Research Article:

The Effect of Oral Propranolol on Intraoperative Bleeding in Minimally Invasive Gastric Bypass Surgery in Patients Admitted to Rasoul Akram Hospital: A Randomized Clinical Trial

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ABSTRACT

Background: Surgical treatment of patients with morbid obesity is now the most successful way to return to active life and overcome its effects. Complications during surgery still are varied and plentiful. One of the most important of these effects is increased bleeding during surgery, which increases the duration of surgery and possibly the need for reoperation. The use of propranolol in other surgeries has had a beneficial effect in reducing bleeding, a finding that has not yet been investigated in bariatric surgery.

Methods and Materials: In the double-blind study, 82 patients were randomly assigned to two groups receiving propranolol 40 mg or placebo twice daily for one week before surgery. The patients then underwent gastric bypass surgery. The bleeding, the need for hemostasis, and blood loss during surgery were evaluated.

Results: Of the studied patients, 24.4% were male and 75.6% were female. The Mean±SD of BMI in the intervention group was 44.1±4.2 and in the control group was 44.07±3.5 kg/m^2 and no difference was observed between the two groups. The mean number of bleeding was 2.13±0.84 and 2.5±1.03 in the intervention and control groups, respectively, and this difference was statistically significant between the two groups. The time needed for hemostasis in the intervention and control groups was 7.96±3.85 and 9.67±5.01, respectively, which this difference was statistically significant. The type of injury was arterial in 79 patients (96.3%) and venous in 3 patients (3.7%), and no statistically significant difference was seen between the two groups (P=0.967) The mean hemoglobin was 13.6 before surgery and 12.9 after surgery, but there was no significant difference between the level of hemoglobin before and after the surgery.

Conclusion: The results of this study showed that based on the bleeding components in gastric bypass surgery patients, propranolol may be useful for reducing bleeding parameters in gastric bypass surgery.

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ABS ANNALS OF BARIATRIC SURGERY

1. Introduction

Obesity is the second leading preventable cause of death worldwide and surgery is the most definitive and reliable method for treating obesity that is becoming more popular nowadays by introducing minimally invasive (laparoscopic) surgical procedures. Despite different statistics in Iran, the prevalence of obesity is estimated to be 30%. The most common obesity surgeries are gastric banding, sleeve gastrectomy, and gastric bypass, and despite the increasing popularity of sleeve gastrectomy, gastric bypass surgery still remains the gold standard. In this technique, 20-30 cc of the gastric is separated using endo staplers and anastomosed to the jejunum as Roux-en-Y and has both restrictive and malabsorptive properties. One of the relatively common problems with this surgery is staple line bleeding, which not only requires a lot of time during the surgery for acceptable homeostasis but also leads to reoperation to control bleeding. In other surgical procedures, the prophylactic use of propranolol is beneficial in preventing bleeding [1-4]. For instance, Lay et al. in Taiwan demonstrated that this drug can be used conveniently and effectively as vascular ligation and reduced the risk of bleeding in esophageal varices in individuals with liver cirrhosis [5]. Lui et al. in Scotland also found that propranolol is equivalent to ligation and even better than isosorbide mononitrate [6]; however, no study has been conducted to reduce bleeding in gastric bypass surgery. Researchers have only tried to use various artificial and biological staples. For example, Angrisani et al. explained that bovine pericardial staplers reduced bleeding [7]. However, invasive methods have yet been used. We intend to assess the effect of propranolol on intraoperative bleeding in gastric bypass surgery in patients referring to Rasoul Akram Hospital in a clinical trial by combining the above two ideas (reduced intraoperative bleeding in gastric bypass surgery and the use of propranolol).

