

Evaluating the Efficacy of Topical Tranexamic Acid in Neck Dissection to Reduce Post-Operative Drain Output: A Randomized Controlled Trial

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ABSTRACT

Objectives: To assess efficacy of topical “tranexamic acid (TXA)” in neck dissection to reduce drain output.

Study Design: Randomized Controlled Trial (IRCT 20231019059765N1).

Place and Duration of Study: Oral & Maxillofacial Surgery Department of CMH, Lahore Medical College & Institute of Dentistry, Lahore Pakistan, from Aug 2023 to Mar 2024.

Methodology: Fifty patients who were scheduled to undergo “supraomohyoid neck dissection” due to malignancy of oral cavity, head or neck were included in the study and were divided into “TXA Group” and “control Group”. Drain output, intraoperative and post-op parameters were assessed and compared between Groups. Data was analyzed by SPSS 22.00.

Results: Median age was 53.00 (81.00 – 25.00) years. There were 38(76.00%) males and 12(24.00%) were females. Mean drain output in “TXA Group” was 194.56±25.47ml while in “control Group” it was 301.48±49.53ml, ($p<0.001$). Mean duration of drain removal in “TXA Group” was 5.08±0.99 days while in “control Group” it was 8.72±2.18 days, ($p<0.001$).

Conclusion: Topical “TXA” effectively reduces drain output after neck dissection.

Keywords: Neck dissection, Surgical wound infection, Topical, Tranexamic acid.

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INTRODUCTION

Cancer is always a major source of mortality and distress among the ailing patients, particularly, when it involves the visible areas of the body like head, oral cavity and the neck. Amongst malignancies of this region of the body, “oral squamous cell carcinoma (OSCC)” is the most widely encountered, which in Pakistan, has the incidence reported to be among the highest in the world at an approximate of 27.03 per 100,000 population.¹ Like most cancers, malignancies of this region have multiple factors that increase the propensity of their development including alcohol usage, smoking, chewing of certain non-food substances (like arica or beetle nut),² genetic predisposition³ and infection of the “Epstein-Barr virus (EBV)” which has particular significance in the cancer of the nasopharynx.⁴

One of the major and most initial clinical presentation of malignancies of the head and neck regions of the body is the enlargement of cervical lymph nodes located in the neck. Different structures in the mouth, head and neck region, like the lips, nose,

salivary glands, palate, and other structures drain primarily into these nodes located within the neck and the enlargement of these nodes is due to the spread of tumor.⁵ For this reason, “neck dissection (ND)” is considered as a widely acceptable procedure not only to determine the extent of spread of the head and neck malignancies but also to treat these cancers.⁶ This surgical procedure of neck is associated with myriad of complications including formation of hematoma, development of seroma and infection at the operation site which can delay the healing of surgical wound and to prevent it “closed suction drain placement” is considered highly useful.⁷ Concurrently, measures should be adopted that can provide reduction in the “drain output” and facilitate its early removal as this can speed up the process of healing of surgical wound.⁸

One such measure that has been hypothesized to reduce the “drain output” after the neck dissection is “topical tranexamic acid (TXA)”, however, previous literature have reported quite opposing results. A study reported that use of “topical TXA” can significantly reduce the “drain output” and facilitate earlier drain removal in patients who undergo “neck dissection (ND)” for malignancies of head and neck ($p<0.01$).⁹ On the other hand, a study found no

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significant role of “topical TXA” in reducing the “drain output” in patients who underwent malignancy related “neck dissection (ND)”, ($p=0.54$).¹⁰ Therefore, to address these controversial results this study was conducted with the objective to assess efficacy of “topical tranexamic acid (TXA)” in “neck dissection (ND)” to reduce drain output.

METHODOLOGY

This randomized controlled trial (IRCT 20231019059765N1) was conducted at “Oral & Maxillofacial surgery department of CMH, Lahore Medical College & Institute of Dentistry Lahore, Pakistan from August 2023 to March 2024” (ERB #: 683/ERC/CMH/LMC). Appropriate sample size was calculated using the formula. For calculations, following assumptions were used; “level of significance of 5%”, “power of 99%” and “anticipated mean drain output in TXA Group” of 208.29 ± 84.18 ml and “anticipated mean drain output in control Group” of 344.56 ± 110.93 ml.⁹ This gave a sample size of 50 (25 in each Group).

$$n = \frac{2\sigma^2(z_{1-\alpha/2} + z_{1-\beta})^2}{(\mu_1 - \mu_2)^2}$$

Inclusion Criteria: Patients were over the age of 18 years, both males and females, without any significant morbidity, who were scheduled to undergo “supraomohyoid neck dissection” due to malignancy of oral cavity, head and neck were included.

