Effectiveness of prophylactic doses of tranexamic acid in reducing hemorrhagic events in sleeve gastrectomy

Paweł Lech1 · Maciej Michalik2 · Kamil Waczyński1 · Karolina Osowiecka3 · Natalia Dowgiało-Gornowicz1

Received: 4 January 2022 / Accepted: 27 July 2022 / Published online: 3 August 2022
© The Author(s) 2022

Abstract
Purpose Laparoscopic sleeve gastrectomy (LSG) is currently the most common bariatric surgery in the world. Although it appears to be a safe treatment for obesity, it is still at risk of complications. The latest literature shows that postoperative bleeding occurs in 2–4% of cases, and up to 3% of cases requires reoperation for hemostasis. The aim of the study is to assess the effect of tranexamic acid (TXA) on hemorrhagic events and the reoperation rate in patients undergoing LSG.

Methods The study was designed as a retrospective analysis of patients undergoing LSG. We investigate the patients 6 months before and 6 months after introducing the prophylaxis doses of TXA into our bariatric protocol (non-TXA group vs TXA group).

Results Three hundred fourteen patients underwent LSG in a high-volume center from 2016 to 2017. After introducing TXA, a statistically significant reduction in the incidence of hemorrhage during surgery was observed (22.3% vs 10.8%, p = 0.006). There was a statistically significant reduction in the need for the staple line oversewing (10.2% vs 1.9%, p = 0.002). The mean operating time and the mean length of hospital stay were significantly higher in the non-TXA group than TXA group (63.1 vs 53.7 min, p < 0.001; 2.3 vs 2.1, p = 0.02). In both groups of patients, no venous thromboembolism or other complications occurred within 6 months after the surgery.

Conclusions The prophylactic doses of TXA may be useful in reducing the hemorrhagic events during LSG. It may also shorten the length of hospital stay and the operating time.

Keywords Tranexamic acid · TXA · Hemorrhagic events · Laparoscopic sleeve gastrectomy

Introduction
Laparoscopic sleeve gastrectomy (LSG) is currently the most common bariatric surgery in the world [1]. Although it appears to be a safe treatment for obesity, it is still at risk of complications. The latest literature shows that postoperative bleeding occurs in 2–4% of cases, and up to 3% of cases requires reoperation for hemostasis [2–4].

By introducing to our daily practice enhanced recovery after bariatric surgery, we focus on the quick mobilization of the patient, shortening the length of hospital stay and discharge from the hospital on the first postoperative day [5]. Undoubtedly, it is beneficial both from the point of view of the patient and the economy of the facility. However, it gives less insight into the occurrence of possible complications, including hemorrhagic complications. Therefore, ways of reducing these risks are sought, such as the staple line oversewing, the use of reinforcement materials or fibrin sealants [6–8].

One of the effective methods of reducing the risk of postoperative bleeding is using tranexamic acid (TXA) [9]. It has been well described in cardiac or orthopedic surgery [10, 11]. TXA is an antifibrinolytic drug, a synthetic analog of lysine [12]. It prevents lysine binding sites on plasminogen by blocking plasmin formation and thus
fibrinolysis. There are only a few reports of the use of TXA in postoperative bleeding following bariatric surgery [13–15].

The aim of the study is to assess the effect of TXA on hemorrhagic events and the reoperation rate in patients undergoing LSG.

**Materials and methods**

The study was designed as a retrospective analysis of patients undergoing LSG. Patients were qualified for surgery according to national and international criteria. We investigate the patients before and after introducing the prophylaxis doses of TXA into our bariatric protocol (non-TXA group vs TXA group). To avoid potential bias due to the learning curve, experience, and time of treatment, the same team of surgeons performed the surgery. The surgeons’ experience is over 150 procedures a year. Additionally, we include patients operated 6 months before and after the introduction of TXA.

