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Drug Utilization of Tranexamic Acid in the Department of Surgery

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Abstract | **Original Research Article**

Synthetic lysine derivative tranexamic acid reversibly blocks plasminogen lysine binding sites, hence inhibiting fibrinolysis. In order to halt bleeding, antifibrinolytics encourage blood coagulation. During surgery, tranexamic acid dramatically lowers blood loss. The study's objective was to ascertain how often tranexamic acid was used in the surgery department. The study used observational methods. The study was carried out at Rajajinagar, Bengaluru's ESIC MC-PGIMSR. 28 participants (88%) in the trial received TXA after surgery, 3 (9%), during surgery, and 1 (3%), both during and after surgery. seventeen (53%) belonged to the 25–34 age range, seven (22%) to the 35–44 age range, and eight (25%) to the 18–24 age range. There were 13 (41%) females and 19 (59%) males. 23 individuals (72%) received 500 mg, 9 subjects received 1g, 29 subjects (91%) received BD (bis in die), 2 subjects (6%) received STAT, and 1 subject (3%) received SOS in this study. Of the 32 participants, 22 (69%) had an infection of the gastrointestinal system, 3 (9%) had endocrine disease, 3 (9%) had cancer, 3 (9%) underwent surgery for diabetic foot problems, and 1 (3%) had soft tissue damage. Of the thirty-two individuals, twenty-four (75%) spent six to ten days in the hospital, four (13%) stayed one to five days, three (9%) stayed eleven to fifteen days, and one (3%) stayed for the maximum duration of sixteen to twenty days. Concluding that TXA was given to most patients after surgery, it may be assumed that most blood loss happens after surgery. TXA was not given to any of the research participants during surgery. This study demonstrates the requirement for an antifibrinolytic TXA in cases where post-operative bleeding continues.

Keywords: Tranexamic acid, Drug utilization review, surgery, Antifibrinolytic agent, Post-operative, and Blood loss.

INTRODUCTION

Tranexamic acid [TXA] is a synthetic derivative of the amino acid lysine that inhibits fibrinolysis by reversibly blocking lysine binding sites on plasminogen molecules [1]. It belongs to a class of drugs known as antifibrinolytics, and it aims to promote blood coagulation, so preventing bleeding. Tranexamic acid lowers blood loss dramatically in a variety of surgical procedures. Bleeding is a surgical complication that can result in significant morbidity and mortality. Post-operative bleeding is regarded as a primary cause of trauma-related mortality worldwide. If left untreated, severe or chronic hemorrhaging can cause organ failure, seizures, coma, external bleeding, and death. Even with treatment, internal bleeding is frequently lethal, with an increased risk of postoperative mortality [2]. Fluid may collect inside the body in the operative location after surgery. This increases the likelihood of infection or other issues. A surgical drain permits liquids to drain. A thin, flexible rubber tube is inserted into the part of your body where the fluid is likely to gather. A surgical drain is a thin plastic tube that is often used after an operation. It is implanted into the patient by the doctor during the surgery and will stick out of the body until it is removed, which is generally a few days later. It is linked to a little plastic bag that collects any fluid or air that has drained away from the area where the patient had the operation. Not all operations necessitate the use of a drain; the surgeon will notify the patient if one is required. Normal wound drainage [Serosanguineous & serous exudate] and aberrant wound drainage [Sanguineous, hemorrhage, and purulent pus] are two forms of wound drainage. A drug usage review (DUR) is an authorized, systematic, continuing review of prescription prescribing, dispensing, and use. DUR entails a drug review against predetermined criteria, which results in drug therapy modifications when these criteria are not met. It entails a thorough examination of the patient's prescription and drug data before to, during, and after dispensing in order

to ensure optimal medication decision-making and beneficial patient outcomes. DUR programmed give corrective action, prescriber feedback, and additional evaluations as a quality assurance measure [3]. Clinically substantial bleeding can occur as a result of surgery, trauma, obstetric problems, anticoagulation, and a wide range of hemostasis diseases. Because the reasons of bleeding are numerous and not always obvious, the availability of a safe, effective, and non-specific hemostatic drug is critical in a variety of clinical contexts, and antifibrinolytic medicines are frequently used for this purpose. Tranexamic acid is a widely used and investigated antifibrinolytic drug, with well-defined roles in postpartum hemorrhage, menorrhagia, trauma-associated hemorrhage, and surgical bleeding. However, Tranexamic acid's utility extends beyond these conventional indications, with mounting evidence indicating its capacity to control bleeding and improve clinical outcomes in the face of a wide range of hemostatic difficulties without a clear increase in thrombotic risk. Similarly, there are numerous additional surgeries that result in severe life-threatening consequences as a result of significant bleeding. This study's primary goal is to support the use of tranexamic acid in perioperative, intraoperative, and postoperative surgery to provide meaningful clinical outcomes in total operative time required to perform surgery, to reduce bleeding complications, and to shorten hospital stays following surgery. This study will aid in providing an overview of the indications, delivery methods, safety, and clinical effects of tranexamic acid used in various surgical subspecialties. In surgery, tranexamic acid continues to be a safe and efficient way to encourage hemostasis and minimize intraoperative and postoperative blood loss.

MATERIALS AND METHODS

Study Centre:

The study was carried out in the inpatient Department of General surgery, ESIC PGIMSR. Rajajinagar, Bengaluru.

Sample Size: A total of 32 subjects were included in the study.

Study Duration: Study was conducted for a period of 6 months.