2. Materials and Methods

In this double-blind placebo-controlled randomized clinical trial, patients (82 patients) who were candidates for gastric bypass surgery were included. The inclusion criteria were patients who were candidates for bypass surgery, Body Mass Index (BMI) above 40 or above 35 with type 2 diabetes, and poorly controlled hypertension, Nonalcoholic Fatty Liver Disease (NAFLD), nonalcoholic steatohepatitis (NASH), Obstructive Sleep Apnea (OSA). Exclusion criteria were patients with open surgery and those who were prohibited from taking propranolol, such as cases with Chronic Obstructive Pulmonary Disease (COPD), hyperthyroidism, Congestive Heart Failure (CHF), and glaucoma.

Patients were randomly divided into the test (receiving 40 mg propranolol twice a day one week before surgery) and control (receiving 40 mg placebo twice a day one week before surgery) groups by the secretary of the department using random number tables. The project nurse followed the patients to make sure that the prescribed medicine or placebo to be used one week before the surgery. All surgeries were conducted by one surgeon to eliminate the confounding factors. The surgeon was blind to randomization and allocation and had no idea which group the patient belonged to. The presence/extent of bleeding was determined based on the number of bleeding points requiring homeostasis in the view of the surgeon and the time the surgeon spent to control. It was estimated to be fixed based on the surgeon's opinion to eliminate the confounding factors. The information was given to the secretary of the department and he/she entered the coded data in the designed questionnaires. The bleeding rate was determined based on the following criteria: 1. The number of bleeding points requiring homeostasis; 2. The time needed for homeostasis; and 3. Difference between hemoglobin levels measured before surgery and 8 hours after surgery [3].

Because the intraoperative intervention was considered, no patient lost the follow-up; however, if a patient found any complications during the laparoscopic surgery that made us end the surgery or convert the laparoscopic to open surgery, he/she was excluded from the study and another patient was replaced to avoid the reduced number of samples.

Statistical analyses

Data analysis was performed using SPSS statistical software version 16. In this study, a p-value less than 0.05 was considered statistically significant. The normality of the data was assessed using the Kolmogorov-Smirnov test or Histogram Chart. The Chi-square test was used to compare qualitative variables between groups. To compare the means of quantitative variables between the studied groups, the t-test (data with normal distribution) or the Mann-Whitney test (data with no normal distribution) were used.

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3. Results

In this study, 82 patients who underwent bypass surgery were included, of whom 41 cases were in the group receiving propranolol (first group) and 41 patients were in the placebo group (second group). The mean age of subjects was 35.2±6.7 years ranging from 25 to 48 years (Table 1). A total of 20 patients (24.4%) were male and 62 patients (75.6%) were female and no significant difference was seen in sex ratio between the two groups (P= 0.399). The Mean±SD height of patients was 165.5±7.2 cm ranging from 149 to 182 cm. Also, the mean weight of patients was 121.3±16.8 kg ranging from 94 to 167 kg. The Mean±SD BMI of patients was 44.1±4.2 kg/m^2 ranging from 36 to 57 kg/m^2. No statistical difference was seen between the two groups in terms of height, weight, and BMI (Table 2).

The Mean±SD number of bleeding points was 2.32±0.96, which was 2.13±0.84 in the propranolol group and 2.5±1.03 in the placebo group, and no statistical difference was seen between the two groups (P=0.108) (Figure 1). The Mean±SD time required for homeostasis was 9.5±5.44, which was 3.85±7.96 in the propranolol group and 9.67±5.01 in the placebo group, and no statistical difference was seen between the two groups (P=0.149) (Figure 2). The type of injury was arterial in 79 patients (96.3%) and venous in 3 patients (3.7%), and no statistically significant difference was seen between the two groups (P=0.967) (Figure 3). Regarding causes of injury, the most common cause was adipose tissue damage, which was observed in 37 cases.

The mean hemoglobin before surgery was 13.6±1.8 g/dL, which reached 12.9±1.5 g/dL after surgery, and the difference between before and after surgery was at the borderline level (P=0.091). Hemoglobin level before surgery was 13.9±1.3 g/dL in the propranolol group and 13.3±2.2 in the placebo group and there was no statistically significant difference between the two groups (P=0.122). Hemoglobin level after surgery was 13.2±1.8 g/dL in the propranolol group and 12.7±1.18 g/dL in the placebo group and no statistically significant difference was seen between the two groups (P=0.145) (Figure 4).