Following our bariatric protocol, 1 g of intravenous TXA (Exacyl ®) was routinely administered as an induction to all LSG patients and three times after the surgery every 8 h. As written in our national Summary of Product Characteristics. In parallel, as part of thrombolytic prophylaxis, 40 mg of low molecular weight heparin (Clexane ®) was administered subcutaneously 12 h before the surgery, 12 h after the surgery, and once a day for 10 days after the discharge from the hospital. Patients were discharged on the first postoperative day, when they were able to self-mobilize and consume adequate amounts of oral fluids. Otherwise, or in the event of complications, they stay in the hospital longer. Thirty days after surgery, each patient showed up for a personal, routine, post-surgery visit to the outpatient clinic. A physical examination and laboratory tests were performed. The subsequent visits in the 6th, 12th month, and annually after the surgery can take place during both personal visits and telephone consultations.

**Surgical technique**

All LSGs were performed according to the standard procedure described by Bhandari et al. [16]. An ultrasonic dissection device (Medtronic, Covidien, Inc.) and a 36-F bougie size were used. The sleeve started 2–4 cm from pylorus. The Endo GIA™ Ultra Universal Staplers (Medtronic, Covidien, Inc.) were used with 60-mm cartridge depending on stomach thickness. Typically, 3 purple and 2 blue cartridge were used. No staple line reinforcement or buttressing was used. Before the end of surgery, the pneumoperitoneum was lowered to 10 mmHg to check for evidence of bleeding. The clips were placed in case of bleeding points of staple line. If the bleeding cannot be controlled by clipping, the surgeon decided to perform the staple line oversewing with 3–0 PDS stitch. The intra-abdominal drainage was not used routinely.

**Outcomes measured**

We analyzed the number of hemorrhagic events during and after the surgery. We divide it into 3 groups, Fig. 1. The first is bleeding from the staple line requiring more than one load of clips (>8 clips). Second, there is bleeding from the staple line, which requires oversewing the staple line for hemostasis. Third is a postoperative bleeding requiring reoperation. Secondary outcomes included the pre- and postoperative levels of hemoglobin, hematocrit, and red blood cells; operating time, length of hospital stay, and the occurrence of 30-day complications, and venous thromboembolism within 6 months after surgery. Anemia 30 days after the surgery was defined as hemoglobin < 10 mg/dL.

**Statistical analysis**

The data was calculated using descriptive statistics. The chi-square test was used to compare the proportion between non-TXA and TXA group due to various factors. The differences in mean age, body mass index, operating time, length of hospital stay, and laboratory parameters between non-TXA
and TXA group were assessed using Student \( t \) test. A \( p \) value < 0.05 was considered significant. The analysis was conducted using Statistica (data analysis software system), version 13, http://statistica.io (accessed on 1 October 2021) TIBCO Software Inc., Krakow, Poland (2017).

### Results

Three hundred fourteen patients underwent LSG in a high-volume center from 2016 to 2017. Twenty-three patients were lost in follow-up at the 6th month. The follow-up rate was 92.7%. The first group of patients (non-TXA group) consisted of 124 women and 33 men (79%, 21%) and was operated without introducing the prophylactic doses of TXA. The second group (TXA group) had 124 women and 33 men (79%, 21%) and was operated using the prophylactic doses of TXA. The TXA group was statistically older than non-TXA group (\( p = 0.048 \)), but there were no significant differences in body mass index, type 2 diabetes mellitus, and arterial hypertension (\( p > 0.05 \), Table 1).

After introducing TXA as a prophylaxis into standard management, a statistically significant reduction in the incidence of hemorrhage during surgery was observed (22.3% vs 10.8%, \( p = 0.006 \)). There was a statistically significant reduction in the need for the staple line oversewing (10.2% vs 1.9%, \( p = 0.002 \)). However, no significant differences in the use of clips and reoperation rate were observed. Nevertheless, the reoperation rate in the analyzed time decreased to 0, \( p = 0.08 \). Only one patient required a transfusion in

