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Use of Topical Insulin vs Placebo for reducing Median Sternotomy Complications after Cardiac Surgery in Diabetic Patients

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[1,3]Conceptualized the study, curated the data, visualization, investigations, and methodology, [4,5]analysed the data and did the writing of the original draft, [2]Supervised the project ,Literature review

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A B S T R A C T

Objective To assess the potential benefits of adding topical insulin to standard postoperative care in diabetic patients undergoing cardiac surgery.

Methodology: A quasi-experimental study was conducted in the Department of Cardiac Surgery, Cardiac Center, Pakistan Institute of Medical Sciences, Islamabad from 01-6-2022 to 30-5-2023. Patients in the intervention group received a spray consisting of 1 cc of 0.9% saline mixed with 10 units (0.1 cc) of insulin per 10 cm^2 of the wound area during sternal closure. This topical application on the wound was continued twice daily for 30 days postoperatively. The control group received standard of care sternal closure and treatment. Patients were monitored for 30 days following surgery. Primary outcomes included wound healing, the occurrence of deep and superficial infections and hospital re-admissions within the 30-day period.

Results: Mean age of patients in insulin treated and control group was 59.31±6.16 years vs 59.82±6.17 years (p=0.683). Although not statistically significant, the Insulin treated patients showed better results as compared to the control group with reduced sternal wound infections (2.0% vs 8.2%, p=0.168), less delayed healing (6.1% vs 14.3%, p=0.182) and lower readmissions (4.1% vs 6.1%, p=0.646).

Conclusion: The application of topical insulin to median sternotomy wounds in diabetic patients showed improved results with better healing and reduced complications within the 30-day postoperative period.

Keywords: Cardiac Surgical Procedures; Coronary Artery Bypass; Insulin; Wound healing.

Introduction

Median sternotomy is regarded as the gold standard incision technique, offering low rates of complications and excellent long-term outcomes in cardiac surgical procedures. Deep sternal wound infections are common post-surgical complications in these patients however, the overall incidence of complications is quite low.[1] The 4-year survival rate was higher (more than 80%) in people who had no complications post sternotomy as compared to those with complications post procedure.[2] Deep sternal wound infections have been observed in about 0.5 to 3% cases after their sternal surgery procedures. Sternal surgical site wound infections can either be deep or superficial infections. Some risk factors have been identified that contribute to the post cardiac surgery/sternotomy related complications like use of steroids, elderly individuals, cigarette smoking and diabetes.[3] Wound healing time is an important entity that predicts the success rate of surgery, as delayed wound healing is associated with increased risk of developing complications. Delayed wound healing is affected by various factors like infections, which affects the quality of life and increase the overall cost of healthcare.[4] Insulin can be administered into the LIMA (left internal mammary artery) bed to promote neovascularization and accelerate the healing process, thereby reducing the risk of deep sternal wound infections, sternal dehiscence, and the need for re-operation due to postoperative complications. The administration of topical insulin has been found to be quite effective in accelerating the wound healing by many ways including neovascularization and wound remodeling via cytokines.[5,6] Median sternotomy is being used for both cardiac as well as the non-cardiac procedures. It is also considered as an emergency procedure for major mediastinal bleeds.

Deep sternal wound infections can be prevented or reduced in multiple ways. Early detection is the key step in management with surgical debridement and using muscular flaps can improve the outcomes and healing process.[7] External fixation corsets have been used post sternotomy and showed reduced incidence of deep wound infections.[8] It is crucial for the cardiac surgeon to recognize the symptoms of deep sternal wound infections which commonly includes fever,

elevated leukocyte count, sternal click and purulent discharge from the wound site.[9]

As a growth factor and peptide hormone, insulin promotes the repair of epidermal injuries. Its cost-effectiveness also makes it an attractive option for incorporation into wound dressings to accelerate the healing process. While systemic insulin therapy has been shown to enhance wound healing and reduce postoperative infections in diabetic patients, it carries the risk of adverse effects such as hypoglycemia and hypokalemia hence the topical route is preferable. Some recent advancements like use of nanotechnology-based insulin delivery systems have improved the desired amount delivery of topical Insulin at wound site thus promoting quick healing with minimal side effects.[10] The safety profile of topical Insulin is excellent when used for wound healing, no serious adverse effects are seen.[11] In topical application over a wound, Insulin promotes healing via fibroblast proliferation, keratinocytes stimulation and angiogenic actions. The main purpose of this study was to compare the complications associated with topical insulin versus the standard technique following median sternotomy over a 30-day period in our population.

Methodology

This quasi-experimental study was conducted at the department of Cardiac surgery, Cardiac Center, Pakistan Institute of Medical Sciences (PIMS) Hospital, Islamabad from 01-6-2022 to 30-5-2023 after ethical approval from the Ethical Review Board (ERB) of Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, Pakistan (Ref No. F.1-1/2015/ERB/SZABMU/931 dated 31-01-2022).

A total of 98 diabetic patients aged 45–72 years undergoing cardiac surgery through median sternotomy were enrolled using non-probability consecutive sampling and the alternate allocation method for grouping. The sample size was determined using the WHO sample size calculator, considering a 5% significance level, 80% study power, and a population standard deviation of 1.3. The anticipated reduction in wound diameter was estimated at 7.15 mm in the topical insulin group (P1) and 7.89 mm in the control group (P2). Those, who were active smokers, taking steroids, had chronic lung disease or osteoporosis were excluded from the study. Written Informed consent was obtained from all the participants before the start of the study. Cardiac surgery was done as per protocol and the wounds were closed in layers using absorbable sutures and then dressed with steri-strips, gauze, and paper tape. In addition, the study group received a spray of 1 cc of 0.9% saline per 10 cm^2 of wound area, combined with 10 units (0.1 cc) of insulin applied to the sternum and surrounding soft tissue during sternal closure. This insulin-saline spray was also applied topically to the wound twice daily following surgery. Primary outcome was measured as frequency of sternal wound complications in terms of delayed healing, superficial infection, deep infections and readmission rate including mediastinitis in 30-day period post-surgery.