4. Discussion

In addition to considerable and lasting weight loss, the surgery also is associated with other important benefits to the patient. Recent studies have shown that it can entirely treat diabetes [8], improve the progression of cardiovascular diseases [9], and reduce the risk of death by 35% over time [10, 11]. In a joint study conducted at several centers on 4776 obese patients undergoing weight loss surgeries, the mortality rate was 0.03 during 30 days and serious complications were reported in 4.1% of patients, which is similar to other important surgeries [12, 13]. From 1998 to 2004, the number of weight loss surgeries was increased by 800% and reached 121500 [14] and then, 171000 cases in the following year [9]. Since 2005, the number of surgeries for obesity has been increasing day by day, particularly due to the failure of non-surgical weight loss procedures (diet, change of habits, exercise, and drug treatments) [15, 16]. There are numerous surgical methods for managing morbidity

Table 1. The age of participants in the two groups

Group	Mean±SD	P
Propranolol	35.7±7.02	0.482*
Placebo	34.7± 6.4	

*Independent samples t-test

Table 2. Anthropometric characteristics of the two groups

Variable	Mean±SD		P*
	Propranolol	Placebo	
Height (cm)	166.1±8.03	164.8±6.4	0.441
Weight (kg)	122.5±19	120.1±14.5	0.521
BMI (kg/m^2)	44.1±4.2	44.07±3.5	0.900

*Independent sample t-test

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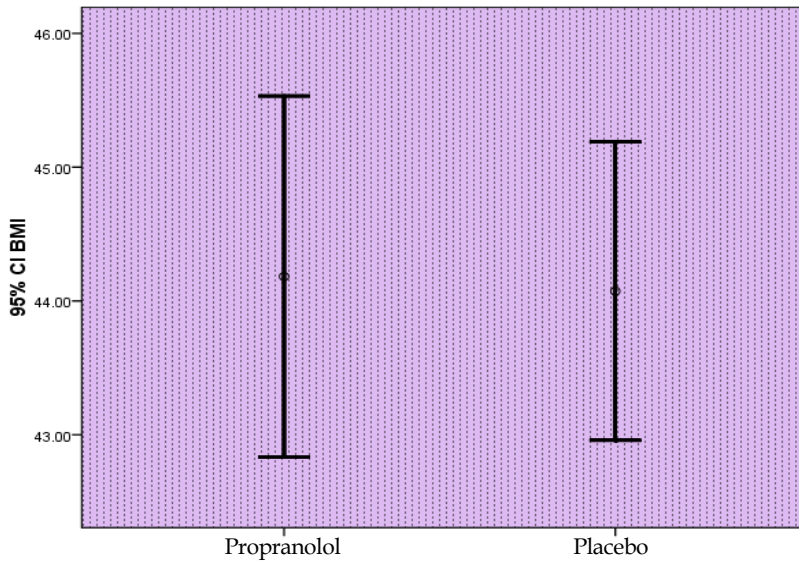

Figure 1. The mean number of bleeding points in the two groups

in obese patients. These surgeries use restrictive procedures, such as laparoscopic adjustable gastric band and malabsorption procedures, such as jejunoileal bypass. Some procedures also aim to limit/cause malabsorption. These surgeries include LRYGB, biliopancreatic bypass, and duodenal switch, of which LRYGB is the standard bariatric surgery procedure that accounts for above 70% of bariatric surgeries [17]. The surgeon's caution in bariatric surgeries is necessary and he should be aware of the potential side effects of these procedures to reduce these complications and improve the control of patients. Bleeding is very rare after gastric bypass surgery and especially, during surgery and could be life-threatening for the patient; thus, bleeding control is still being debated. This is becoming more important with an increase in the number of bariatric surgeries in recent years. Bleeding (in the first 24 hours) requires a blood transfusion and could take the patient back to the operating room. Propranolol is used in various studies as a placebo in reducing bleeding and is associated with contradictory results. However, this medicine has not been studied in laparoscopic and gastric bypass surgery.