Inclusion Criteria:

a. Patients receiving tranexamic acid will be included in the study.
b. Patients who have undergone surgery in the in-patient ward of Surgery department.
c. Patients of age above 18 years will be included in the study.
d. Patients of any gender will be included in the study.

Exclusion Criteria:

a. Individuals not willing to provide information.
b. Patients who are diagnosed with anemia before surgery will be excluded in the study.
c. Patients with known allergy to tranexamic acid & its excipients will be excluded from the study.

Study Tools:

The following tools were employed to obtain information pertaining to the study:

1. Self-designed patient demographic form.

Ethical Approval: The study was approved by Institutional Ethics Committee of ESIC PGISMR, Rajajinagar, Bengaluru in accordance with the guidelines issued by ICMR. (No.532/L/11/12/Ethics/ESICMC&PGIMSR/Estt. Vol.-I

Study Procedure:

Subjects for the study were identified by the investigators based on the inclusion and exclusion criteria. The patients who have undergone surgery & was administered with tranexamic acid was identified & considered as the study sample. The patients were explained the purpose of the study and the informed consent was obtained. Relevant data (demographic details) was recorded with the help of data collection form which was designed to collect the specific samples to obtain relevant information. The data thus obtained was entered in a Microsoft Excel sheet and appropriate analysis was performed.

Statistical Analysis:

All recorded data such as Distribution of subjects for various categories including age, gender, time of administration, type of dose, type of frequency, disease pattern, length of hospital stay & number of days drug administered was entered using MS Excel software and percentages were calculated. Relevant charts were applied to find the nature of data distribution. Type of surgery with length of hospital stay & length of stay with number of days administered was correlated and analyzed using Chi-square test for determining the statistical significant.

RESULTS

The study was conducted in the In-patient department of general surgery, ESI PGIMSR, Rajajinagar who were fulfilling the inclusion criteria and had provided the informed consent to participate in the study.

Age Distribution of Subjects:

Out of 32 study subjects, majority of them 17 (53%) were from the age group of 25-34 years, while the least with 7 subjects (22%) were from the 35-44 and 8 subjects (25%) were from the age group of 18-24 years.

Table 1: Age Distribution of Subjects

Age groups	Number of subjects	Percentage %
18-24	8	25
25-34	17	53
35-44	7	22
TOTAL	**32**	**100**

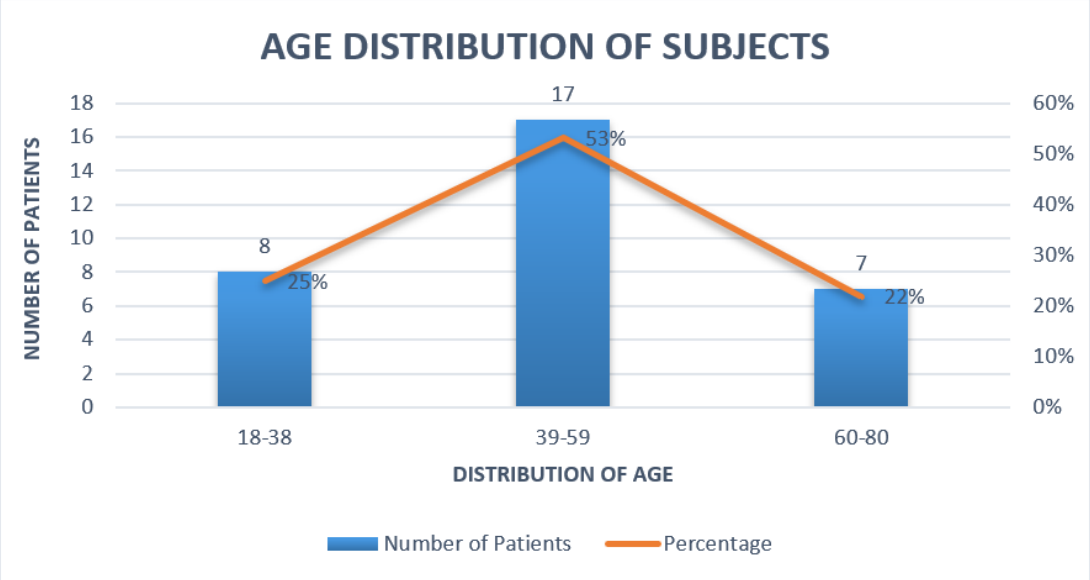

Figure 1: Age Distribution of Subjects

Distribution of Subjects by Gender:

Out of 32 subjects included in the study, the majority of the subjects 19 (59%) were males & 13 (41%) females included in the study were lesser than the males.

Table 2: Distribution of subjects by gender

Gender	Number of subjects	Percentage%
Male	19	59
Female	13	41
Total	**32**	**100**

