients' skin integrity in Palestine. Further, this study will increase knowledge and awareness of health care providers regarding Pressure ulcer care and management to provide a high quality of skin care. Moreover, implementation of the topical insulin in Pressure ulcers will reduce Pressure ulcer incidence rates, morbidity, mortality, pain, and length of stay. This study will reduce the costs and increase the quality of care for healthcare organizations by considering it as a reliable benchmark that can

be used to compare with other Pressure ulcer researches in the Intensive care unit.

1.5 Aims of the study

To assess the effectiveness of using topical insulin on the healing of Pressure ulcer among ICU patients at An-Najah National University Hospital (NNUH) (cardiac intensive care unit, surgical intensive care unit and medical intensive care unit).

1.6 Null Hypothesis

1. There are no significant differences in push score (at $P<0.05$) related to the topical insulin dressing use in pressure ulcer.
2. There are no significant differences in push score (at $P<0.05$) related to the topical insulin dressing use in pressure ulcer among diabetes and non-diabetes patients.
3. There are no significant differences in push score (at $P<0.05$) related to gender.
4. There are no significant differences in random blood sugar on the first day and the seventh day before insulin intake (at $P<0.05$) related to two hours after insulin intake.

Chapter Two
Literature Review

In order to acquire the required knowledge about effectiveness of using topical insulin on healing of Pressure ulcers, the researcher has collected the required information from the academic databases such as google scholar, science direct and HENARI, and by using several keywords as follows: (insulin, topical insulin, pressure ulcer, bed sore, decubitus ulcer, decubitus, chronic wound, healing and wound healing) between (1930 - 2020)

Table 1; key words used in research

	Term	Combined with
1	pressure ulcer, OR bed sore, OR decubitus ulcer, OR decubitus OR chronic wound	AND
2	Insulin OR topical insulin	
3	healing OR wound healing	

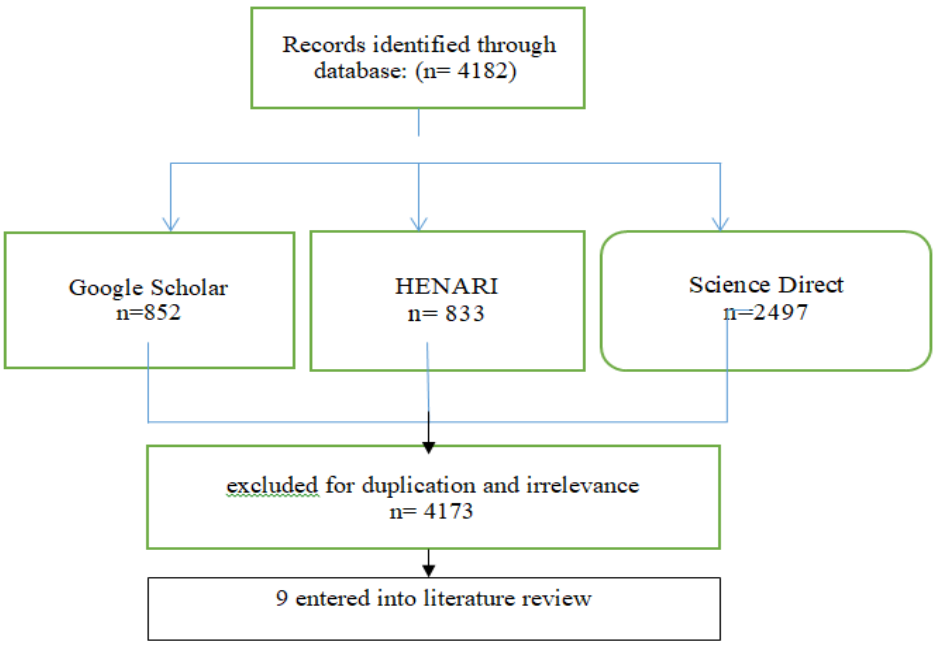


Figure 1: systemic review searching finger.

Table 2: The Characteristics of Included Studies (systemic review).

stage	Number of subject		intervention	control	Outcomes	Reference
	intervention	control				
stage 2 and 3 pressure ulcer	30	30	topical insulin dressing	ordinary hospital dressing	topical insulin dressing was effective and safe method to accelerate pressure ulcers healing	(El-said et al., 2017)
stage 2 or stage 3 pressure ulcer	25	25	Topical Insulin	Normal Saline (nacl 0.9%)	Treatment with topical insulin safe and effective compared with normal saline	(Stephen et al., 2016)
Pressure ulcers (no information about stages included)	22	22	insulin group	normal saline group (NaCl 0.9%)	abatement in wound size was moderately better with insulin using but this difference was not statistically significant	(Ebrahimifard et al., 2015).
All chronic ulcers types	25	25	insulin group	Normal Saline (nacl 0.9%) group	days required for wound healing in insulin group was less than normal saline group and rate of healing was faster in insulin group and days of hospitalization in insulin group was significantly less than the second group	(Goenka et al., 2014).
stage 2 or stage 3 pressure ulcer	_	_	Insulin	hyperosmotic glucose solution	They found for grade 2 pressure sores no statistically significant difference between them. but the average healing time for grade 3 pressure sore in the insulin group was faster	(Zhou et al., 2001)
All stages of pressure ulcers	5	5	Insulin complexation with hydroxypropyl-beta-cyclodextrin	Carbopol 940 polymer	Using of stabilized insulin will progress the healing of wounds	(Valentini et al., 2015).

Not specific stage	6	8	insulin	Other (not mentioned)	Using of insulin was safe and effective in the treating of small and uncomplicated Pressure ulcer.	(van & Gerber 1976)
Not specific stage	15	14	insulin	ordinary dressing	whileusing topical insulin dressing, number of days decreased and the rate of healingincreased.	(Gerber & Van 1979)
Not specific stage	5	0	insulin		using of insulin is effective treatment of Pressure ulcer.	(Joseph, 1930).

In the literature review, quantitative studies are included; some articles were excluded after review of the abstract reviewed and some were excluded after the full article had been reviewed.

A Quasi-experimental study was conducted in Egypt in Neurological wards in one center, on 60 clients divided into two clusters; a cluster with topical insulin use and the cluster that received the usual hospital method, two kinds of insulin have been used, act rapid and Mixtard 30/70. That was applied to 30 clients in each group. Assessment of the wound in both clusters for two times done, one time immediately before intervention on the first day and second time after one week of intervention, the result showed there was a significant decrease in Pressure Ulcer Scale for Healing (PUSH) for topical insulin cluster than another cluster and highly significant improvement in PUSH score for Mixtard subgroup (El-saidet al., 2017).

Another important randomized controlled trial on 50 patients, was performed in the trauma center in India. It sought to measure the effect of topical Insulin vs NaCl0.9% solution in Pressure ulcer healing. The statistical results show that there was a significant decrease in PUSH score and wound size. This result supports the researcher’s idea about the association between the use of Topical Insulin and Pressure ulcer healing (Stephen et al., 2016).

A study that was conducted at Shahid-Modarres Hospital, Tehran, Iran and was designated to determine the effect of topical insulin on bed sores healing. an experimental double-blinded clinical trial on 44 cases, cases were randomly divided into two groups. normal saline group and insulin group. They found that abatement in wound size was moderately better with insulin using but this difference was not statistically significant. (Ebrahimifard et al., 2015).

In another hospital in Brazil, they sought to evaluate complexation containing insulin for healing of Pressure ulcers, and they find that Using of stabilized insulin will progress the healing of wounds. (Valentini et al., 2015).

A study was conducted at Padmashree, Pimpri, Pune, India; The purpose of the study was to determine the effectiveness of using topical insulin on chronic ulcer healing. A prospective study on 50 patients was randomly allocated to two groups, the first one received insulin dressing and the second one received normal saline dressing. They found that the days required for wound healing in the insulin dressing group was significantly less as compared to the normal saline dressing group, the rate of healing of wounds was faster in the insulin dressing group and days of hospitalization in the insulin dressing group was significantly less than the second group (Goenka et al., 2014).

A study that is entitled “Insulin and hyperosmotic glucose solution topical use for treating Pressure ulcer” was conducted in China in 2001, to compare the effect of use insulin with hyperosmotic glucose solution and use of moist burn ointment in terms of average healing time. They found for grade 2 pressure sores no statistically significant difference be¬tween them. but the average healing time for grade 3 pressure sore in the insulin with hyperosmotic glucose group more significantly de¬creased than that of the moist burn ointment group (Zhou et al., 2001).

A pilot study on 14 subjects in 1976 by van & Gerbershowed that insulin was safe and effective in the healing of uncomplicated Pressure ulcer. (van& Gerber 1976)

A study that is entitled “Topical use of insulin in Pressure ulcers.” was conducted on Twenty-nine geriatric subjects, and they find that number of days decreased and the rate of healing increased. (Gerber& Van 1979)

A study that conducted on 5 non-diabetic cases 1 male patient and 4 female patients in1930 by Barnet Joseph in New York, Observation of the size of ulcer over time indicates whether wound healing is occurring, and the study found that the use of insulin is an effective treatment of bedsores. (joseph, 1930).