In the present study, there was no significant difference between the two groups in the number of bleeding points, the time required for homeostasis, type of vas-

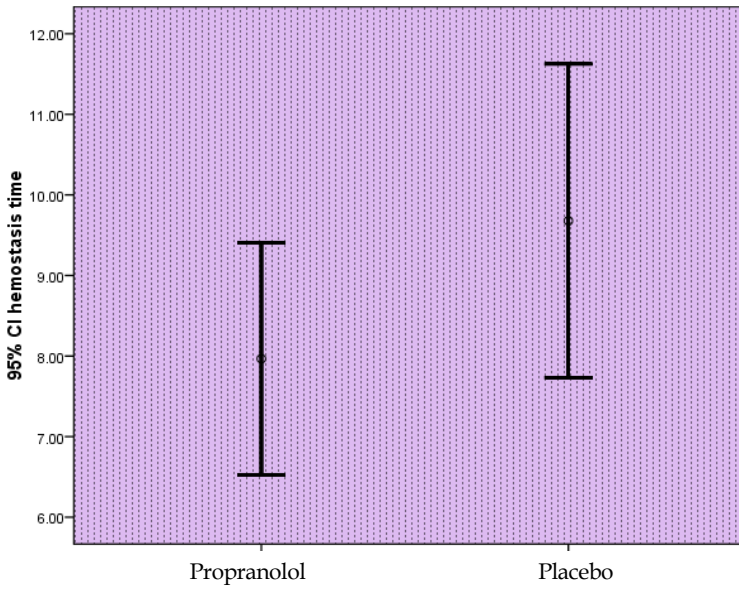

Figure 2. The mean time (g/dl) required for homeostasis in the two groups

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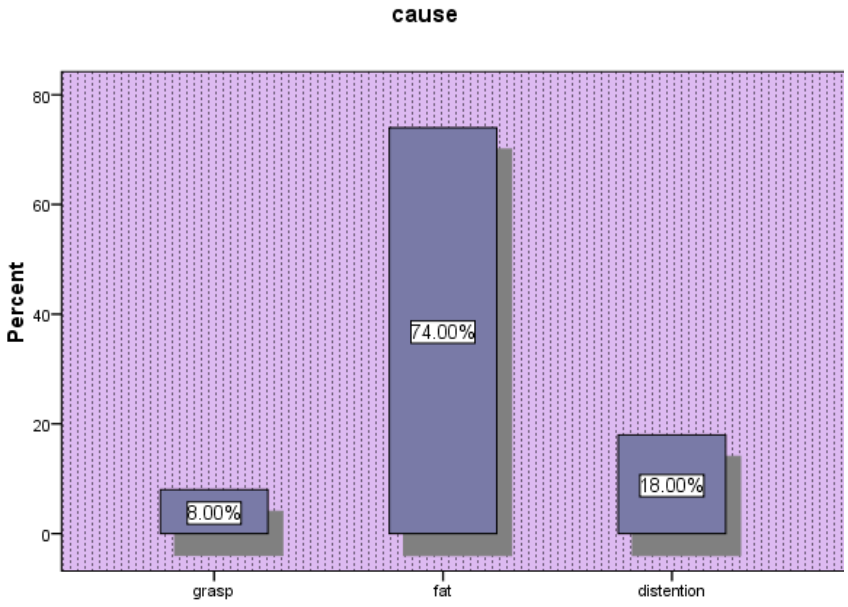

Figure 3. The causes of bleeding

cular injury, and mean hemoglobin before and after surgery. However, the overall outcomes of the propranolol group were better than the placebo group.