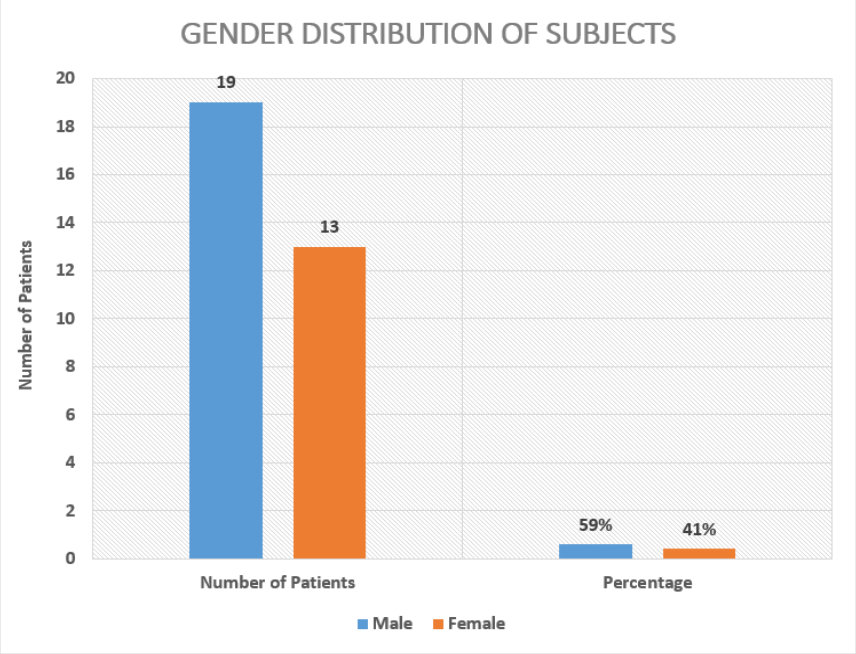

Figure 2: Distribution of subjects by gender

Distribution of Subjects by the Time of Administration Oof Txa:

Out of 32 subjects included in the study, majority of the subjects 28 (88%) were administered with TXA post operatively, 3 subjects (9%) were administered intra operatively & 1 of the subject (3%) was administered both intraoperative & postoperatively whereas none of the study subjects were administered with TXA perioperatively. In this study,

Table 3: Distribution of Subjects by the time of Administration of TXA

Time of administration of TXA	Number of subjects	Percentage %
Peri Operative	0	0
Intra Operative	3	9
Post Operative	28	88
Intra Operative + Post Operative	1	3
Total	**32**	**100**

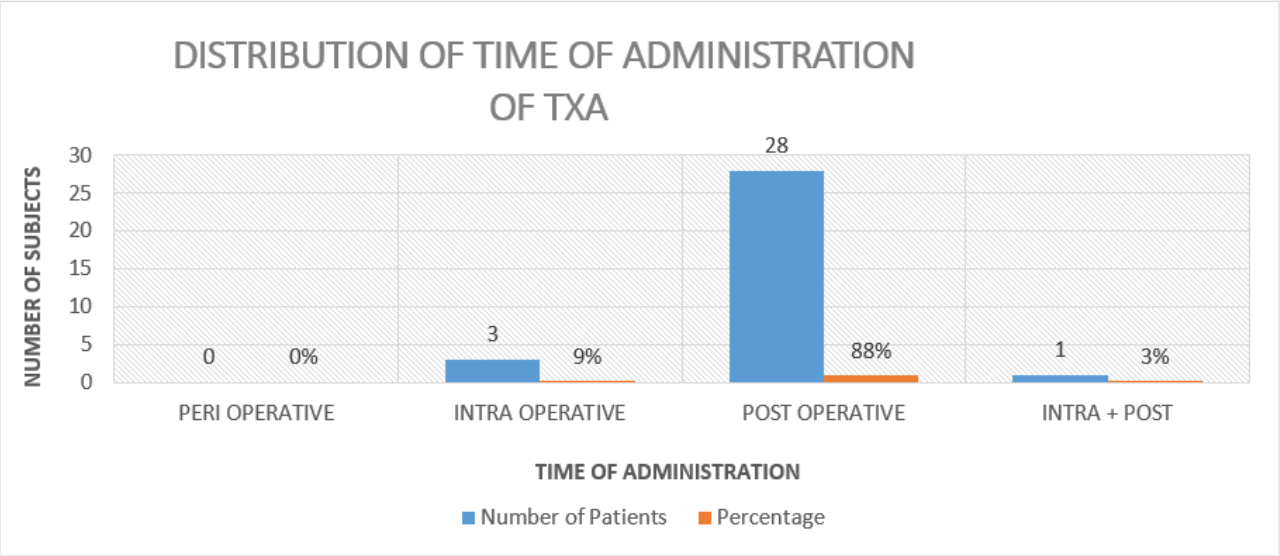

Figure 3: Distribution of Subjects by the time of Administration of TXA

Distribution of Subjects by the Type of Dose Administered:

Out of 32 subjects which was included in the study, majority of the subjects 23 (72%) were administered with 500 mg dose & the remaining 9 subjects were administered with 1g.

Table 4: Distribution of type of Dose Administered

Dose Administered	Number of subjects	Percentage %
500 mg	23	72
1 g	9	28
Total	**32**	**100**