PUSH Tool that developed in 1997 consists of three parameters: length (cm) times width (cm) (length x width) scored from zero to ten, exudate amount (none, light, moderate, and heavy) scored from 0 to 3, and tissue type (necrotic tissue, slough, granulation tissue, epithelial tissue, and

closed) scored from 0 to 4. the sum of the three parameters is a total score of wound status. (Thomas et al., 1997).

Data indicate that changes in Pressure ulcersize while using insulin topically over a one-week are associated with the ulcer's healing (El-said et al., 2017). Other randomized, controlled trials indicate that insulin facilitates pressure ulcer healing During the 7-day study (Stephen et al., 2016). In Hillingdon Hospital, united Kingdome a study applied on chronic wounds and they find that the proper administration concentration dose to promote healing of topical insulin is 1International unit of human soluble insulin (actrapid)in 10 ml for 7 days and the amount of solution depends on

wound size, and it is safe and no systemic hypoglycemia effect (Wilson et al., 2008), the same concentration of topical insulin (1International unit of human soluble insulin (actrapid)in 10 ml) and amount of solution depend on wound size, and it is safe and no systemic hypoglycemia effect (El-said et al., 2017).

Braden Scale developed in 1987 it was used for predicting pressure ulcer risk, used by health care providers to evaluate the risk of developing a pressure ulcer(Bergstrom, Braden et al.,1987). The Braden Scale it is a tool that was used for predicting pressure ulcer risk, in 1998 they did a multisite study to assess the validity of the tool then it was approved. Braden Scale consists of six subcategories as shown in Annex4, (Bergstrom & Braden 1998). The cut-off score is 18 Lower scores mean a higher risk (Braden & Bergstrom, 1994). Patients will divide into 4 subcategories: mild-risk

patients (ranging from 15 to 18), moderate-risk patients (ranging from 13 to 14), high-risk patients (ranging from 10 to 12), and very high-risk patients (9 or below). The Braden Scale can clarify clients who are at risk of pressure ulcerdevelopment in the intensive care units (Pancorbo- Hidalgo et al., 2006).

Chapter Three
Methodology

Methodology chapter includes: Study design, Study site and setting, Population, Sample and sampling, Sample size, Inclusion criteria, Exclusion criteria, Randomization, Tools, Ethical considerations, Data collection procedure, Data analysis plan, Validity and reliability of the data sheet, the reliability of the data sheet, Cronbach's alpha Correlation Coefficient and Missing data:

3.1 Study design

A prospective true experimental used, involves the Randomization, manipulation of an independent variable, and Control group to minimize bias.

Definition of research methodology: general approach the researcher takes in carrying out the research project. In quantitative research collection of data will be quantified and statistically analyze to support or refuse, by using mathematical issues we analyze the data, which is consists of three parts; design, measurement and test procedures, and statistical analysis. There are many types of quantitative research: descriptive, experimental, and causal-comparative, in experimental research, the researcher investigates the treatment of an intervention into the study group and then measures the outcomes of the treatment, true experimental design is one of three types of exploratory approaches, which provides a higher degree of control in the experiment and produces a higher degree of validity. The true

experimental designs result in a systemic approach to quantitative data collection involving mathematical models in the analyses. (Williams, 2007), A diagrammatic representation of the design is given below.

Table 3: study design

	EXPERIMENTAL	CONTROL	
PRE-TEST	O1	O1	
INTERVENTION	X		
POST-TEST	02	02	

Prospective, randomized, controlled study.

3.2 Study site and setting

An-Najah National University Hospital (NNUH), cardiac intensive care unit, surgical intensive care unit and medical intensive care unit.

3.3 Population

The study conducted at NNUH, data collected from critical care unites, (cardiac intensive care unit, surgical intensive care unit and medical intensive care unit).

3.4 Sample and sampling

To find the optimal sample magnitude for the research trial that safeguard an adequate effect to clarify statistical significance, the effect of the trial was measured at 80% power, with alpha levels as ($p < 0.05$). Sample magnitude was measured as 31 clients in study group and 31 clients control group.

3.5 Sample size

The sample size was measured by using the tool at https://clincalc.com/stats/samplesize.aspx , evidence-based calculators for medical professionals. The following assumptions were used to calculate the sample size:

- The accepted alpha is 5% and the beta is 20%.
- A prevalence of pressure ulcers in the ICU department in Palestine was 33% in all stages of pressure ulcer and the prevalence of 2nd and 3rd stages pressure ulcers in the ICU department in Palestine was 7.57%(Omar & Jamal, 2018).
- in a review of nine articles (Table 2), seven of them mention the number of participants the total number was 136 cases took topical insulin dressing, they found it was effective on 130 cases of them, it means The median incidence of 2nd and 3rd stages expected to go down to 0.365%. A sample size of 31 subjects in each group would be required to detect this difference.
- According to this tool and these assumptions, we decide to take 31 patients per group (a total of 62 participants) by using inclusion criteria.

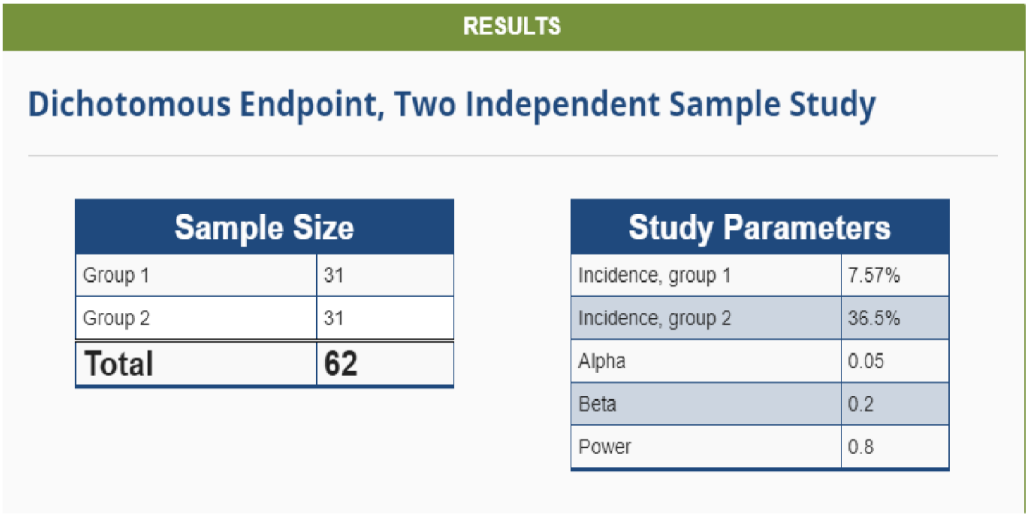


Figure 2: sample size calculation

3.6 Inclusion criteria for the two groups (experimental and control)

clients who met the inclusion criteria will be in research:

- 18-70 years old, both gender.
- Patients have pressure ulcers stage 2 and 3.
- wound size less than 10 cm2.

3.7 Exclusion criteria for the two groups (experimental and control)

- Patients under 18 years and over 70 years of age.
- Patients who have pressure ulcers grade 1, 4 and unstageable.
- Patients who have insulin allergy.
- Patients who have vascular disease (Arterial insufficiency, Buerger'sdisease).
- Immunodeficiency, pregnancy, osteomyelitis, varicose and burns ulcers.

- patient with hypotension.
- Patients with hemoglobin levels <12.0 g/dL

3.8 Randomization

Randomization list formatted by www.randomization.com -which developed by Gerard in 2008 (Gerard, 2008), the selected patients were divided randomly into two groups:

1. Experimental group: Those patients who were given Topical insulin (10 IU/100ml NaCl 0.9%) will be utilized in dressing 2 times per day for one week
2. Control group The patient received the usually routine hospital dressingthe following table showed the randomized selection of each group

Table (4): The computerized online randomized list.

N	Group	N	Group	N	Group	N	Group
1	insulin	17	control	33	Insulin	49	Insulin
2	control	18	Control	34	Control	50	Control
3	Control	19	Control	35	Control	51	Control
4	Control	20	Insulin	36	Insulin	52	Control
5	Insulin	21	Control	37	Control	53	Control
6	Insulin	22	Insulin	38	Insulin	54	Control
7	Insulin	23	Insulin	39	Insulin	55	Insulin
8	Control	24	Insulin	40	Control	56	Control
9	Insulin	25	Insulin	41	Control	57	Control
10	Insulin	26	Insulin	42	Control	58	Insulin
11	Insulin	27	Control	43	Insulin	59	Insulin
12	Insulin	28	Insulin	44	Control	60	Insulin
13	Control	29	Insulin	45	Control	61	Insulin
14	Insulin	30	Control	46	Control	62	insulin
15	Insulin	31	Control	47	control		
16	control	32	Control	48	Insulin		

3.9 Tools

Tool 1: Socio-demographic characteristics

Including: age, sex.etc.

