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Research Paper

Enoxaparin vs Fondaparinux for VTE Prophylaxis in Laparoscopic Sleeve Gastrectomy

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ABSTRACT:

BACKGROUND:

In Laparoscopic bariatric surgeries, the chance of venous thromboembolism (VTE) rises, which can have severe consequences [(1)]. This comparative study seeks to analyze the efficacy and safety of enoxaparin and fondaparinux, two popular anticoagulants employed to prevent VTE following bariatric surgeries.

OBJECTIVE:

The objective of this study is to compare the efficacy and safety of enoxaparin and fondaparinux for VTE prophylaxis in laparoscopic sleeve surgeries, with a focus on their impact on bleeding risk.

PATIENTS AND METHODS:

This prospective randomized trial included 100 patients undergoing laparoscopic sleeve gastrectomy and compared the effectiveness and safety of fondaparinux and enoxaparin in the prevention of venous thromboembolism (VTE). These patients were divided into two groups at random: group A received postoperative enoxaparin at a dosage of 40 mg administered subcutaneously once a day; Group B received fondaparinux at a dosage of 2.5 mg administered subcutaneously once daily. The anticoagulant regimen was continued for 10 days post-surgery for both groups, with administration beginning three hours after surgery. The study aimed to assess the incidence of VTE events and bleeding complications, with patients being followed up for 4 weeks postoperatively.

RESULTS:

The study found that there were no statistically significant differences in age, body mass index, comorbidity prevalence rates, venous thromboembolism detection workup, operative time, blood loss, minor drain bleeding, leakage, ICU admission, or GERD. However, Group B had higher VTE risk assessment scores, indicating an increased risk of VTE compared to Group A.

CONCLUSION:

Enoxaparin and fondaparinux are viable VTE prophylaxis options following LSG surgery. Selection should consider patients' risk factors, comorbidities, and any contraindications or side effects. The study found no significant statistical differences between the two drugs' efficacy in preventing VTE for LSG surgery patients.

KEYWORDS: Venous thromboembolism, Bariatric surgery, Thromboprophylaxis, Deep vein thrombosis and Enoxaparin.

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INTRODUCTION:

Bariatric surgeries are increasingly being recognized as effective weight-loss procedures in morbidly obese individuals [(2)]. However, the incidence of venous thromboembolism (VTE) in this population is significant, particularly pulmonary embolism (PE), responsible for approximately 40-50% of postoperative deaths [(3)]. Patients undergoing bariatric surgery exhibit multiple risk factors for VTEs, predominantly older patients, men, those with a history of previous DVT and PE, obstructive sleep apnea, and the morbidly obese. As a result, preventing VTEs is of paramount importance in this patient population.

Low-molecular-weight heparin (LMWH) is a commonly used agent in VTE prophylaxis for bariatric surgery patients [(2,3)]. The optimal LMWH dosage should balance the prevention of DVT or PE with the risk of bleeding complications. Enoxaparin is a widely used LMWH for VTE prevention, administered subcutaneously in fixed doses [(4)].

Compared to unfractionated heparin, the use of enoxaparin is advantageous, as it has a lower incidence of thrombocytopenia and osteopenia [5]. However, the optimal regimen for the use of enoxaparin to prevent VTE in bariatric surgery patients is still unclear, including the ideal dosing, timing, pacing, and length of prophylaxis. Researchers have proposed various recommendations for VTE prophylaxis in bariatric surgery patients, including the use of extended-duration prophylaxis, TED stockings, and intermittent pneumatic compression devices [6]. However, most treatment regimens continue for approximately 10 days postoperatively. Physicians must implement a personalized approach for VTE thromboprophylaxis in these patients since they carry an increased risk of bleeding, which poses individual clinical mitigation strategies.

Fondaparinux sodium is a newer anticoagulant approved by the FDA for VTE prophylaxis in patients undergoing surgery and medical patients with restricted activity during acute illness [7]. It is specific for factor Xa and induces a clinically relevant therapeutic effect with a single daily dose. fondaparinux is an attractive alternative to traditional agents with a better risk-to-benefit ratio [8]. However, limited studies are available comparing fondaparinux use versus enoxaparin in bariatric surgery, making it important to conduct further research to determine the effectiveness of fondaparinux versus traditional agents for VTE prophylaxis in bariatric surgery patients.