### Table 1 Characteristics of groups (results in bold indicate statistical significance, \( p < 0.05 \))

|                          | Non-TXA group | %     | TXA group  | %     | \( p \) |
|--------------------------|---------------|-------|------------|-------|---------|
| Sex                      |               |       |            |       |         |
| Woman                    | 124           | 79    | 124        | 79    |         |
| Man                      | 33            | 21    | 33         | 21    |         |
| Mean age (± SD) (years)  | 39 (11.2)     |       | 41.6 (11.5)|       | 0.048   |
| Mean BMI (± SD) (kg/m²)  | 44.6 (6.6)    |       | 46.0 (9.6) |       | 0.16    |
| Diabetes mellitus type 2 |               |       |            |       |         |
| Yes                      | 26            | 16.6  | 33         | 21    | 0.31    |
| No                       | 131           | 83.4  | 124        | 79    |         |
| Arterial hypertension    |               |       |            |       |         |
| Yes                      | 67            | 42.7  | 73         | 46.5  | 0.5     |
| No                       | 90            | 57.3  | 84         | 53.5  |         |
| Mean operating time (± SD) (min) | 63.1 (19.2) | 53.7 (14.5) |       | < 0.001 |
| Mean length of hospital stay (± SD) (days) | 2.3 (0.9) | 2.1 (0.4) |       | 0.02    |
| Hemorrhagic incidents    |               |       |            |       |         |
| Yes                      | 35            | 22.3  | 17         | 10.8  | 0.006   |
| No                       | 122           | 77.7  | 140        | 89.2  |         |
| Bleeding                 |               |       |            |       |         |
| Yes                      | 16            | 10.2  | 14         | 8.9   | 0.7     |
| No                       | 141           | 89.8  | 143        | 91.1  |         |
| Oversewing               |               |       |            |       |         |
| Yes                      | 16            | 10.2  | 3          | 1.9   | 0.002   |
| No                       | 141           | 89.8  | 154        | 98.1  |         |
| Reoperations             |               |       |            |       |         |
| Yes                      | 3             | 1.9   | 0          | 0     | 0.08    |
| No                       | 154           | 98.1  | 157        | 100   |         |
| Anemia                   |               |       |            |       |         |
| Yes                      | 11            | 7.0   | 4          | 2.5   | 0.06    |
| No                       | 146           | 93.0  | 153        | 97.5  |         |

\( SD \) standard deviation, \( BMI \) body mass index, \( RBC \) red blood count, \( Ht \) hematocrit, \( Hb \) hemoglobin.
the non-TXA group and none in the TXA group; this is of no clinical significance and not statistically significant. We found no changes in mean difference in hemoglobin, hematocrit, and red blood cell levels before and after the surgery (p > 0.05). The mean operating time and the mean length of hospital stay were significantly higher in the non-TXA group than TXA group (63.1 vs 53.7 min, p < 0.001; 2.3 vs 2.1, p = 0.02), Table 1.

In both groups of patients, no evident, clinically noticeable venous thromboembolism or other complications occurred within 6 months after the surgery. The incidence of anemia in the first 30 days after surgery was lower in TXA group (2.5% vs 7%, p = 0.06), but not statistically significant, Table 1.

Discussion

Our study analyzed the effect of TXA on perioperative bleeding in patients undergoing LSG. There are many reports in the literature regarding the use of TXA in various fields of surgery. However, little is known about its effects on bariatric surgery. To our knowledge, this is the first report to compare such a large group of bariatric patients to provide objective evidence.

TXA is synthetic lysine analog that inhibits the activation of plasminogen to plasmin [12]. It is routinely used in orthopedic and cardiac surgery to reduce the perioperative bleeding [9, 10]. Although the efficacy of TXA has been confirmed in studies, current studies have focused on effective dose adjustment as well as careful evaluation of use in elderly patients [10, 17]. Recent reports have shown that TXA can be safely used in elderly patients without increasing the risk of thrombotic complications [17, 18].

In a recent randomized controlled trial by Oseni et al., a significant reduction in blood was observed in women undergoing emergency caesarean section after a prophylactic dose of TXA [19]. This was noticeable in reducing both intraoperative blood loss and postoperative hemoglobin levels.

The first report of the use of TXA in the prophylaxis of LSG was described by Chakravatty et al. [14]. They compared 25 patients who received 1 g of TXA intravenously as induction with the control group. They noticed that the introduction of TXA significantly decreases intraoperative bleeding and time of surgery, which is consistent with our observations. Hussain et al. showed in a letter to the editor that they also observed that the use of TXA may reduce postoperative transfusion rates and reoperation [13].