Tool 2: medical datasheet

diagnosis, date of admission, past medical history, Braden scale score, site of pressure ulcers, the shape of pressure ulcers, degree of pressure ulcers, using pressure-relieving devices and types of them, and random blood sugar level.

Tool 3: PUSH

The patient were assessed two times before the beginning of topical insulin dressing and after seven days of dressing ended, Tool that was developed in 1997 consists of three parameters: length (cm) times width (cm) (length x width) scored from zero to ten, exudate amount (none, light, moderate, and heavy) scored from 0 to 3, and tissue type (necrotic tissue, slough, granulation tissue, epithelial tissue, and closed) scored from 0 to 4. the sum of the three parameters is a total score of wound status. (Thomas et al., 1997).

3.10 Ethical considerations

The institutional Review Board of NNU accept the research, as well as the approval, was taken from the hospital. every patient takes a Consent form, information about the aim, objectives, collecting information, and taking pictures of bedsores, before participating in the study.

3.11 Data collection procedure

After the Institutional review board of An-Najah National University approval obtained and the ministry of health approve the research, every patient takes a Consent form, information about the aim, objectives, collecting information and take pictures of bedsores, before participating in the study, coordination with the chief of Nursing and Medical director in An-Najah National University Hospital (NNUH), introduce name of researchers, goals, and mechanism of collecting data from each institution then all the legal papers that allow starting research has been shown then data collected from all critical care units, the researcher did a continuous checking for patients who were admitted to the critical care units at NNUH trough the period of august 2020-November2021. Any patient who was admitted with pressure ulcer and who met the inclusion criteria was included in the study. The researcher then asked the patient to participate in the study and took the consent form after explaining the aim of the study while reassuring the patients about the confidentiality and anonymity of their participation. Patients were informed in details about the use of insulin in the dressing of their ulcer and that the dressing will be done by

the doctor who is responsible, The file will be checked for the Braden and Push scale calculated before starting the procedure.

The field of working includes pre-procedure, procedure, and post-procedure.

Pre-procedure:

1. Doctor who has the responsibility to do the dressing write-down the order of using topical insulin, how to administer, time of doing that, order of random blood sugar before dressing and 2 hours after dressing, in the patient file or any tool used in the hospital as order sheet for nurses, and write down all things that makes the order valid depends on hospital policy.

2. The researcher then asked the patient to participate in the study and took the consent form after explaining the aim of the study while reassuring the patients about the confidentiality and anonymity of their participation. Patients were informed in details about the use of insulin in the dressing of their ulcer and that the dressing will be done by the doctor who is responsible, The file will be checked for the Braden and Push scale calculated before starting the procedure.

3. On the first day of dressing for the study group these data were obtained from the patient file: Date of admission, Patient diagnosis, Site of bedsores, Braden Scale Score, degree of bedsores, use of pressure-relieving devices, random blood sugar before dressing.

4. at the first day before the intervention, the wound will evaluate.

Procedure:

1. in study group: cleaning the wound with NaCl 0.9%, then gauze with insulin with a concentration of 1 International unit of human soluble insulin (act rapid) in 10 ml NaCl 0.9%, then covered with a sterile dressing.

2. in the control group: usually routine hospital dressing is applied; i.e cleaning the wound with saline, then covering the wound with sterile gauze.

3. Dressing done 2 times per day for one week in 2 groups. With 12 hours between them by the same researcher.

Post-procedure:

one week after intervention, the wound was evaluated for the second time in both groups.

3.12 Data analysis plan

After collection of the data, it was analyzed using the statistical package of social science “SPSS” software version 25. this chapter includes two sections. Section one for Descriptive statistics in the form of frequencies and percentages for quantitative data and means and standard deviations and medians and interquartile ranges for quantitative variables. Section two Quantitative continuous data were compared using the non-parametric

Mann-Whitney test and Wilcoxon, for parametric paired t-test and independent t-test. using the chi-square test the qualitative categorical variables were compared. Statistical significance was considered at p-value <=0.05.

3.13 Validity and reliability of the datasheet

The content validity of the tool that was used in the research was created depending on recommendations of a panel of three experts who have doctoral degrees in the nursing field, one internal medicine specialist doctor, one surgical specialist doctor, and one plastic surgeon doctor, nothing to add after the audit.

3.14 The reliability of the datasheet

To determine the reliability of the study instrument we use piloting of the tool on 10% of the sample size who were in the study later on. Piloting is the pre-testing or trying out for the study tool (Bannister T, et al.,2021).; it explores where study failed or inappropriate questions. Therefore, the piloting of the questionnaire is a tool for assessing and developing the study instrument to ensure confidential scientific information collected by a standardized questionnaire was gathered (Bannister T, et al.,2021). After the piloting of the study data sheet on 10% of the sample, nothing was added or modified.

3.15 Cronbach's alpha Correlation Coefficient

We use Cronbach's alpha to evaluate the reliability of the tool, when values are more than 0.7 they are reliable (Cronbach&Warrington, 1951). the evaluated tool showed that it is valid and reliable, depending on factor analysis and Cronbach's alpha (for 7 items the Cronbach's alpha is = 0.86; scores above 0.7 are generally considered reliable).

3.16 Missing data

The researcher filled in the datasheet because of the client's critical health condition, so there was no missing data.

Chapter Four
Result and Discussion

4.1 Result

After collection of the data, it was analyzed using the statistical package of social science “SPSS” software version 25. this chapter include two sections. Section one for Descriptive statistics in the form of frequencies and percentages for qualitative data and means and standard deviations and medians and inter quartile ranges for quantitative variables. Section two Quantitative continuous data were compared using the non- parametric Mann-Whitney test and Wilcoxon, for parametric paired t-test and independent t-test. Qualitative categorical variables were compared using chi-square test. Statistical significance was considered at p-value <=0.05, The results were supported by taken pictures for patients bed sores at day one and after procedure at day seven as shown in last section (Figure 4), (Figure 5).

4.1.1 Descriptive statistics

The aim of the present study is to assess the effectiveness of using topical insulin on healing of pressure ulcers in intensive care unit patients. To evaluate the insulin effect on healing pressure ulcers, a prospective true experimental will be used in this study. Sample of this study comprised of 62 patients of both sexes, had pressure ulcers stage 2 or 3with or without diabetes mellitus. They were divided into two equal groups; Experimental group with the use of topical insulin treatment and control group who

received ordinary hospital treatment, all patients were selected from all critical care unites in Najah National University hospital NNUH, Table (5) showed demographic data for two groups.

Table (5): Demographic data for two groups

Characteristics	Experimental Group (n=31) 50%	Control Group (n=31) 50%	P *
Mean age± SD (yrs.)	55.55 ± 16.82	50.16 ± 12.50	0.014
Mean Push 1st day ±SD	8.84 ± 2.38	7.61 ± 2.64	0.037
Mean Push 7th day± SD	5.19 ± 2.44	9.45 ± 3.65	0.000
Gender (Male/Female)	13/18 21%/29%	20/11 32%/18%	N /A
DM (Yes/No)	14/17 22.5%/27.5%	15/16 24%/26%	N /A

* Mann-Whitney U test was conducted, since the data not normally distributed

As we see from table 5, mean age for experimental group is 55 years, while control group is 50 years, and that is significant difference between two groups, since p-value less than 0.05. mean push score at day one for experimental group is 8.8, while control group is 7.6, and that is significant difference between two groups, since p-value less than 0.05. mean push score at day 7 for experimental group is 5.19, while control group is 9.45 years, and that is significant difference between two groups, since p-value less than 0.05. 42% from experimental group male, while 64% in control group. 45% from patients in experimental group have diabetes mellitus, while 48% from control group, For degree of bedsores, 90% (28) from patients who take insulin with 2nd degree and 10% (3) with 3rd degree at day 1, after 7 days of take insulin 65% (21) with zero degree and 19% (6) with 1st degree, below table show movement of degree of bedsores, Table (6).

Table 6: degree of pressure ulcer at day 1 and 7 in experimental group

degree of pressure ulcer at day 1 in experimental group	2nd degree	28
	3rd degree	3
degree of pressure ulcer at day 7 in experimental group	total	31
	zero	21
	1st degree	6
	2nd degree	3
	3rd degree	1
	total	31

As we see there is positive effect using insulin to treat bedsores. In contrast for patients who didn't use insulin there are 90% (28) from patients who didn't take insulin with 2nd degree, 10% (3) with 3rd degree at day 1, after 7 days 55% (17) there are no change in degree of bedsore, below table show movement of degree of bedsores Table (7).

Table 7: degree of pressure ulcer at day 1 and 7 in control group

degree of pressure ulcer at day 1 in control group	2nd degree	28
	3rd degree	3
	total	31
degree of pressure ulcer at day 7 in control group	zero	0
	1st degree	6
	2nd degree	15
	3rd degree	10
	total	31

4.1.2 inferential statistics

To identify the proper test, first we want to check if the data normally distributed or not, below figure 1 showed the distribution for age all cases, Figure 2 illustrate patients ages under normal distribution curve. According to kolmogrov-smirnov normality test, the significance level (0.001) and that is less than 0.05, which indicates that the distribution of our sample is not normal, which results in the use of nonparametric tests. Since the data

not normally distributed, we will use Wilcoxon test and Mann-Whitney U test to check the hypotheses number 1.