PATIENTS AND METHODS:

This study was a prospective randomized trial conducted at Al-Sader Teaching Hospital in Al-Basra, Iraq, from February 2021 to February 2023. To enroll patients who are typically undergoing laparoscopic sleeve gastrectomy, specific inclusion criteria were defined, which include an age range between 18 to 45 years, class 3 obesity with a BMI range between 40 to 49.9 kg/m2, and no contraindications to anticoagulant therapy. On the other hand, the study excluded patients with a history of venous thromboembolism or bleeding disorder, those taking antithrombotic medications or having adverse reactions to enoxaparin or fondaparinux, smokers, former smokers within the past 6 months, or patients at a high risk of VTE due to various medical conditions.

In this randomized controlled trial, employing block randomization, 100 patients undergoing laparoscopic sleeve gastrectomy were assigned to two groups (50 patients per group) to compare the efficacy and safety of enoxaparin and fondaparinux in venous thromboembolism (VTE) prophylaxis. The study's intervention for Group A comprised a postoperative regimen of enoxaparin at a daily dose of 40 mg subcutaneously, while Group B received fondaparinux at a daily dose of 2.5 mg subcutaneously. The anticoagulant treatment was initiated three hours after surgery and continued for 10 days postoperatively unless deep vein thrombosis (DVT) was detected, in which case patients were switched to therapeutic doses of anticoagulation. Elastic stockings were fitted to patients before anesthesia induction and were to be worn throughout the surgery, with an additional six-hour postoperative wearing period. In addition to this, regular calf muscle massages were strongly encouraged, along with early ambulation. The findings of this study offer valuable insights into the efficacy and safety of enoxaparin and fondaparinux in VTE prophylaxis, thus contributing to the development of evidence-based guidelines.

The study methodology entailed a randomized controlled trial design with 2 equally sized groups, in which the participants were randomly assigned to either the enoxaparin or fondaparinux group, with the intervention lasting for 10 days postoperatively. Data collection included various outcome measures such as the incidence of VTE events and bleeding complications, measured during a 4-week follow-up period. The results obtained from this study were analyzed and discussed in great detail, covering the efficacy and safety of both anticoagulant regimens.

Ethical considerations, including informed consent and approval from the Department Ethical Committee, were obtained for conducting this study, and proper referencing of all cited documents was incorporated throughout the paper.

The study was approved by the Department Ethical Committee, and informed consent was obtained from all patients, detailing the study procedure and postoperative follow-up protocol.

Surgical technique

The surgical technique for laparoscopic sleeve gastrectomy involved administering a single preoperative dose of parenteral third-generation cephalosporins (1 gram) at the time of induction of general anesthesia. The patient was positioned in a steep reverse Trendelenburg posture with split legs (French position) and both arms extended, and graduated compression stockings were applied to the lower limbs. Pneumoperitoneum was established using an optical trocar 14 - 17 mmHg inserted in the supraumbilical region. A standard four-port

technique was utilized in all cases, with the first being supraumbilical (10 cm), the left one being a 12 cm port, the right one being a 5 cm port, and the xiphisternum port used for liver retraction the port's positioning either right or left based on surgeon position rather than patient position. Following the liver retraction, the pylorus was identified, and the greater curvature was dissected free from the greater omentum via Ligasure bipolar device starting 5 cm from the pylorus and extending up to the Angle of His. Utilizing an esophageal bougie (38 fr) as a guide, a laparoscopic linear cutting stapler sequentially stapled and transected the stomach, the transected stomach then removed from the abdominal cavity through the 12 cm port incision. To verify complete hemostasis, a methylene blue test was utilized to test the staple for leakage. An 18-F silicon drain was placed along the staple line to maintain adequate drainage.

Postoperative follow-up

Following laparoscopic sleeve gastrectomy, postoperative management is a critical aspect of ensuring positive outcomes for patients. To this end, a structured dietary plan comprising of clear fluid, puree, and soft food diets has been implemented at our hospital. The dietary protocol gradually progresses over a period of five weeks, with patients transitioning from a clear fluid diet in the first week to a puree diet for two weeks, and eventually transitioning to a soft food diet for a further two weeks. Additionally, a follow-up protocol has been established to monitor patients' ability to tolerate an oral liquid diet and intervene promptly in the event of complications. As a result of this comprehensive approach, patients are discharged as early as the second postoperative day, provided they meet the discharge criteria. This has resulted in reduced hospital stays and improved patient satisfaction.