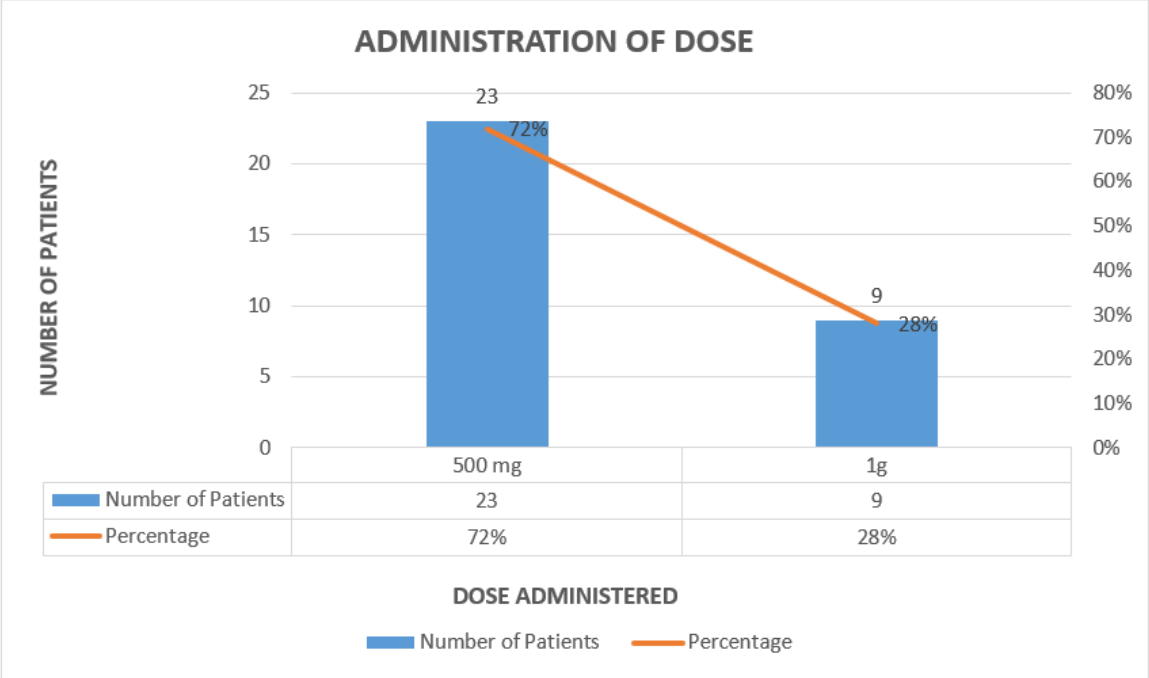

Figure 4: Distribution of type of Dose Administered

Distribution of Subjects by the Type of Frequency Period:

Out of 32 subjects included in the study, majority of them 29 (91%) were administered with BD (bis in die) or twice a day while the other 2 (6%) were administered with STAT which means to administer immediately or without delay & 1 (3%) subject was administered SOS which means to administer when necessary, depending upon the bleeding condition.

Table 5: Distribution of Frequency Period

Frequency	Number of subjects	Percentage %
BD	29	91
SOS	1	3
STAT	2	6
TOTAL	**32**	**100**

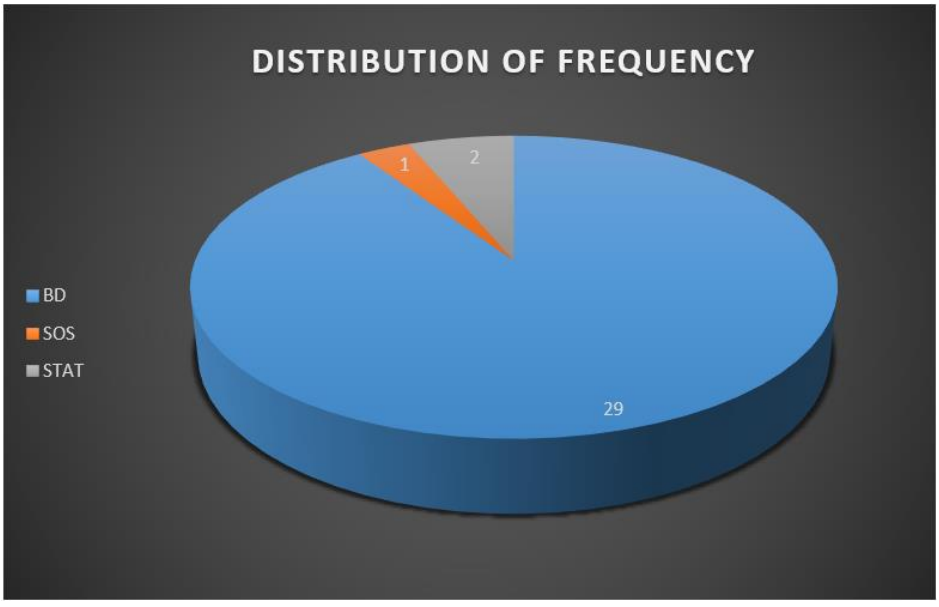

Figure 5: Distribution of Frequency period

Distribution of Disease Pattern in the Subjects:

Out of 32 subjects included in the study, majority of them 22 (69%) had Gastrointestinal tract infection, 3 (9%) subjects had endocrine disease, 3 (9%) had cancer & 3 (9%) had diabetic foot surgery respectively & 1 (3%) of the subject had soft tissue injury.

Table 6: Distribution of Disease Pattern

Disease Pattern	Number of subjects	Percentage %
Diabetic foot surgery	3	9.3
Soft tissue injury	1	3
Cancer	3	9.3
Endocrine	3	9.3
GIT	22	69
Total	**32**	**100**

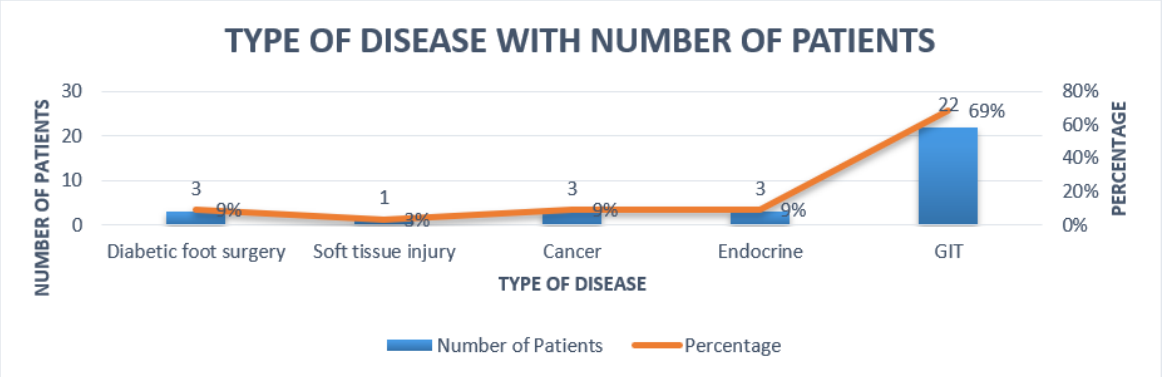

Figure 6: Distribution of Disease Pattern

Distribution of Length of Hospital Stay in the Subjects:

Out of 32 subjects included in the study, majority of the subjects 24 (75%) had hospital stay between 6 to 10 days, 4 (13%) subjects had stay between 1 to 5 days, 3 (9%) subjects had hospital stay between 11 to 15 days, whereas 1 (3%) subject had lengthiest stay of 16-20 days.