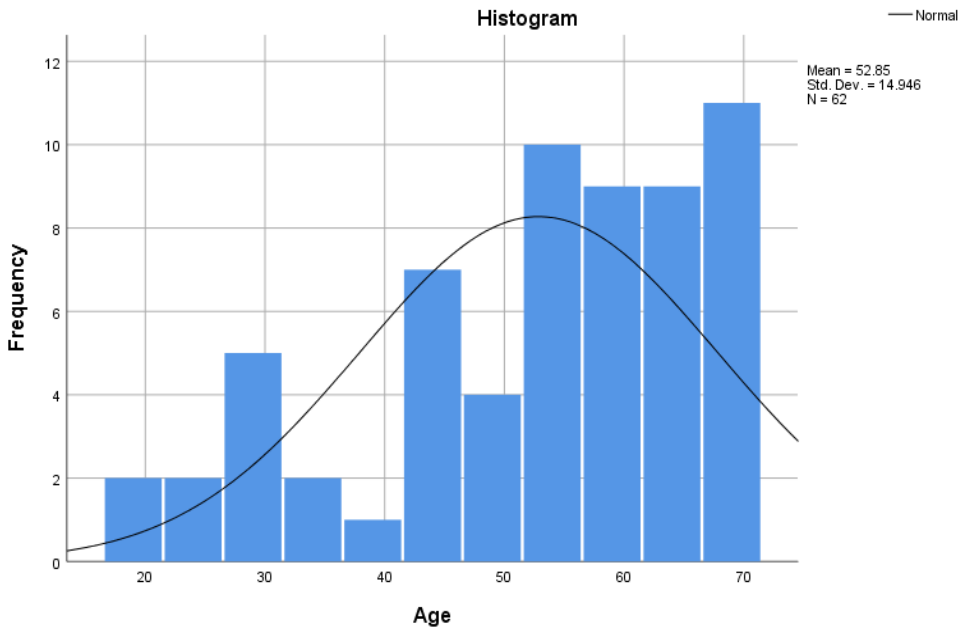


Figure 3: distribution of patients ages under normal distribution curve.

In this section we will test the below null hypotheses

1. There are no significant differences in push score (at $P<0.05$) related to the topical insulin dressing use.

2. There are nosignificant differences in push score (at $P<0.05$) related to diabetes mellitus**.**

3. There are no significant differences in push score (at $P<0.05$) related to gender.

4. There are nosignificant differences random blood sugar in first day and seventh day before insulin intake (at P<0.05) related to two hours after insulin intake.

1. **There are no significant differences in push score (at P<0.05) related to the topical insulin use**

To check if there is significant difference in push score between two groups, we will conduct Wilcoxon test and Mann-Whitney U test, since the data that we have is non-parametric, below table 8 represent Wilcoxon test and Mann-Whitney U test.

Table 8: Comparison of Pressure Ulcer Scale of Healing PUSH) between Experimental and control group at day one and day seven

Timing	**Experimental Group (n=31)**	**Control Group (n=31)**	**p-value**
	Mean ± SD, Median		
Day 1	8.84 ± 2.38, 9	7.61 ± 2.64, 7	0.037
Day 7	5.19 ± 2.44, 5	9.45 ± 3.65, 11	0.000
P-value	0.000	0.122	

As we see from table (8), there was a significant improvement in PUSH for experimental group than control group. where, there is statistically significant difference in PUSH score between the experimental and control groups at day one, and there is statistically significant decreased in experimental group at day 7 but in control group it was increased. Based on that we reject H0: “There are no significant differences in push score (at P<0.05) related to the topical insulin and healing of pressure ulcers.”, since the p-value for is less than 0.05 in experimental group, while in control group is greater than 0.05. in conclusion the insulin is effective to healing the pressure ulcers, for degree of bedsores, 90% of patients who take insulin with 2nd stage and 10% with 3rd stage at day 1, after 7 days of take insulin 65% with zero stage and 19% with 1st stage, show movement of degree of bedsores in Table (6), there is positive effect using insulin to treat

bedsores. In contrast for patients who didn't use insulin there are 90% from patients who didn't take insulin with 2nd stage, 10% with 3rd stageat day 1, after 7 days 55% there are no change in degree of bedsore, show it in Table (7).

2. There arenosignificant differences in push score (at *P*<0.05) related to diabetes mellitus

To check if there is significant difference in push score between two groups (patients with DM, and patients without DM), we will conduct parametric test, since the data that we have is parametric as we will see in figure 3, also based on kolmogrov-smirnov normality test, the significance level (0.200), and that is greater than 0.05, which indicates that the distribution of our is normal, to test if there is significantly difference in PUSH score between patients with DM and patients without DM, we will conduct paired t-test and independent t-test, below table 9 represent the result.

Table 9: Comparison of Pressure Ulcer Scale of Healing PUSH) between patients with DM and patients without DM at day one and day seven

Timing	Patients with DM (n=29)	Patients without DM (n=33)	p-value
	Mean ± SD, Median		
Day 1	8.10 ± 2.59, 8	8.83 ± 2.58, 8	0.855
Day 7	7.41 ± 3.94, 7	7.24 ± 3.6, 6	0.535
P-value	0.284	0.081	

As we see from table (9), there is no statically significant in PUSH score for patients with DM and patients without DM, the p-value 0.284 and 0.081 respectively. There is no statically significant in push score between patients with DM and patients without DM at day one and at day seven, the

p-value 0.855 and 0.535 respectively. Based on that we accept H0: “There are no significant differences push score (at P<0.05) related to diabetes mellitus.” since the p-value for is greater than 0.05.

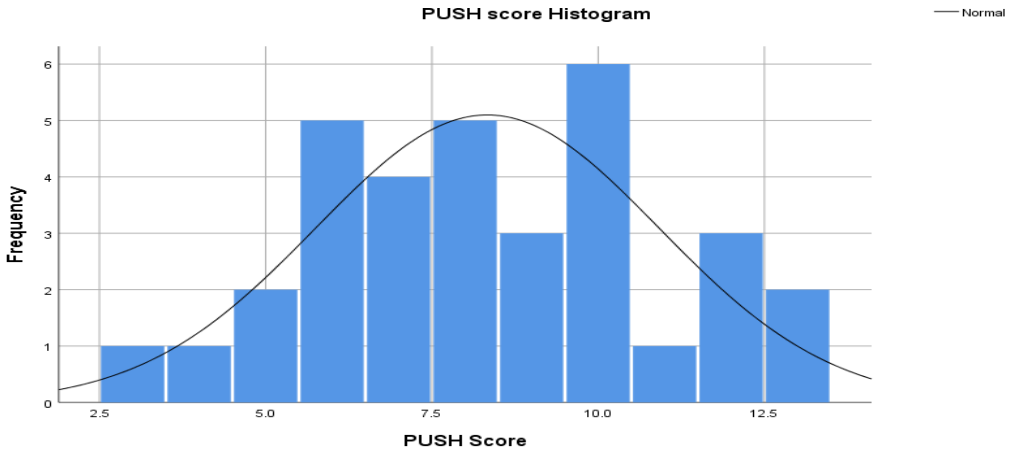


Figure 4: distribution of PUSH score under normal distribution curve

3. There are no significant differences in push score (at P<0.05) related to gender.

To test if there is significantly difference in PUSH score between male or female with insulin intake, we will conduct paired t-test and independent t-test, below table 10 represent the result.

Table 10: Comparison of Pressure Ulcer Scale of Healing PUSH) between male and female with insulin in take at day one and day seven

Timing	Male with insulin intake (n=13)	Female with insulin intake (n=18)	p-value
	Mean ± SD, Median		
Day 1	8.85 ± 1.72, 9	8.83 ± 2.81, 9.5	0.988
Day 7	4.85 ± 2.41, 5	5.44 ± 2.5, 5	0.510
P-value	0.000	0.000	

As we see from table (10), there is significant in PUSH score for male and female, the p-value 0.000 and 0.000 respectively, which mean the insulin is effective for both male and female. Based on that we reject H0: “There are no significant differences push score who used insulin (at P<0.05) related to gender.”, since the p-value for is less than 0.05. there is no statically significant in push score between male and female at day one and at day seven, the p-value the p-value 0.988 and 0.510 respectively.

4. There are no significant differences in random blood sugar in first day and seventh day before insulin intake (at *P*<0.05) related to two hours after insulin intake

To test if there is significantly difference in random blood sugar in first day and seventh day before insulin intake related to two hours after insulin intake, we will conduct paired t-test and independent t-test, below table 11 represent the result.