Klassen et al. analyzed patients who developed hemorrhage after bariatric surgery [15]. Treatment failure was observed in 4 of 44 complicated patients who received TXA after surgery. The authors suggested that TXA appeared to be safe in reducing the reoperation rate for bleeding.

The reported reoperation rate for bleeding in bariatric surgery ranges from 0.5 to 3% [3, 4]. In our study, the reoperation rate was 1.9% and it decreased to 0% after TXA in the presented group, but it was not statistically significant. In addition, we also noted shortening the operating time and the length of hospital stay. In our bariatric protocol, each patient requires 4 TXA ampoules, which costs less than PLN 10 (EUR 2.1). In contrast, buttressing materials or fibrin sealants cost about PLN 1000 (EUR 210). The use of TXA may be useful in reducing the overall costs of hospitalization in bariatric units. That may have a positive impact on the hospital’s finances. Importantly, we did not observe any evident thromboembolic events until 6 months after surgery.

Our study has several limitations. It includes the subjective definition of hemorrhage events, retrospective, and non-randomized character. However, to minimize the risk of bias, we included patients operated within 6 months before and after the introduction of TXA into the bariatric protocol. The team of bariatric surgeons in our department consists of two experienced surgeons who have operated for over 5 years and perform over 150 operations a year. The surgeons were not blinded, which may have influenced the decision to use more clips or to perform the staple line oversewing. But the statistics on reoperation rate and postoperative hemoglobin levels were absolute. However, a randomized controlled trial with blind surgeons appears to be an ideal model to conduct the trial, as proposed by Leeman et al. [20].

Conclusions

The prophylactic doses of TXA may be useful in reducing the hemorrhagic events during LSG. It may also shorten the length of hospital stay and the operating time. However, more randomized controlled trials are needed.

Author contribution Study conception and design: Paweł Lech, Natalia Dowgiallo-Gornowicz. Acquisition of data: Kamil Waczyński. Analysis and interpretation of data: Karolina Osowiecka. Drafting of manuscript: Paweł Lech, Natalia Dowgiallo-Gornowicz. Critical revision of manuscript: Maciej Michalik.

Declarations

Ethics approval This observational study was conducted retrospectively from data obtained for clinical purposes. Due to study design, it was not formally supervised by an Institutional Review Board in line with its policy.

Conflict of interest The authors declare no competing interests.
Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