Table 7: Distribution of Length of Hospital Stay

Length of stay (days)	Number of subjects	Percentage %
1 to 5	4	13
6 to 10	24	75
11 to 15	3	9
16 to 20	1	3
Total	**32**	**100**

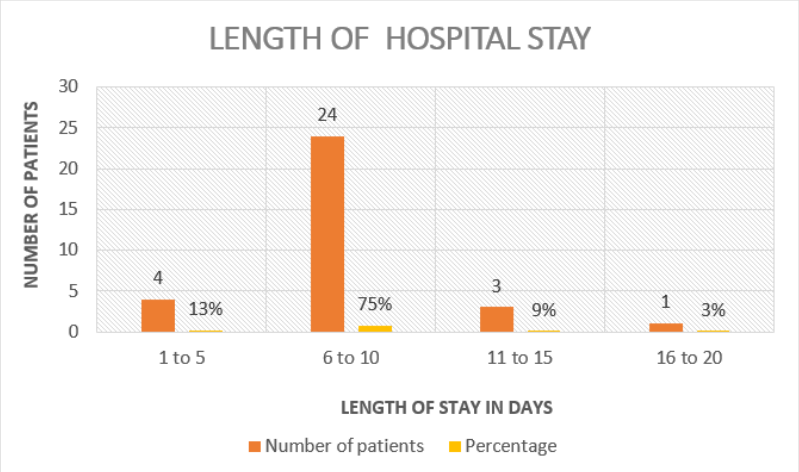

Figure 7: Distribution of length of hospital stay

Distribution of Subjects with Number of Days Ondrug Administered:

Out of 32 study subjects included, majority of the subjects 12 (38%) was administered for 3 days, 9 (28%) subjects were administered for 2 days, 8 (25%) subjects were administered for 4 days, 2 (6%) subjects were administered for one day & 1 subject (3%) was administered for 5 days.

Table 8: Distribution of Subjects with Number of Days on Drug Administered

Number of days drug administered	Number of subjects	Percentage %
One	2	6
Two	9	28
Three	12	38
Four	8	25
Five	1	3
Total	**32**	**100**

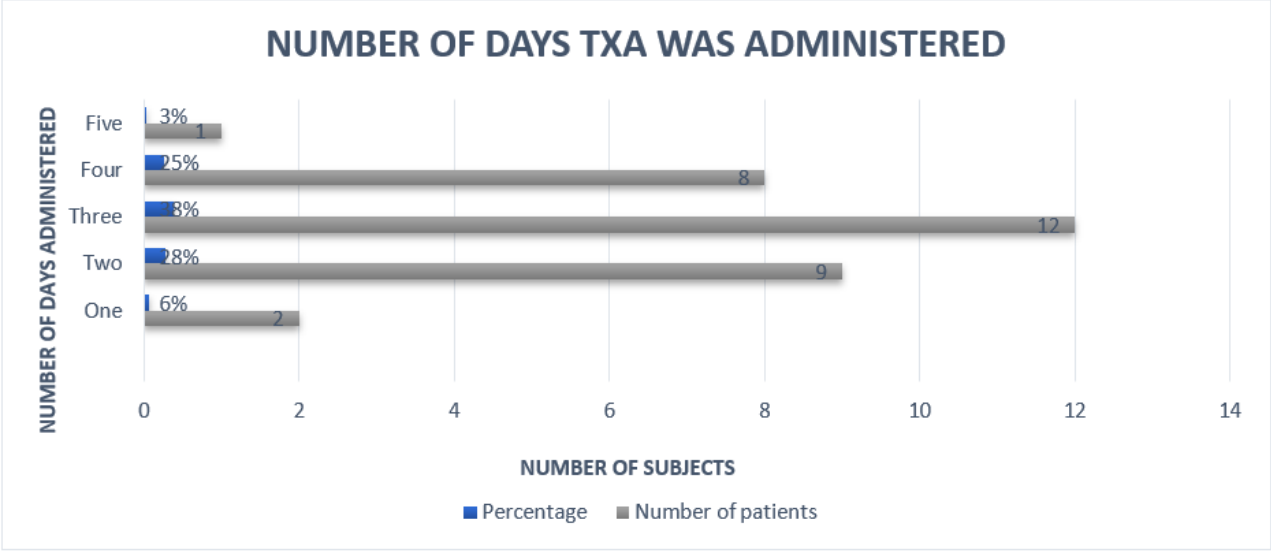

Figure 8: Distribution of Subjects with Number of Days on Drug Administered

Distribution of Subjects with Type of Surgery Performed with the Length of Stay:

In this study, 32 subjects were included for which 12 different type of surgeries was performed, & majority of the subjects (24) had a hospital stay between 6 to 10 days, 4 subjects had a stay between 1 to 5 days, 3 subjects had a stay between 11 to 15 days & only 1 subject had the lengthiest hospital stay between 16 to 20 days.