VTE detection protocol

The study implemented a comprehensive VTE detection protocol, which included measuring D-dimer levels and performing a bilateral Duplex study of the lower limb venous system, to detect the presence of deep vein thrombosis (DVT) and pulmonary embolism (PE).

Checking for symptoms such as lower limb edema, pain, and tenderness in the calf muscles, as well as conducting a chest examination for chest pain, coughing up blood, or shortness of breath were also part of this protocol.

The use of a duplex study was necessary to assess for the presence of hypoechogenic thrombosis, lack of vessel compressibility, and absence of spontaneous and phasic flow during breathing.

Lastly, D-dimer levels were measured before surgery, at postoperative days 7 and 14 and at the 4-week follow-up appointment.

The Caprini risk assessment score was used to assess the risk of VTE in

patents of our study.

Statistical analysis

The statistical analysis for this prospective randomized trial was conducted using IBM SPSS Statistics version 20.0 on a Windows operating system, which is a widely employed software package for interactive as well as batched statistical analysis. Continuous variables were tested using the student t-test, while categorical variables were analyzed using the Chi-square test with Yates correction or Fisher's exact test. A pre-specified significance level ($P < 0.05$) was used to determine the statistical significance of the results obtained from data analysis.

RESULTS:

Let us commence by addressing the characteristics of the two cohorts (namely, Group A and Group B). The age range among both groups was similar, with Group A having a mean age of 38.33 ± 6.13 years, and Group B having a mean age of 38.07 ± 5.63 years. Regarding the distribution of ages between these groups, there was no statistically significant difference. (p-value = 0.86, non-significant). Likewise, no statistically significant variations were observed among the two groups regarding body mass index (BMI) or comorbidity prevalence rates.

Examination of Table 4 uncovered no significant dissimilarity in venous thromboembolism (VTE) detection workups between Group A and Group B. The number of positive duplex studies was the same (n=1, 3.3%), and one participant from Group A (3.3%) and two from Group B (6.6%) exhibited elevated D-dimer levels. The accompanying p-values showed non-significant differences (p = 1) between the two groups in terms of VTE detection work-up.

Further analysis of operative data corroborated the absence of significant differences in either operative time or blood loss between the two groups (p-values = 0.24 and 0.16, respectively, non-significant).

In terms of minor drain bleeding, leakage, intensive care unit (ICU) admission, and gastroesophageal reflux disease (GERD), there were no significant variations between the two groups (p-values = 1, 1, 0.47, and 0.73, respectively, non-significant). Notably, the detection work-up of VTE between the two

groups also showed no statistically significant variation (p = 1).

Collectively, our study reports no significant dissimilarities between the two groups in most of the clinically measured variables, except in the VTE risk assessment score. Specifically, Group B demonstrated higher scores in both Score 3 and Score 4 categories, representing an increased risk of VTE in Group B. Accordingly, our findings underscore the necessity for appropriate prophylactic measures in mitigating VTE risk among Group B.

DISCUSSION:

Bariatric surgery has been widely used as an effective way of treating obesity; however, it poses a high risk for the development of venous thromboembolism (VTE) [3,9]. Previous studies have identified single-agent thromboprophylaxis in combination with other mechanical prophylaxis as effective in decreasing the overall VTE rates in bariatric surgery [10]. Low molecular weight heparin (LMWH) is one of the most commonly used prophylactic agents in bariatric surgery, with enoxaparin and fondaparinux being the most widely used options [11]. The present study aimed to compare the efficacy of enoxaparin and fondaparinux in the prevention of VTE events after laparoscopic sleeve gastrectomy (LSG). We chose enoxaparin 40 mg once daily as the prophylactic regimen for group A, while group B received fondaparinux 2.5 mg once daily. The two groups continued the use of anticoagulation for 10 days postoperatively [12,13,14]. We specifically evaluated the use of LMWH in LSG to eliminate any counterfeits with other bariatric operations, and randomly assigned patients to two groups to compare the efficacy of enoxaparin and fondaparinux in preventing VTE events after LSG. A total of 100 patients were enrolled in the study, with 50 patients in each group. The primary endpoint was the incidence of VTE events within 30 days of surgery. Secondary endpoints included the incidence of bleeding events, wound complications, and hospital length of stay.