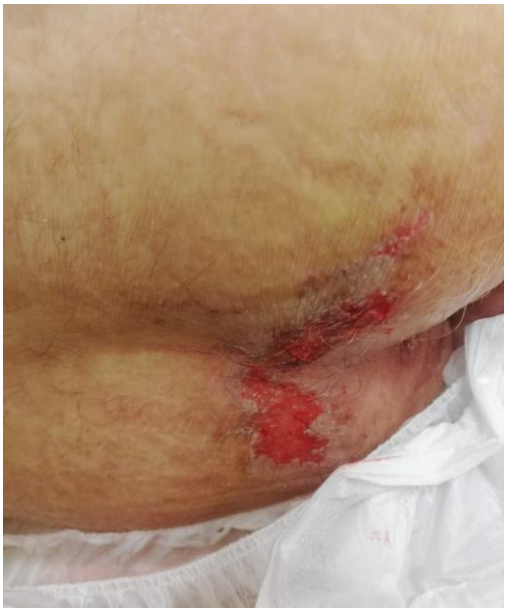
Table 11: Difference between Random sugar level before and after insulin intake among study group at the 1st and 7th day (n=31).

Timing	Mean ± SD, of RBS	p-value
Before insulin intake at Day 1	142.2 ± 38.2	0.580
Two hours after insulin intake at Day 1	139.6 ± 41.8	
Before insulin intake at Day 7	134.7 ± 37.6	0.758
Two hours after insulin intake at Day 7	135.7 ± 37.1	

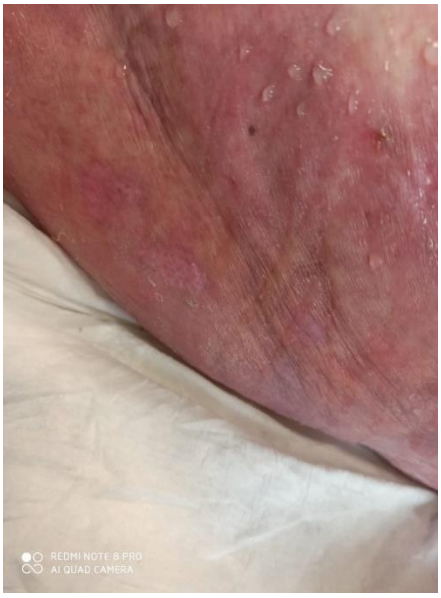
As shown from table 11, the random blood sugar values in first day before insulin intake was (142±38.2) whereas after insulin intake was (139.6±41.8) which was statistically non-significant (p=0.580). In day

seven the random blood sugar values before insulin intake was (134.7±37.6) whereas after insulin intake was (135.7±37.1) which was statistically non-significant (p=0.758).

4.1.3 pictures

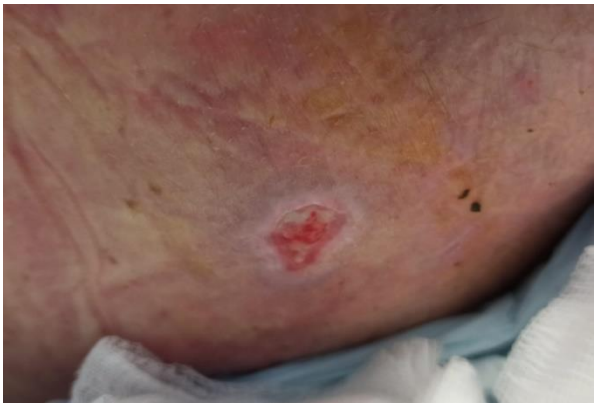


Case A1: an experimental group participant pressure ulcer picture at day 1 before dressing

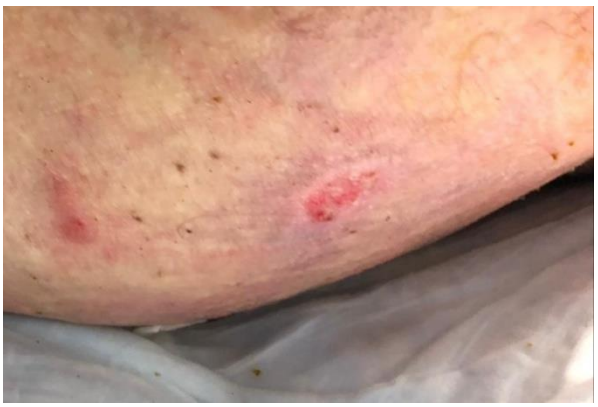


Case A2: an experimental group participant pressure ulcer picture at day 7 after using topical insulin dressing for all period**.**

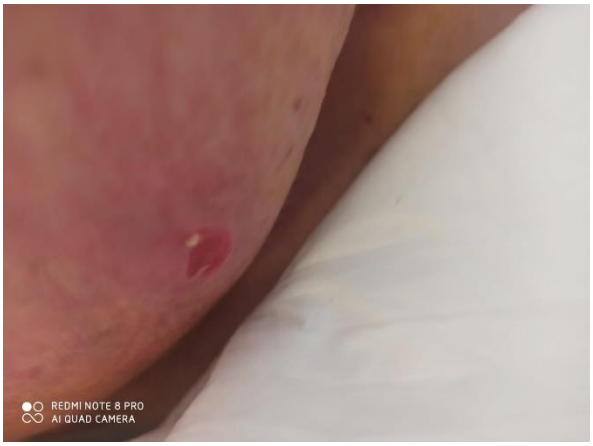
Figure 5: case A1&2: an experimental group participant pressure ulcer pictures at day 1 before dressing and at day 7 after using topical insulin dressing for all period.



Case B1: an experimental group participant pressure ulcer picture at day 1 before using topical insulin dressing



Case B2: an experimental group participant pressure ulcer picture at day 3 after using topical insulin dressing.



Case B3: an experimental group participant pressure ulcer picture at day 7 after using topical insulin dressing for all period.

Figure 6: case B 1-3: an experimental group participant pressure ulcer pictures at day 1 before dressing, day 3 and at day 7 after using topical insulin dressing for all period.

4.2 Discussion

As a result of the current study, it was determined that topical insulin was a more effective and safe method of accelerating the healing of pressure ulcer than a hospital routine. pressure ulcers can obstruct a patient's functional recovery, be complicated by infection and pain, and contribute to a longer hospital stay. Because the presence of bedsores is a predictor of poor overall prognosis and may lead to early mortality in some patients, insulin

was utilized in wound treatment. Insulin is a growth factor that influences the proliferation, migration, and secretion of keratinocytes, endothelial cells, and other cell types, and fibroblasts. (Ebrahimifard et al., 2015) In ICU departments in Palestine, the prevalence of pressure ulcers was 33%, which was greater than in China and Jordan but lower than in Western Europe and was influenced by duration of stay in the hospital, wetness, and friction. Where do the most common pressure ulcer risk factors occur (Omar & Jamal, 2018) Approximately 1.3 to 3 million persons suffer from pressure ulcers, with each ulcer costing between $500 and $40,000 to treat; hence, discovering novel low-cost strategies for treating and preventing pressure ulcers is useful to the human being. (Ebrahimifard et al., 2015) We did our research on humans with pressure ulcers in the 2nd or 3rd stage, similar to (El-said et al., 2017; Stephen et al., 2016; Ebrahimifard et al., 2015), but others only included the 2nd stage (Zhou et al., 2001). When others exclude diabetic patients (Ebrahimifard et al., 2015; Goenka et al., 2014; Gerber & Van 1979; van & Gerber 1976), we include diabetic and non-diabetic clients (Ebrahimifard et al., 2015; Goenka et al., 2014; Gerber & Van 1979; van & Gerber 1976). (El-said et al., 2017; Joseph, 1930; Stephen et al., 2016; Valentini et al., 2015). 46.5 percent of them, on the other hand, had diabetes, with a median age of 53 years.

1. healing of pressure ulcer and use of topical insulin dressing

On day 7, mean PUSH scores in the control group increased from 7.61 2.64 to 9.45 3.65 (P = 0.122), whereas in the insulin group, they decreased from 8.84 2.38 to 5.19 2.44 (P less than 0.01), indicating that there are

significant differences in push scores (at P0.05). On day 1, 90 percent (28) of patients on insulin had 2nd-degree bedsores, and 10% (3) had 3rd-degree bedsores. After 7 days, 65 percent (20) had zero-degree bedsores, and 19 percent (6) had 1st-degree bedsores. As you can see, utilizing insulin to treat bedsores has a good effect. Patients who did not use insulin, on the other hand, account for 90% (28) of those with 2nd-degree diabetes and 10% (3) With 3rd-degree bedsore on day 1, after 7 days 55 percent (17) have no change in the degree of bedsore, our findings contradict most of the human publications we discovered. El-said et al., 2017 clarified that using the same tool to assess pressure ulcer healing (PUSH), there was no significant difference in PUSH score between the insulin and normal saline groups on the first day, but the score was statistically significantly decreased in the study group (insulin) on the seventh day, but increased in the control group (normal saline), implying that wounds in the insulin group healed faster than wounds in the control group (El-said et al., 2017 In another study of 50 patients, the mean PUSH scores decreased from 10.52 2.37 to 10.36 2.40 on the last day in the normal saline group (P = 0.475), and increased from 10.28 1.10 to 8.52 1.58 on the last day (P less than 0.01) in the insulin group, indicating that pressure ulcers in the insulin group healed more quickly than those in the saline group (Stephen et al., 2016). The ratio of wound healing was 8.7% in the normal saline group and 10% in the insulin dressing group (P > 0.05) in a study comparing the effect of insulin solution on wound healing compared to normal saline (Ebrahimifard et al., 2015), A similar article found insulin was effective that which evaluate Insulin and hyperosmotic glucose solution for treating