Data were entered and analyzed using SPSS version 23. Qualitative variables such as sex, superficial wound infection (SWI), deep sternal wound infection (DSWI), delayed wound healing, and readmission were presented as frequency distributions. Quantitative variables, including age and cost, were expressed as means with standard deviations. The chi-square test was used to compare the incidence of SWI, DSWI, and delayed wound healing between the two groups. A *p*-value of less than 0.05 was considered statistically significant for all analyses.

Results

A total of 98 patients were enrolled in the study, with 49 patients assigned to each group. The mean age in the study group was 59.31 ± 6.16 years, while in the control group it was 59.82 ± 6.17 years ($p = 0.683$). Table 1 shows the male-female distribution of cases in the study and control groups indicating comparable gender distribution between the two groups ($p=0.541$).

Table I: Gender distribution in study and control groups

Gender	Groups		Total n (%)	*p*-value
	Study Group n (%)	Control Group n (%)		
Male	26 (53.1%)	29 (59.2)	55	0.541
Female	23 (46.9%)	20 (40.8%)	43	
Total	100.0%	100.0%		

Table II: Distribution of wound-related complications in study and control group.

Wound		Groups n (%)		Total	*p*-value
		Study Group	Control Group		
DWSI	Yes	00	02 (4.1)	02 (2.0)	0.153
	No	49 (100)	47 (95.9)	96 (98.0)	
SWI	Yes	01 (2.0)	04 (8.2)	05 ()	0.168
	No	48 ()	45 ()	93 ()	
Delayed WH	Yes	3 ()	7 ()	10 ()	0.182
	No	46 ()	42 ()	88 ()	
Total					

No cases of Deep Sternal Wound Infection (DSWI) were reported in the study group, compared to 2 cases (4.1%) in the control group (p=0.153). Superficial Wound Infection (SWI) was observed in 1 patient (2.0%) in the study group and 4 patients (8.2%) in the control group (p=0.168). Delayed Wound Healing occurred in 3 patients (6.1%) in the study group versus 7 patients (14.3%) in the control group (p=0.182). Although none of the differences were statistically significant, the study group receiving topical insulin demonstrated a trend toward improved outcomes in both primary and secondary endpoints compared to the control group (Table II).

Discussion

Sternal wound infections are the most commonly observed complications after median sternotomy procedures done for cardiac surgery. They are not only associated with increased morbidity and mortality, but the overall cost of treatment is also increased including the length of hospital stay. This study was conducted to see the effects of topical insulin in wound healing in people undergoing cardiac surgery. The results showed that topical Insulin is slightly more effective when considering the wound healing including the development of deep sternal wound infections and time of wound healing. Although the results were not statistically significant, the analysis of study results revealed a trend towards better outcome in patients who received topical insulin when compared with the control group.

As prevention is always better than treatment, strategies should be devised to minimize the risk of complications particularly wound infections after the procedure. A study conducted in Islamabad revealed that topical Insulin is quite effective in wound healing and repair.[12] Insulin- soaked dressings have been found to be more effective compared with conventional dressing in treating diabetic foot wounds with reduced duration of wound healing[13] indicative of the beneficial effects of topical insulin in wound care. Topical Insulin has been found to be effective in promoting wound healing in diabetics.[14] Wound healing and post-operative complications after sternal surgical procedures are more frequent in diabetic individuals.[15]

Nutrition, rigid sternal fixation and good pre/post-operative hospital care can reduce the risk of complications after cardiac surgery.[16] Topical Insulin has already been used and has a proven efficacy in the treatment of diabetic foot ulcers,[17] which suggests its potential role in wound healing. Deep sternal wounds and mediastinitis are the common and serious post-operative complications in patients undergoing sternotomy and they pose a significant health burden. Orlandi and colleagues conducted a microcosting analysis on deep sternal wound infections after coronary surgery and showed that DSWIs increased the cost of health care by more than 150%.[18] Topical Insulin has been found to improve the wound healing in diabetics by its anti-inflammatory properties.[19,20] Some of the most important limitations regarding the use of topical insulin included the stability of peptide and sterility of the medication.[21] There are some other factors affecting the wound healing post operatively in cardiac surgery patients like appropriate topical antibiotics, early initiation of broad spectrum cephalosporins, patients with Methicillin resistant Staphylococcus Aureus wounds,[22] but these factors were not studied in the present study. A recent comparative study conducted in India also showed good efficacy of Topical Insulin in wound healing.[23] Ramirez-GarciaLuna et al. in a systematic review and meta-analysis assessing the safety and effectiveness of local insulin concluded that its use improves wound healing without any side effects,[24] a finding similar to this study.

LIMITATIONS: This study had few limitations. It was a single center study with a relatively smaller sample size therefore a multi-centre study with a larger sample is recommended to validate the findings of this study. The effects of possible confounders affecting wound healing like duration of surgical procedure, BMI, HBA1C, antibiotic selection and glycemic control, were not studied. As diabetes delays wound healing after surgery, so further studies should be done preferably in both diabetics and non-diabetics.

Conclusion

Application of topical Insulin on wounds post-operatively can be useful in improving wound healing in diabetic patients undergoing sternotomy.

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