Modified radical mastectomy was performed for 3 subjects diagnosed with breast cancer out of which 2 subject had a hospital stay between 6 to 10 days & 1 subject had a hospital stay between 1 to 5 days.

Laparoscopic or open retro rectus mesh was performed for 2 subjects out of which 1 subject had a hospital stay between 1 to 5 days & the other subject had a stay between 6 to 10 days.

Laparoscopic cholecystectomy was performed for the majority of the subjects (8) included in the study, out of which 4 subjects had a hospital stay between 6 to 10 days, 2 subjects had stay between 1 to 5 days, & other 2 subjects had stay between 11 to 15 days.

Laparotomy was performed for 2 of the subjects where both the subjects had a hospital stay between 6 to 10 days.

Hernioplasty was performed for total of 5 subjects where all the 5 subjects had a hospital stay between 6 to 10 days.

Laparoscopic cyst gastrostomy was performed for 2 subjects where 1 subject had hospital stay for 6 to 10 days & the other subject had a hospital stay between 16 to 20 days.

Diabetic foot surgery was performed for 1 subject & had a hospital stay between 6 to 10 days.

Hemorrhoidectomy was performed for 2 subjects where both the subjects had a hospital stay between 6 to 10 days.

Emergency debridement & fasciotomy was performed for 2 subjects where 1 subject had a stay between 6 to 10 days, & the other subject had a stay between 11 to 15 days. Total thyroidectomy was

performed for 3 subjects & all the 3 subjects had a hospital stay between 6 to 10 days.

Fistulotomy was performed for 1 subject & had a hospital stay between 6 to 10 days.

Soft tissue surgery was performed for 1 subject & had a hospital stay between 6 to 10 days.

Table 9: Distribution of type of surgery with length of stay

Type of Surgery	Length of Hospital Stay (days)			
	1 to 5	6 to 10	11 to 15	16 to 20
Modified Radical Mastectomy	1	2	0	0
Laparoscopic or Open retro rectus mesh	1	1	0	0
Laparoscopic Cholecystectomy	2	4	2	0
Laparotomy	0	2	0	0
Hernioplasty	0	5	0	0
Laparoscopic Cyst gastrostomy	0	1	0	1
Diabetic Foot surgery	0	1	0	0
Haemorrhoidectomy	0	2	0	0
Emergency debridement & fasciotomy	0	1	1	0
Total Thyroidectomy	0	3	0	0
Istulotomy	0	1	0	0
Soft tissue surgery	0	1	0	0

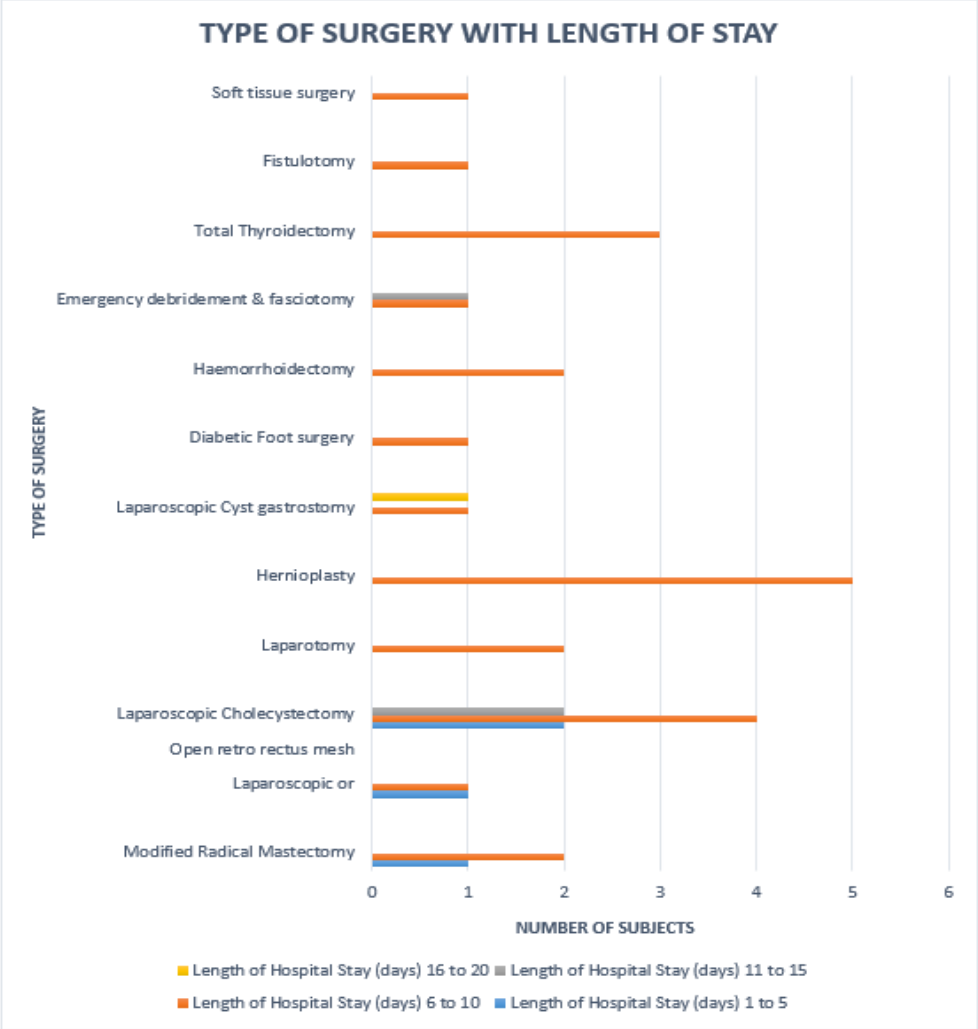

Figure 9: Distribution of type of surgery with length of stay

Distribution of Subjects with the Length of Stay & Number of Days Drug Administered:

Out of 32 subjects included in the study, TXA was administered to the subjects for a minimum of 1 day to maximum of 5 days depending on the severity of the bleeding, majority of the subjects (12) was administered with TXA for 3 days, 9 subjects received TXA for 2 days, 8 subjects received TXA for 4 days, 2 subjects received TXA for 1 day & only 1 subject with complicative bleeding received TXA for 5 days.