Exclusion Criteria: Patients who had evidence/history of previous thromboembolic disorder, history of hypercoagulability disease, history of bleeding disorder, pregnant women and hypersensitivity to “tranexamic acid (TXA)” were excluded.

Patients were selected by using “non-probability consecutive sampling technique”. Baseline characteristics of the patients including age, gender and laterality of neck dissection were documented. All patients received preoperative evaluations according to the established protocol at “CMH, Lahore” with preliminary hematologic investigations (like complete blood count, renal/hepatic function tests and coagulation profile), electrocardiogram (ECG) and an X-ray of the chest. After that, primary researcher explained patients regarding the surgical procedure and the purpose of study. Patients were then randomly (using randomizer mobile application) divided into two equal Groups of 25 patients each namely “TXA Group” and “control Group”. Only the patients were blinded regarding the Group assigned to

them while operating team knew drug status. All the procedures were performed under general anesthesia, induced and maintained by a consultant anesthesiologist with minimum 2 years of experience. All the surgeries were performed by a single surgical team headed by a senior surgeon having more than 10 years of experience by utilization of standard “modified Crile’s incision” followed by dissection with the help of cautery.⁹ Intraoperative parameters including the “operative time” and “number of lymph nodes resected” were documented by primary researcher. Once hemostasis was achieved, in “TXA Group”, 20ml of topical “tranexamic acid (TXA)” solution was sprayed over the field of operation which was prepared by taking 5ml injection of TXA having a concentration of 100mg/5ml and diluting it into 15ml of normal saline while in “control Group” equivalent amount of normal saline was sprayed. After this, a closed suction drain was placed at the operative site and closing of neck wound was performed using standard “two layers suturing” technique. “Drain output (in ml)” was documented on daily basis till the removal of drain by primary researcher. Criteria which was set for drain removal was “presence of <20ml drain output for two consecutive days”. Number of days after which drain was removed was also documented by primary researcher. After this patients were discharged for home and were followed up till day 30 of “neck dissection” to observe for any post-procedural complications. In case of any complication, appropriate care as per patient’s need and consultant surgeon’s opinion was administered to the patients.

A CONSORT diagram below exhibits the PICO protocol used in this trial (Figure).

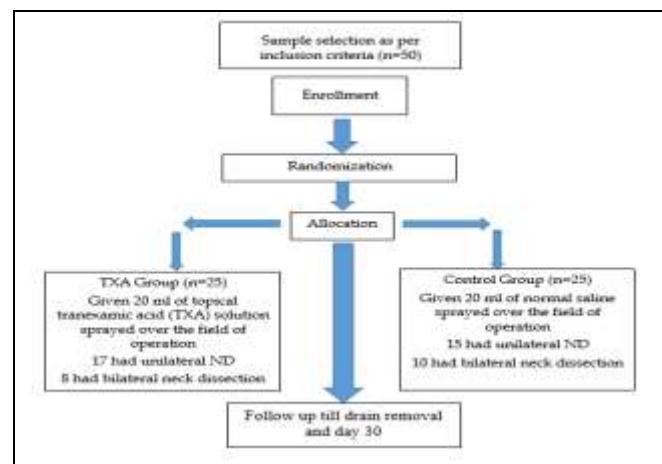


Figure: CONSORT Flow Diagram

Data analysis was performed using Statistical package for Social Sciences version 20. Age found to be non-normally distributed so median was calculate for age. Quantitative data was represented using Mean $\pm$ SD. Qualitative data was represented by using percentage and frequency. Comparison of qualitative variables between Groups was performed using Chi-square test while for quantitative variables, Sample t-test was used. The $p \leq 0.05$ was taken as significant.

RESULTS

In this study, 50 patients (25 in each Group) were included. Median age was 53.00 (81.00 – 25.00) years. There were 38(76.00%) males and 12(24.00%) were females. 32(64.00%) patients had unilateral neck dissection while 18(36.00%) had procedure bilaterally. Comparison of baseline characteristics between Groups is summarized in tabulated form in Table-I.