pressure ulcer the average healing time of 2nd stage bed sore in insulin group was 11.6 +/- 2.7 days, while in the hyperosmotic glucose solution group 12.9 +/- 3.4 days, the difference was not statistically significant, the average healing time of 3rd stage bed sore in insulin group 22.3 +/- 4.3 days it was significantly shorter than that of the hyperosmotic glucose solution group 24.8 +/- 3.9 days, ($P < 0.05$) it means both of solutions are effective in treating bedsore. (Zhou et al., 2001), In 2015 a hospitalized patients of the Intensive Care Unit with 2nd stage of bedsore divided into two groups, patients treated with a gel containing insulin 5 patients of them and patients treated with the Carbopol 940 polymer gel 5 patients of them, on the first day in insulin group the pressure ulcer showed the presence of necrotic and devitalized tissues, and after 15 days' new epithelial tissue created in the edge of the sore and sore size shrink. In patients treated with the Carbopol 940 polymer gel 5 patients, on the first day the pressure ulcers showed loss of dermal thickness and the presence of blood. After 15 days, wound size increased and the formation of white and dark edges with devitalized tissue attached to the surface and necrotic tissues appeared (Valentini et al., 2015), Another pilot study was conducted on Decubitus ulcers of 6 experimental patients were treated with a topical application of ten units of regular insulin twice a day for five days; 8 control group patients received one of a variety of topical therapies other than insulin for 15 days, data analysis showed that insulin was an effective agent in the healing of small, uncomplicated pressure ulcers. (Van & Gerber 1976), another article shows the effectiveness of using topical insulin on day 7 and day 15 applied on 29 geriatric patients 15 of them in the insulin group, they

find that there was a direct correlation between the number of days of treatment and the rate of healing which supports our results. (Gerber & Van 1979) And the oldest research found in a database that mentioned before about using insulin to treat pressure ulcer that article in 1930 by Observe the size of ulcer overtime for 5 patients, they found that wound healing is occurring, and they found that the use of insulin is an effective treatment of bedsores. (joseph, 1930).

2. healing of pressure ulcer and diabetes mellitus

In our study we include diabetic and non-diabetic clients, then we found that there is no statically significant PUSH score for patients with diabetes and patients without diabetes, the p-value 0.284 and 0.081 respectively, there is no statically significant push score between patients with diabetes and patients without diabetes at day one and at day seven, the p-value 0.855 and 0.535. Other researchers exclude diabetic patients (El-said et al., 2017; Joseph, 1930)., another researcher were excluding diabetes mellitus patients, persons with immunodeficiency, pregnancy, osteomyelitis, and peripheral vascular illness (Stephen et al., 2016). Others mention that Hyperglycemic clients and those with bedsores other than stage2 were excluded from the study but at the end of the study, they found that it did not alter the blood glucose level of clients, and therefore it did not have a hypoglycemic reaction (Valentini et al., 2015). but in a study concerning insulin solution effect on wound healing compared with normal saline for 44 patients including half of them had diabetes mellitus regarding diabetic patients and wound healing the difference was not significant between

them. (Ebrahimifard et al., 2015), Another article on 50 patents 66% of them had diabetes clarify that number of days required for healing was 38 ± 17.03 days in the Group of insulin dressing for diabetic patients and 30.5 ± 13 days in the Group of insulin dressing for non-diabetic patients Whereas the number of days required for healing was 44.3 ± 17.5 days in Group of normal saline dressing for diabetic patients. and 40 ± 18.8 days in Group of normal saline dressing for non-diabetic patients which were comparable and statistically significant, and the healing in insulin group was faster, (Goenka et al., 2014).

Others did not mention the description of samples like inclusion and exclusion criteria (Zhou et al., 2001) others do that for diabetic and non-diabetic participants they administer insulin dressing at mealtime to avoid hypoglycemia and do blood sugar level test before dressing then two hours after dressing end, but no significant defiance observed between the healing of pressure ulcer and diabetes mellitus (Gerber & Van 1979) other study was undertaken to determine the effect of hydrogen peroxide versus topical insulin on the healing rate of pressure ulcers applied on both five diabetic and ten non-diabetic clients, but only one client has had a symptom of diabetes mellitus, during the study determined by fasting blood glucose, due to a blood level of 130 mg. per-cent. However, it is not possible to infer from the statistics that this is evidence of diabetic control or to observe a significant difference between diabetic clients. (van& Gerber 1976).

3. healing of pressure ulcer and gender

Our study clarifies that there was a significant difference in PUSH score for male and female, which mean the insulin is effective for both male and female since the p-value for it was less than 0.05.there is no statically significant in push score between male and female at day one and day seven, the p-value 0.988 and 0.510. Previous research by Gerber & Van (1979) about topical insulin effectiveness and study of its extraneous variables clarify that gender was a significant factor in the rate of pressure ulcer healing, male patients healed significantly faster than female patients. In El-said et al., (2017) Study on 60 participants with 2nd and 3rd stage of bedsore with 70% of them were female they conclude insulin use is effective in both male and female clients but the difference between gender not studied. In another study on 50 patients with 80% male found the same result in both of them but searching of deference between them was not included (Stephen et al., 2016). A study conduct on 44 patients including 50% males and 50% clarify it was effective to use insulin in both male and female patients but the difference between them was not clarified (Ebrahimifard et al., 2015), As same as that article applied to both male and female gender to test effectiveness and safety of using insulin to treat pressure ulcers, they found out it was safe and effective in both of them without clarifying difference between gender (Valentini et al., 2015; Zhou et al., 2001; van & Gerber 1976; joseph, 1930). another did not mention how many males or females participated but they found topical insulin safe

and accelerated wound healing in chronic ulcers without any side effect and reduced length of hospital staying. (Goenka et al., 2014).

4. random blood sugar in the first day & seventh day before insulin intake and two hours after insulin intake

To test safety we check random blood sugar before and after dressing in the experimental group and no one become hypoglycemic after doing that in all experimental cases, and we analyze data for two days, on day one and day seven if there is a significant difference in random blood before insulin intake related to two hours after insulin intake, the random blood sugar values in the first day before insulin intake was (142±38.2) whereas after insulin intake was (139.6±41.8) which was statistically non-significant (p=0.580), in day seven the random blood sugar values before insulin intake was (134.7±37.6) whereas after insulin intake was (135.7±37.1) which was statistically non-significant (p=0.758).In our study we found that no statically significant push score between patients with diabetes and patients without diabetes at day one and at day seven, Our results are inconsistent with many articles that we found research assesses the safety of topical insulin(1 U/cm2 wound area) by check blood glucose levels with a glucometer 10 minutes before and 1 hour after the topical insulin application in the insulin group total of 350 reads of blood glucose level was obtained, Mean blood glucose levels (mg/dL) before and after intervention were 130.62 ± 24.94 and 128.82 ± 25.14, respectively. Paired t-test confirm that a slight decrease in blood glucose was not significant (P >0.05), no one of the clients in the insulin group developed

hypoglycemia (Stephen et al., 2016). but in El-said et al., (2017), to check the safety of topical insulin use, the random blood sugar results in 1st day as an example before dressing was (190±78.7) whereas after the dressing was (177.2±67.7) which was statistically significant (p=0.050) but no read of hypoglycemia recorded, on the second day, there was no significant difference in random blood glucose levels before and after dressing. The same In one study, half of the patients had diabetes., Fasting blood sugar and (HBA1C) glycosylated hemoglobin were measured in both groups to assess the effect of insulin on blood glucose and to compare its effect on wound healing in patients with and without diabetes after insulin administration. Blood glucose was measured twice on the first day and once on the second day, which revealed no hypoglycemia. (Ebrahimifard et al., 2015). No significant adverse reactions were observed, and no one had adverse systemic effects such as hypoglycemia, headache, or vertigo. The blood sugar level before dressing was 119.3+/–40.1 mg/dl, whereas after the dressing was 120+/–39.7 mg/dl in insulin dressing, which was comparable and statistically not significant. (Goenka et al., 2014). The topical insulin use had been assessed as part of the risk assessment analysis on a sample of non-diabetic clients by monitoring blood sugar levels four times per day to assess whether the topical insulin caused the hypoglycemic effect, and it confirmed that there was no significant difference among both blood sugar levels and all patients analyzed.. (Valentini et al., 2015)others do that for the experimental group they were measuring blood sugar level before insulin dressing and mealtime to avoid as they mention ‘absorption of insulin through the ulcer’ then two hours after dressing end blood sugar

measured again, as a result of that they found that no significant defiance observed between the healing of pressure ulcer and diabetes mellitus (Gerber & Van 1979). In Van & Gerber (1976) none of the experimental group who received topical insulin developed allergic reaction or hypoglycemia it would appear that topical insulin use overpressure ulcers is not absorbed systemically but they mention that, they can't say that conclusively because they encourage clients to eat after dressing with topical insulin.