In Subjects who was administered with TXA for 1 day, both the 2 subjects had a hospital stay between 6 to 10 days.

Out of 9 subjects who was administered with TXA for 2 days, 2 subjects had stay between 1 to 5 days, 6 subjects had stay between 6 to 10 days, & 1 subject had stay between 11 to 15 days.

Out of 12 subjects who was administered with TXA for 3 days, 1 subject had a hospital stay between 1 to 5 days, 9 subjects had a stay between 6 to 10 days, 1 subject had a stay between 11 to 15 days & 1 more subject had a stay between 16 to 20 days.

Out of 8 subjects who was administered with TXA for 4 days, 1 subject had stay between 1 to 5 days, 6 subjects had a stay between 6 to 10 days, 1 subject had stay between 11 to 15 days.

1 subject was administered with TXA for 5 days & had a hospital stay between 6 to 10 days.

Table 10: Distribution of length of stay with number of days drug administered

Number of Days drug administered	Length of Hospital stay(days)			
	1 to 5 days	6 to 10 days	11 to 15 days	16 to 20 days
One	0	2	0	0
Two	2	6	1	0
Three	1	9	1	1
Four	1	6	1	0
Five	0	1	0	0

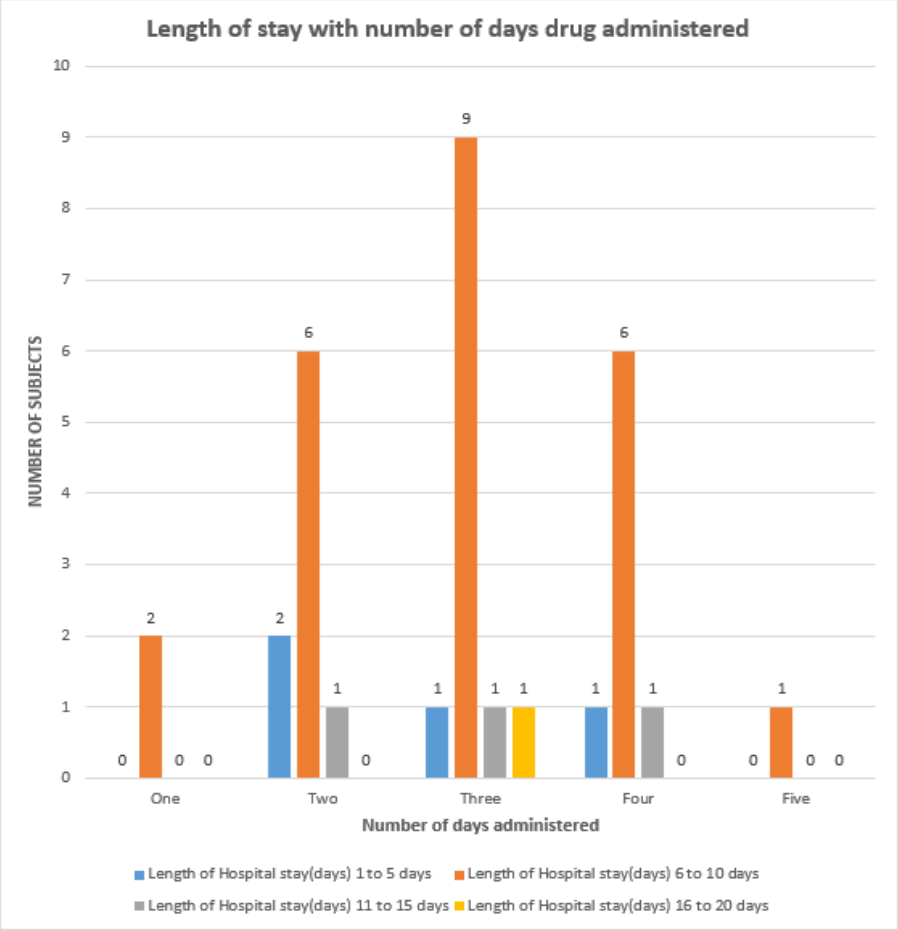

Figure 10: Distribution of length of stay with number of days administered

DISCUSSION

In this study, 32 subjects were included for which 12 different type of surgeries was performed, modified radical mastectomy was performed for 3 subjects diagnosed with breast cancer out of which 2 subject had a hospital stay between 5 to 10 days & 1 subject had a hospital stay between 1 to 4 days. Laparoscopic or open retro rectus mesh was performed for 2 subjects out of which 1 subject had a hospital stay between 1 to 4 days & the other subject had a stay between 5 to 10 days. Laparoscopic cholecystectomy was performed for the majority of the subjects (8) included in the study, out of which 4 subjects had a hospital stay between 5 to 10 days, 2 subjects had stay between 1 to 4 days, & other 2 subjects had stay between 11 to 20 days. Laparotomy was performed for 2 of the subjects where both the subjects had a hospital stay between 5 to 10 days. Hernioplasty was performed for total of 5 subjects where all the 5 subjects had a hospital stay between 5 to 10 days. Laparoscopic cyst gastrostomy was performed for 2 subjects where 1 subject had hospital stay for 5 to 10 days & the other subject had a hospital stay between 20 to 30 days. Diabetic foot surgery was performed for 1 subject & had a hospital stay between 5 to 10 days. Hemorrhoidectomy was performed for 2 subjects where both the subjects had a hospital stay between 5 to 10 days. Emergency debridement & fasciotomy was performed for 2 subjects where 1 subject had a stay between 5 to 10 days, & the other subject had a stay between 11 to 20 days. Total thyroidectomy was performed for 3 subjects & all the 3 subjects had a hospital stay between 5 to 10 days. Fistulotomy was performed for 1 subject & had a hospital stay between 5 to 10 days. Soft tissue surgery was performed for 1 subject & had a hospital stay between 5 to days. The following comparison between type of surgery & length of hospital stay was statistically analyzed using Chi-square test. Actual range is the range of data that contains observations to test against expected values, expected range is the range of data that contains the ratio of product of row totals & column totals to the grand total. After analyzing the actual range with expected range, the formula result was found to be 1 which is the Chi-Square score. Returns the test for independence: the value from the Chi-squared distribution for the statistic & the appropriate degrees of freedom. The degree of freedom was calculated using the following formula: Degrees of freedom in the DF box (DF = (NColumns-1) * (NRows-1) for chi-square test for independence) & DF was found to be 33. After converting the chi-square score to P-value, With the significance level of 0.05 the P-value was found to be 1. The result is not significant at $P < 0.05$ Since the P value is greater than 0.05 the result is not significant. Out of 32 subjects included in the study, TXA was administered to the subjects for a minimum of 1 day to maximum of 5 days depending on the severity of the bleeding, majority of the subjects (12) was administered with TXA for 3 days, 9 