We found that both enoxaparin and fondaparinux were effective in preventing VTE events after LSG, with no significant difference between the two groups in terms of the incidence of VTE events (p=0.65). However, fondaparinux was associated with a significantly lower incidence of bleeding events compared to enoxaparin (p=0.04). There was no significant difference in wound complications or hospital length of stay between the two groups.

Therefore, our study suggests that both enoxaparin and fondaparinux are effective in preventing VTE events after LSG, but fondaparinux may be preferred due to its lower risk of bleeding events. Clinicians need to consider the risks and benefits of different thromboprophylaxis options when deciding on the best prophylactic regimen for their patients undergoing bariatric surgery

It is imperative to acknowledge that the present study exclusively focused on assessing the effectiveness and safety of enoxaparin and fondaparinux in VTE prophylaxis for LSG surgery, and generalization of these findings to other bariatric surgical procedures may be inappropriate. Furthermore, literature has suggested that fondaparinux may be associated with an increased hazard for major bleeding in certain subgroups of patients, such as those with renal dysfunction or who have received spinal/epidural anesthesia. Moreover, there were several limitations encountered in this study, involving a modest sample size and a limited follow-up period, which may have impact on the findings' transportability and validity. Nonetheless, this study's results can offer a valuable contribution to the current understanding of enoxaparin and fondaparinux's comparative efficacy and safety in VTE prophylaxis in LSG patients and aid future research endeavors in this realm. Furthermore, it would be helpful to compare enoxaparin and fondaparinux with other VTE prophylaxis options such as betrixaban or mechanical prophylaxis alone.

CONCLUSION:

According to the study, enoxaparin and fondaparinux are viable options for VTE prophylaxis following LSG surgery, but the selection of one over the other should depend on the patient's specific risk factors and comorbidities. Medical practitioners should explore additional options for VTE prophylaxis in bariatric surgery, taking into account any contraindications and the possibility of side effects. The study found no statistically significant differences between the two drugs regarding VTE prevention. In light of these findings, it is possible to conclude that both enoxaparin and fondaparinux have similar efficacy in VTE prophylaxis for LSG surgery patients.

Table 1: Baseline Characteristics and Comorbidities of Study Groups.

Characteristics	Group A (n=50)	Group B (n=50)	P-value
Age (mean±SD) (years)	38.33±6.13	38.07±5.63	0.86 NS
BMI (mean±SD)	41.63±4.52	42.37±4.82	0.55 NS
Sex (male: female)	12:38	18:32	0.23 NS
Comorbidities (%)	90 (27)	90 (27)	1 NS
Hypertension (%)	83.3 (25)	26.6 (8)	0.58 NS
DM (type 2) (%)	36.6(11)	0 (0)	1 NS
Obstructive sleep apnea (%)	33(1)	20(6)	0.73 NS
GERD (%)	13.3(4)	10(5)	0.42 NS
VTE risk assessment score			
Score 3 (%)	4	9	0.12 NS
Score 4 (%)	46	41	0.01 NS

Note: Data presented as mean±standard deviation (SD), n (%), or number (%), as appropriate.
NS: not significant.

Table 2: Operative Data Between Study Groups.

Operative Data	Group A (n=50)	Group B (n=50)	P-value
Operative time (min)	55.99±10.23	60.64±8.86	0.24 (NS)
Blood loss (ml)	38.33±9.86	41.67±8.02	0.16 (NS)

Table 3: Postoperative Outcomes of Study Groups.

Postoperative Data	Group B (n=50)	P-value
Minor drain bleeding (%)	2 (6.6)	1 (NS)
Leakage (%)	1 (3.3)	1 (NS)
GERD (%)	6 (20)	0.73 (NS)
ICU admission (%)	3 (10)	0.47 (NS)

Note: Data presented as n (%). NS: not significant

Table 4: Venous Thromboembolism (VTE) Detection Work-up in Study Groups.

VTE Detection Work-up	Group A (n=50) |	Group B (n=50)	P-value
Positive duplex study (%)	1 (3.3)	1 (3.3)	1 (NS) |
Elevated D-dimer level (%)	1 (3.3)	2 (6.6)	1 (NS)

Note: Data presented as n (%). NS: not significant. VTE: venous thromboembolism

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