References

1. Welbourn R, Hollyman M, Kinsman R, Dixon J, Liem R, Ottosson J, Ramos A, Väge V, Al-Sabah S, Brown W, Cohen R, Walton P, & Hippens J (2019) Bariatric surgery worldwide: baseline demographic description and one-year outcomes from the fourth IFSO Global Registry Report 2018. Obes Surg 29:782–795. https://doi.org/10.1007/s11695-018-3593-1
2. Zellmer JD, Mathiason MA, Kallies KJ, Kohthri SN (2014) Is laparoscopic sleeve gastrectomy a lower risk bariatric procedure compared with laparoscopic Roux-en-Y gastric bypass? A meta-analysis. Am J Surg 208:903–910. https://doi.org/10.1016/j.amjsur.2014.08.002
3. Kitahama S, Smith MD, Rosencreantz DR, Patterson EJ (2013) Is bariatric surgery safe in patients who refuse blood transfusion? Surg Obes Relat Dis 9:390–394. https://doi.org/10.1016/j.soard.2012.02.008
4. Mocanu D, Dang J, Ladak F, Switzer N, Birch DW, Karmali S (2019) Predictors and outcomes of bleed after sleeve gastrectomy: an analysis of the MBSAQIP data registry. Surg Obes Relat Dis 15:1675–1681. https://doi.org/10.1016/j.soard.2019.07.017
5. Małczak P, Piasarska M, Piotr M, Wysocki M, Budzyński A, Pęczwiatori M (2017) Enhanced recovery after bariatric surgery: systematic review and meta-analysis. Obes Surg 27:226–235. https://doi.org/10.1007/s11695-016-2438-z
6. Cunningham-Hill M, Mazzei M, Zhao H, Lu X, Edwards MA (2019) The impact of staple line reinforcement utilization on bleeding and leak rates following sleeve gastrectomy for severe obesity: a propensity and case-control matched analysis. Obes Surg 29:2449–2463. https://doi.org/10.1007/s11695-019-03883-8
7. Roy S, Wang Y, Mallampati R, Johnstone S (2020) Surgical outcomes, health care utilization, and costs associated with staple line buttressing among primary sleeve gastrectomy patients. Obes Surg 30:4935–4944. https://doi.org/10.1007/s11695-020-04917-2
8. Chen Y, Loh E, Shen S, Su Y, Tam K (2021) Efficacy of fibrin sealant in reducing complication risk after bariatric surgery: a systematic review and meta-analysis. Obes Surg 31:1158–1167. https://doi.org/10.1007/s11695-020-05098-8
9. Yao Y, He L, Tan J (2020) The effect of tranexamic acid on the values of activated clotting time in patients undergoing cardiac surgery: a PRISMA-compliant systematic review and meta-analysis. J Clin Anesth 67:110020. https://doi.org/10.1016/j.jclinane.2020.110020
10. Zufferery PJ, Lanoiselle J, Graouch B, Vieille B, Delavenne X, & Ollier E (2021) Exposure-response relationship of tranexamic acid in cardiac surgery. Anesthesiology 134:165–178. https://doi.org/10.1097/ALN.0000000000003633
11. Leow L, Ng J, Luo HD, Choong AM, Mithirian H, Kofidis T, & Tam J (2021) Antifibrinolytics reduces blood loss in thoracic surgery: a systematic review and meta-analysis. ANZ J Surg 91:1251–1259. https://doi.org/10.1111/ans.16909
12. Ng W, Jerath A, Wąsowicz M (2015) Tranexamic acid: a clinical review. Anaesthesiol Intensive Ther 47:339–350. https://doi.org/10.5603/AIT.a2015.0011
13. Hussain A, Ali-Shoek I (2017) El-Hasani S (2017) The use of tranexamic acid in sleeve gastrectomy. Obes Surg 27:198–199. https://doi.org/10.1186/s40608-018-0213-5
14. Chakravartty S, Sarma DR, Chang A, Patel AG (2016) Staple line bleeding in sleeve gastrectomy—a lower cost and effective solution. Obes Surg 26:1422–1428. https://doi.org/10.1007/s11695-015-1986-y
15. Klaassen R, Selles C, van den Berg J, Poelman M, van der Harst E (2018) Tranexamic acid therapy for postoperative bleeding after bariatric surgery. BMC Obes 5:36. https://doi.org/10.1186/s40608-018-0213-5
16. Bhanderi M, Fobi MA, Buchwald J (2019) Bariatric Metabolic Surgery Standardization (BMSS) working group standardization of bariatric metabolic procedures: World Consensus Meeting Statement. Obes Surg 29:309–345. https://doi.org/10.1007/s11695-019-04032-x
17. Luo X, Huang H, Tang X (2020) Efficacy and safety of tranexamic acid for reducing blood loss in elderly patients with intertrochanteric fracture treated with intramedullary fixation surgery: A meta-analysis of randomized controlled trials. Acta Orthop Traumatol Turc 54:4–14. https://doi.org/10.5152/aott.2020.01.88
18. Reale D, Andriolo L, Gursoy S, Bozkurt M, Filardo G, Zaffagnini S (2021) Complications of tranexamic acid in orthopedic lower limb surgery: a meta-analysis of randomized controlled trials. Biomed Res Int 2021:6961540. https://doi.org/10.1155/2021/6961540
19. Oseni RO, Zakari M, Adamou N, Umar UA (2021) Effectiveness of preoperative tranexamic acid in reducing blood loss during caesarean section at Aminu Kano Teaching Hospital, Kano: a randomized controlled trial. Pan Afr Med J. 39:54. https://doi.org/10.11604/pamj.2021.39.34.21938
20. Leeman M, Huisbrink J, Wijnand JMA, Biter Lu, Verbrugge SJc, Dunkelgrun M, Apers JA (2020) Trial protocol: preoperative administration of tranexamic acid in sleeve gastrectomy (PATAS) to reduce haemorrhage rates. A randomised controlled trial BMJ Open 10:e034572. https://doi.org/10.1136/bmjopen-2019-034572

Publisher’s note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.