Avgerinos et al. examined the effect of propranolol as an additive on sclerotherapy in cirrhotic esophageal varices and showed that it was not effective on sclerotherapy [18]. Wilbur et al. studied 106 cirrhotic patients, 60% of whom underwent propranolol prophylaxis. The bleeding rate was 41% in patients receiving propranolol prophylaxis and 73% in other patients and the difference between the two groups was statistically significant (p-value=0.04). They concluded that beta-blockers could be used as a preventative measure for bleeding in esopha-

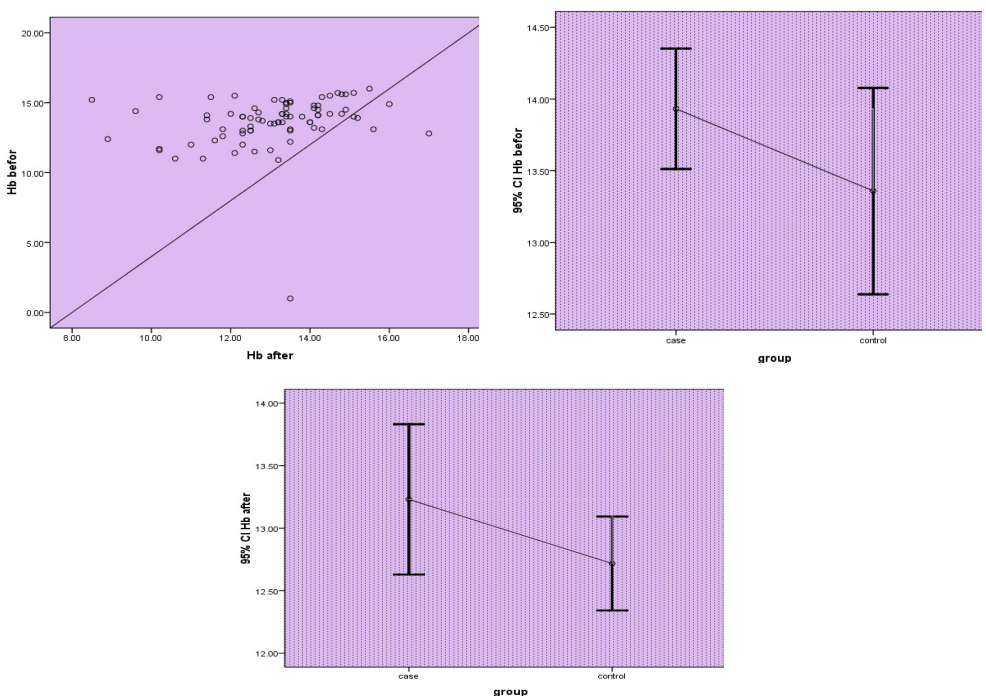

Figure 4. Mean difference in hemoglobin levels (g/dl) between the two groups and hemoglobin levels before and after surgery between the two groups

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geal varices [19]. The results of this study demonstrated that propranolol is an effective drug on bleeding, which was in contrast to the present study. This could be owing to the bleeding rate in two different study cases, as bleeding rate and its prevalence were very high in esophageal varices, and using a drug to reduce this rate with the least effect could be the most important therapeutic option. No case of severe bleeding was seen in the present study and there was a small number of bleeding points at the operation site. However, in the present study, no cases of severe bleeding were observed and the number of bleeding points at the surgical site, in general, was small, which in these conditions and the sample size of these changes were not significant. However, this study did not reject the positive effect of this drug on bleeding components, and as mentioned, a positive effect was seen in these components compared to the placebo.

Limitations /strengths

Because the outcome of the intervention during surgery is estimated, we did not lose the follow-up. However, if during the laparoscopic surgery, the patient had a complication that we had to end the surgery or the surgery was changed to open surgery, the patient was excluded from the study and another patient was replaced to compensate so that the sample size was the same.

5. Conclusion

The results of this study demonstrated a positive effect of propranolol on bleeding components in patients undergoing gastric bypass surgery, but this difference was not statistically significant. Because this is the first study in this field and the initial results indicated a positive effect of this medicine, the results of this study seem to prove the necessity of further studies with larger sample sizes.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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