4.3 Conclusion

Our results of this trial on 62 participants of human beings with 2ndor 3rdstage pressure ulcers with 53% of them were female, 46.5% of all of them had diabetes, with a median for the age was 55.55 years, indicate that insulin is an effective and safe to use topically over pressure ulces, that will facilitate pressure ulcer healing when compared to the group didn't take insulin. During seven days of research, statistically significant differences in wound size and PUSH score were observed between the controlled group (didn't take insulin) and experimental group (take insulin), and by the way, there is no statically significant push score between patients with diabetes and patients without diabetes and there is no statically significant in push score between male and female and the random blood sugar before insulin intake related to two hours after insulin intake was statistically non-significant.

4.4 Limitation

1. The lack of capacity for ICU patients in the hospital in which the research was conducted

2. The doctor was late in writing the medical order and the length of the period before the procedure was taking a lot of time before the intervention was performed.

4.5 Recommendation

1. Assessment of patients' skin from the moment they enter the hospital using assessment tools and risk monitoring models such as push score and Braden scale

2. Increasing the awareness and knowledge of the medical staff, especially the nursing staff, of the importance of evaluating ulcers and how to deal with them and treating them, and conducting continuous awareness seminars.

3. Recommendation of using topical insulin dressing for patients with Pressure ulcer typ2 and 3.

4. Increasing the awareness and knowledge of adequate nutrition for the prevention of pressure ulcers.

5. Application in large communities from different countries.

6. Application on pediatric patients with pressure ulcers.

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Appendices

Annex (1) Consent form

نموذج طلب موافقة على المشاركة في بحث علمي

عنوان الدراسة: تقييم الاستخدام الموضعي للانسولين لشفاء القرحة الجلدية لدى المرضى في اقسام العناية الحثيثة باستخدام التجربة المنضبطة العشوائية.

اسم الباحث الرئيسي: وفاء قيسي

المشرفين على البحث: د. إيمان الشاويش(مشرفاً اكاديمياً).

المشاركين في البحث: ابراهيم غول

ملخص البحث: نقوم بهذه الدراسة استيفاء لمتطلبات التخرج من برنامج ماجستير العناية المكثفة للتمريض في جامعة النجاح الوطنية وهي دراسة سريرية لاستخدام الأنسولين الموضعي على التقرحات الجلدية ويتم مراقبة التقرحات يوميا ويتم التغير عن القرحة مرتين في اليوم ويتم متابعة نسبة السكري للتأكد من عدم تأثره.

معلومات عن العينة المنتقاة والفترة الزمنية المقدرة لاستكمال المقابلة أو الاستبيان:

تم اختيار فئة المرضى الذين لديهم تقرحات من الدرجة الثانية الى الدرجة الثالثة، وستبدأ الدراسة من لحظة دخول المشارك الى المستشفى وصولا الى خروجه من المستشفى.

المخاطر المتوقعة والخصوصية:

ليست هنالك اي مخاطر للدراسة سواء نفسية ام جسدية, سيتم حفظ خصوصيتك كمشارك بالدراسة وسوف يتم التكتم على هويتك وسيبقى اسمك طي الكتمان والمكان الوحيد الذي سيتم ذكر اسمك فيه هو نموذج الموافقة على المشاركة في الدراسة. سوف يتم التعامل مع العينة والمعلومات الخاصة بك

بطريقة الترميز حماية لخصوصيتك، ويحق لك الانسحاب من البحث متى شئت من دون أن يأثر ذلك عليك او على الرعاية الطبية التي سوف تتلقينها.

المنافع المتوقعة:

استخدام الانسولين الموضعي يزيد من احتمالية التئام التقرحات ويحد من نسب حدوث المضاعفاتوزيادة درجة التقرح .

طريقة التواصل مع الباحث:

إذا كانت لديك اي سؤال او استسفار عن الدراسة يمكنك التواصل مع الباحث (وفاء قيسي) بكل رحابة وفي اي وقت عن طريق (الهاتف:0569045318)أو
البريدالإلكتروني(wafaa.qaysi123@gmail.com)

توقيع المشاركة في البحث:

لقد حصلت على شرح مفصل عن الدراسة وأهدافها وإجراءاتها، ومنافعها، والمخاطر المحتملة. ولقد فهمت كافة المعلومات التي قدمت لي وتمت الإجابة كل أسئلتي. لذا فأنني أوافق وبمحض ارادتي على ألمشاركة في هذه الدراسة.

الاسم:.....

التوقيع:.....

التاريخ:.....

Annex (2) Data Collecting Sheet

Tool I: Socio-demographic data

ToolII: Medical data sheet

Date of admission								
Patient diagnosis								
Past medical and surgical history								
	Day 1	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**	**Day 7**	**Day 8**
Braden Scale Score		***		***		***		***
degree of bedsores		***	***	***	***	***	***	
using pressure relieving devices and types of them								

day	**random blood sugar level**

Socio-demographic data	
Initial litters of patient name	
Randomly number	
Age	
Sex	

	Before	**After 2 h**	**Before**	**After 2 h**
1				
2				
3				
4				
5				
6				
7				

<u>ToolIII</u>: Pressure Ulcer Scale for Healing (PUSH Tool)

Pressure Ulcer Scale for Healing (PUSH Tool)				
Day	LENGTH x WIDTH	EXUDATE AMOUNT	TISSUE TYPE	TOTAL PUSH Score
1 (Before intervention)				
7 (After intervention)				

Annex (3) PUSH Tool

NATIONAL PRESSURE ULCER ADVISORY PANEL

Pressure Ulcer Scale for Healing (PUSH)
PUSH Tool 3.0

Patient Name_____ Patient ID# _____

Ulcer Location _____ Date _____

Directions:
Observe and measure the pressure ulcer. Categorize the ulcer with respect to surface area, exudate, and type of wound tissue. Record a sub-score for each of these ulcer characteristics. Add the sub-scores to obtain the total score. A comparison of total scores measured over time provides an indication of the improvement or deterioration in pressure ulcer healing.

LENGTH X WIDTH (in cm²)	**0** 0	**1** < 0.3	**2** 0.3 – 0.6	**3** 0.7 – 1.0	**4** 1.1 – 2.0	**5** 2.1 – 3.0	Sub-score
		6 3.1 – 4.0	**7** 4.1 – 8.0	**8** 8.1 – 12.0	**9** 12.1 – 24.0	**10** > 24.0	
EXUDATE AMOUNT	**0** None	**1** Light	**2** Moderate	**3** Heavy			Sub-score
TISSUE TYPE	**0** Closed	**1** Epithelial Tissue	**2** Granulation Tissue	**3** Slough	**4** Necrotic Tissue		Sub-score
							TOTAL SCORE

Length x Width: Measure the greatest length (head to toe) and the greatest width (side to side) using a centimeter ruler. Multiply these two measurements (length x width) to obtain an estimate of surface area in square centimeters (cm²). Caveat: Do not guess! Always use a centimeter ruler and always use the same method each time the ulcer is measured.

Exudate Amount: Estimate the amount of exudate (drainage) present after removal of the dressing and before applying any topical agent to the ulcer. Estimate the exudate (drainage) as none, light, moderate, or heavy.

Tissue Type: This refers to the types of tissue that are present in the wound (ulcer) bed. Score as a "4" if there is any necrotic tissue present. Score as a "3" if there is any amount of slough present and necrotic tissue is absent. Score as a "2" if the wound is clean and contains granulation tissue. A superficial wound that is reepithelializing is scored as a "1". When the wound is closed, score as a "0".

- **4 – Necrotic Tissue (Eschar):** black, brown, or tan tissue that adheres firmly to the wound bed or ulcer edges and may be either firmer or softer than surrounding skin.
- **3 – Slough:** yellow or white tissue that adheres to the ulcer bed in strings or thick clumps, or is mucinous.
- **2 – Granulation Tissue:** pink or beefy red tissue with a shiny, moist, granular appearance.
- **1 – Epithelial Tissue:** for superficial ulcers, new pink or shiny tissue (skin) that grows in from the edges or as islands on the ulcer surface.
- **0 – Closed/Resurfaced:** the wound is completely covered with epithelium (new skin).