subjects received TXA for 2 days, 8 subjects received TXA for 4 days, 2 subjects received TXA for 1 day & only 1 subject with complicative bleeding received TXA for 5 days. In Subjects who was administered with TXA for 1 day, both the 2 subjects had a hospital stay between 5 to 10 days. Out of 9 subjects who was administered with TXA for 2 days, 2 subjects had stay between 1 to 4 days, 6 subjects had stay between 5 to 10 days, & 1 subject had stay between 11 to 20 days. Out of 12 subjects who was administered with TXA for 3 days, 1 subject had a hospital stay between 1 to 4 days, 9 subjects had a stay between 5 to 10 days, 1 subject had a stay between 11 to 20 days & 1 more subject had a stay between 20 to 30 days. Out of 8 subjects who was administered with TXA for 4 days, 1 subject had stay between 1 to 4 days, 6 subjects had a stay between 5 to 10 days, 1 subject had stay between 11 to 20 days. 1 subject was administered with TXA for 5 days & had a hospital stay between 5 to 10 days. The following comparison between number of days administered & length of hospital stay was statistically analyzed using Chi-square test. Actual range is the range of data that contains observations to test against expected values, expected range is the range of data that contains the ratio of product of row totals & column totals to the grand total. After analyzing the actual range with expected range, the formula result was found to be 0.999999992 which is the Chi-Square score. Returns the test for independence: the value from the Chi-squared distribution for the statistic & the appropriate degrees of freedom. The degree of freedom was calculated using the following formula: Degrees of freedom in the DF box (DF = (NColumns-1) * (NRows-1) for chi-square test for independence) & DF was found to be 12. After converting the chi-square score to P-value, With the significance level of 0.05 the P-value was found to be 0.999986. The result is not significant at $P < 0.05$. Since the P value is greater than 0.05 the result is not significant.

LIMITATIONS

The study has certain limitations

1. The study was carried out for a short duration of time.
2. The samples available was too less to be implicative to a result related to general population.
3. The study was carried out in a single hospital.
4. The data was collected from a single hospital & it may not be a representative of the pattern across the city or across India.
5. The study was carried out only in the In-patient department of Surgery.

CONCLUSION

The current study, which focused on patients who underwent surgery and received tranexamic acid, was carried out in a tertiary care teaching hospital. By temporarily blocking the lysine binding sites on plasminogen molecules, tranexamic acid [TXA], a synthetic lysine derivative, inhibits fibrinolysis. It is a member of the antifibrinolytic drug subclass and works

to encourage blood coagulation, thereby reducing bleeding. When used during a variety of surgical procedures, tranexamic acid significantly reduces blood loss. From this study, we can infer that most of the subjects received TXA after surgery, indicating that the majority of blood loss occurs after surgery, as none of the study subjects received TXA preoperatively. During the study, a high prevalence of patients who underwent laparoscopic cholecystectomy had a higher rate of receiving TXA. Out of the 12 different types of surgeries carried out, we can draw the conclusion that patients who received TXA had shorter hospital stays regardless of the surgery's type; the majority of subjects had stays between 5 and 10 days, and the majority of the subjects received TXA for 3 days regardless of the surgery's type. If a patient bleeds after surgery, the medication can be given, according to this study, and TXA had no negative effects on any of the subjects. It is clear from this study that if the surgical bleeding does not stop after some time, an antifibrinolytic TXA is required to stop the bleeding postoperatively. According to the results of the current study, the surgeons at the ESI hospital prefer the antifibrinolytic drug tranexamic acid for stopping post-operative bleeding. This medication is typically prescribed for 1 to 3 days.

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