Table-I: Comparison of baseline Characteristics between Groups (n=50)

Characteristic	Tranexamic Acid Group (n=25)	Control Group (n=25)	p-value
Median age	51.00 (81.00 – 25.00) years	59.00 (81.00 – 25.00) years	0.580
Gender			
Male	19(76.00%)	19(76.00%)	1.000
Female	6(24.00%)	6(24.00%)	
Laterality of neck dissection			
Unilateral	17(68.00%)	15(60.00%)	0.556
Bilateral	8(32.00%)	10(40.00%)	

Table-II: Comparison of Intra and Post-Operative parameters between Groups (n=50)

Characteristic	Tranexamic Acid Group (n=25)	Control Group (n=25)	p-value
Mean operative time	256.56 $\pm$ 35.20 min	256.32 $\pm$ 38.38 min	0.982
Median number of lymph nodes resected	24.00(27.00–18.00)	24.00(29.00–18.00)	0.961
Mean drain output	194.56 $\pm$ 25.47ml	301.48 $\pm$ 49.53ml	<0.001
Mean duration of drain removal	5.08 $\pm$ 0.99 days	8.72 $\pm$ 2.18 days	<0.001
Complication(s)			
Surgical wound infection	2(8.00%)	3(12.00%)	0.637
Seroma	0(0.00%)	1(4.00%)	0.312
Flap necrosis	1(4.00%)	2(8.00%)	0.552

Mean operative time in “TXA Group” was 256.56 $\pm$ 35.20 minutes while in “control Group” it was 256.32 $\pm$ 38.38 minutes, ($p=0.982$). Mean number of lymph nodes resected in “TXA Group” was 23.76 $\pm$ 2.25 while in “control Group” it was 23.84 $\pm$ 2.64 ($p=0.909$). Mean drain output in “TXA Group” was 194.56 $\pm$ 25.47ml while in “control Group” it was 301.48 $\pm$ 49.53ml, ($p<0.001$). Mean duration of drain removal in “TXA Group” was 5.08 $\pm$ 0.99 days while in “control Group” it was 8.72 $\pm$ 2.18 days, ($p<0.001$). None of the patient of either Group developed hematoma.

Aforementioned and other outcome variables are summarized in Table-II.

DISCUSSION

Cancers of head & neck constitute 7th most common type of malignancy across the globe with predominant histology of “squamous cell carcinoma (SCC)”.^{11,12} In earlier stages of the disease, surgical “neck dissection (ND)” plays a pivotal role in diagnosing, staging and managing patients suffering from cancer of this region.¹³ “Tranexamic acid (TXA)” which is an anti-fibrinolytic drug that acts by inhibiting activation of “plasminogen” through blocking the sites located on the molecules of “plasminogen” where “lysine” binds^{14,15} is considered to be helpful in reducing the post-operative drain output, however, when it comes to its role in reducing “drain output” after ND, literature has been quite controversial. Present study thus focused on answering this research question.

In present study, majority of patients who had malignancy were males. This male predominance have been observed in studies conducted by Manzoor *et al.*,¹⁶ Park *et al.*,¹⁷ and Tan *et al.*,¹⁸ all of which reported higher burden of head and neck cancers in males. In terms of laterality, operative time and mean number of LN being resected there was no significant difference between Groups. Compared to this, Anand *et al.*,⁹ reported that the drain output was significantly lowered by the use of topical TXA while performing ND for head and neck cancers which was similar to the findings of present study. This significant reduction in drain output after surgery has also been reported by Liang *et al.*,¹⁹ and Safran *et al.*,²⁰ but in their study this effect was observed in different types of surgical procedures. Thakur *et al.*,¹⁰ conducted a double-blinded RCT to determine the efficacy of topical TXA in reducing the post-op drain output and reported no role of topical TXA in reducing the “drain output” surgical procedures of head and neck. Compared to this, present RCT was a single blinded trial and exhibit a statistically significant benefit of using topical TXA to reduce post-op drain output. Additionally, topical TXA significantly reduced the duration taken to remove the placed drain at the surgical site, which was similar to findings of Safran *et al.*,²⁰ and Saito *et al.*,²¹ No statistical significance was observed between study Groups in terms of complications, including the SSI, seroma formation, hematoma formation and flap necrosis, within 30-days period after the surgery. This finding is consistent

with the results of studies conducted by Costain *et al.*,²² and Weissler *et al.*,²³ who reported no significant impact of use of TXA in reduction of post-operative complications.

Based on findings of present study, it is clearly evident that use of “topical tranexamic acid (TXA)” plays a crucial role in reducing the “drain output” in patients who undergo “neck dissection (ND)”. Therefore, its use is strongly recommended in future among patients undergoing ND. There were a few limitations of present study including limited sample size, study being confined to single institution and smaller follow up period.

CONCLUSION

In conclusion, utilization of “topical tranexamic acid (TXA)” for reduction of drain output in patients who undergo neck dissection for managing malignancy of oral cavity, head or neck is highly effective.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MAI & AAC: Data acquisition, data analysis, critical review, approval of the final version to be published.

HMJM & MS: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MBN & MAP: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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