(Thomas et al., 1997)

Annex (4) Braden scale

RISK FACTOR	SCORE / DESCRIPTION			
SENSORY PERCEPTION Ability to respond meaningfully to pressure-related discomfort	**1.COMPLETELY LIMITED** – Unresponsive (does not moan, flinch, or grasp) to painful stimuli, due to diminished level of consciousness or sedation, **OR** limited ability to feel pain over most of body surface.	**2. VERY LIMITED** – Responds only to painful stimuli. Cannot communicate discomfort except by moaning or restlessness, **OR** has a sensory impairment, which limits the ability to feel pain or discomfort over ½ of body.	**3. SLIGHTLY LIMITED** – Responds to verbal commands but cannot always communicate discomfort or need to be turned, **OR** has some sensory impairment which limits ability to feel pain or discomfort in 1 or 2 extremities.	**4. NO IMPAIRMENT** – Responds to verbal commands. Has no sensory deficit, which would limit ability to feel or voice pain or discomfort.
MOISTURE Degree to which skin is exposed to moisture	**1.CONSTANTLY MOIST**– Skin is kept moist almost constantly by perspiration, urine, etc. Dampness is detected every time patient is moved or turned.	**2. OFTEN MOIST** – Skin is often but not always moist. Linen must be changed at least once a shift.	**3.OCCASIONALLY MOIST** – Skin is occasionally moist, requiring an extra linen change approximately once a day.	**4. RARELY MOIST** – Skin is usually dry; linen only requires changing at routine intervals.
ACTIVITY Degree of physical activity	**1. BEDFAST** – Confined to bed.	**2. CHAIRFAST** – Ability to walk severely limited or nonexistent. Cannot bear own weight and/or must be assisted into chair or wheelchair.	**3. WALKS OCCASIONALLY** – Walks occasionally during day, but for very short distances, with or without assistance. Spends majority of each shift in bed or chair.	**4. WALKS FREQUENTLY**– Walks outside the room at least twice a day and inside room at least once every 2 hours during waking hours.
MOBILITY Ability to change and control body position	**1. COMPLETELY IMMOBILE** – Does not make even slight changes in body or extremity position without assistance.	**2. VERY LIMITED** – Makes occasional slight changes in body or extremity position but unable to make frequent or significant changes independently.	**3. SLIGHTLY LIMITED** – Makes frequent though slight changes in body or extremity position independently.	**4. NO LIMITATIONS** – Makes major and frequent changes in position without assistance.
NUTRITION Usual food intake pattern 1NPO: Nothing by mouth. 2IV: Intravenously. 3TPN: Total parenteral nutrition.	**1. VERY POOR** – Never eats a complete meal. Rarely eats more than 1/3 of any food offered. Eats 2 servings or less of protein (meat or dairy products) per day. Takes fluids poorly. Does not take a liquid dietary supplement, **OR** is NPO1 and/or maintained on clear liquids or IV2 for more than 5 days.	**2. PROBABLY INADEQUATE** – Rarely eats a complete meal and generally eats only about ½ of any food offered. Protein intake includes only 3 servings of meat or dairy products per day. Occasionally will take a dietary supplement **OR** receives less than optimum amount of liquid diet or tube feeding.	**3. ADEQUATE** – Eats over half of most meals. Eats a total of 4 servings of protein (meat, dairy products) each day. Occasionally refuses a meal, but will usually take a supplement if offered, **OR** is on a tube feeding or TPN3 regimen, which probably meets most of nutritional needs.	**4. EXCELLENT** – Eats most of every meal. Never refuses a meal. Usually eats a total of 4 or more servings of meat and dairy products. Occasionally eats between meals. Does not require supplementation.
FRICTION AND SHEAR	**1. PROBLEM**- Requires moderate to maximum assistance in moving. Complete lifting without sliding against sheets is impossible. Frequently slides down in bed or chair, requiring frequent repositioning with maximum assistance. Spasticity, contractures, or agitation leads to almost constant friction.	**2. POTENTIAL PROBLEM** – Moves feebly or requires minimum assistance. During a move, skin probably slides to some extent against sheets, chair, restraints, or other devices. Maintains relatively good position in chair or bed most of the time but occasionally slides down.	**3. NO APPARENT PROBLEM** – Moves in bed and in chair independently and has sufficient muscle strength to lift up completely during move. Maintains good position in bed or chair at all times.	

(Bergstrom&Braden, 1998)

Annex (5) IRB

An-Najah
National University
Health Faculty of medicine&
Sciences
IRB

جامعة النجاح
الوطنية
كلية الطب وعلوم الصحة
لجنة اخلاقيات البحث العلمي

Ref :Mas July /2020/18

IRB Approval Letter

Study Title:

"Effectiveness of Using Topical Insulin on Healing Of Pressure Ulcers among intensive care unit patients: A prospective observational study".

Submitted by:
Wafaa Qaysi

Supervisor:
Eman Alshawish, Abdelkarim Barqawi

Date Approved:
22nd July 2020

Your Study Title **"Effectiveness of Using Topical Insulin on Healing Of Pressure Ulcers among intensive care unit patients: A prospective observational study".** was reviewed by An-Najah National University IRB committee and was approved on **22nd July 2020**

Hasan Fitian, MD

IRB

IRB Committee Chairman
An-Najah National University

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جامعة النجاح الوطنية

كلية الدراسات العليا

تقييم الاستخدام الموضعي للأنسولين لشفاء القرحة الجلدية لدى المرضى في اقسام العناية الحثيثة باستخدام التجربة المنضبطة العشوائية

إعداد

وفاء قيسي

إشراف

د. إيمان الشاويش

قدمت هذه الاطروحة استكمالاً لمتطلبات الحصول على درجة الماجستير في برنامج تمريض العناية المكثفة، من كلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس- فلسطين.

2021

تقييم الاستخدام الموضعي للانسولين لشفاء القرحة الجلدية لدى المرضى في اقسام العناية الحثيثة باستخدام التجربة المنضبطة العشوائية

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الملخص

الخلفية والأهداف: تعد قرحة الضغط من أكبر التحديات والمشكلات التي تواجه النظام الصحي في المؤسسات، وتسبب عبئًا كبيرا على كل من المريض ونظام الرعاية الصحية، وتتمثل عملية علاج قرحة الضغط في نقاط عديدة ومتنوعة وتتضمن الكثير من الاستراتيجيات، وبالتالي فإن الهدف من هذه الدراسة هو التحقق من فاعلية تطبيق العلاج الموضعي بالأنسولين لتحسين التئام قرح الضغط في مرضى وحدة العناية المركزة في مستشفى جامعة النجاح الوطنية.

الطريقة: تم إجراء تصميم بحث تجريبي حقيقي في وحدات العناية المركزة في مستشفى جامعة النجاح الوطنية. تكونت عينة هذه الدراسة من 62 مريضاً مقسمة إلى مجموعتين متساويتين. مجموعة الدراسة الذين يتلقون ضمادات الأنسولين الموضعية ومجموعة المراقبة الذين يتلقون الضمادات الروتينية في المستشفى. معايير الاشتمال للمجموعتين هي المرضى الذين تتراوح أعمارهم بين 18–70 سنة، كلا الجنسين، قرحة الضغط ذو المرحلة 2 و 3، وحجم الجرح أقل من 10 سم 2. ومعايير الاستبعاد للمجموعتين هي المرضى الذين تقل أعمارهم عن 18 عامًا وأكثر من 70 عامًا، وقرح الضغط ذات الدرجة الأولى والرابعة والغير قابلة للتحديد، والمرضى الذين يعانون من حساسية الأنسولين، وأمراض الأوعية الدموية، ونقص المناعة، والحمل، والتهاب العظم، قرح الدوالي والحروق، مرضى نقص الضغط، المرضى الذين لديهم مستويات هيموجلوبين أقل من 12.0 جم / ديسيلتر.

النتائج: تحسن أكثر أهمية في التئام قرحة الضغط لمجموعة الأنسولين مقارنة بمجموعة التحكم بقيمة($p <0.05$)، لا توجد ذات دلالة إحصائية في مقياس ضغط القرحة للشفاء بين مرضى السكري وغير المصابين بالسكري، لا يوجد دلالة إحصائية في النتيجة بين الذكور والإناث، لم تكن نسبة السكر في الدم العشوائية قبل وضع الأنسولين بساعتين وبعد وضع الأنسولين ذات دلالة إحصائية، والتُقطت صور قرحة الضغط للمشاركين في المجموعة التجريبية في اليوم الأول قبل واستخدام الضمادات وفي اليوم السابع بعد استخدام ضماد الأنسولين الموضعي الذي قدم الدليل لتحسين التئام قرحة الضغط.

الخلاصة: استخدام الأنسولين الموضعي آمن وفعال لتسريع التئام قرحة الضغط ذات الدرجة 2 و3.

التوصيات: نوصي باستخدام ضمادات الأنسولين الموضعية للمرضى الذين يعانون من قرحة الضغط ذات الدرجة 2 و 3، وتقييم جلد المرضى من لحظة دخولهم المستشفى باستخدام أدوات التقييم ونماذج مراقبة المخاطر، وزيادة الوعي والمعرفة للوقاية من قرحة الضغط، إجراء مزيد من الدراسات وتطبيق ضمادات الأنسولين الموضعية للأطفال المصابين بقرحة الضغط وتطبيقها على مجتمع اوسع واكبر.

الكلمات المفتاحية: الأنسولين، الأنسولين الموضعي، قرحة الضغط، قرحة الفراش، قرحة الاستلقاء، الاستلقاء والجرح المزمن.