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RESEARCH ARTICLE

PROSPECTIVE RANDOMIZED STUDY ON EFFECT OF TRANEXAMIC ACID ON WOUND DRAINAGE FOLLOWING MODIFIED RADICAL MASTECTOMY FOR CANCER BREAST

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ABSTRACT

A prospective randomized study has shown that, in 50 women with breast cancer undergoing modified radical mastectomy with level III axillary clearance, perioperative and postoperative administration of tranexamic acid 1 g three times daily resulted in a significant reduction in the mean postoperative drainage volume compared with patient not receiving tranexamic acid (781.4±248.64 vs. 1023±196.3ml; p<0.001). The frequency of post drain seroma formation was increased by tranexamic acid administration (44% vs. 20%). None of the patient developed hematoma, flap necrosis in both the groups. Three patients developed wound infection in the study group and none in the control group. Two patients developed wound dehiscence in study group while 1 in the control group. Stage of breast carcinoma, total number of nodes dissected and number of lymph nodes positive for metastatic diseases does not effect the seroma formation. Tranexamic acid may be used for longer duration to reduce the frequency of postoperative wound complications following surgery for breast cancer.

INTRODUCTION

The most common morbidity after MRM is formation of seroma. Other more serious complications, including flap necrosis, delayed healing of wound, impaired shoulders functions and lymphedema are frequently a consequence of seroma formation. The exact etiology of seroma formation remains controversial but it is considered to be the collection of liquefied fat, serum, inflammatory exudates and lymphatic fluid under skin flap. The fluid is serosanguinous in immediate postoperative period and later on usually it becomes clear, yellow, somewhat viscus (Dayton, 2004). The amount and duration of seroma formation varies and influenced by many factors like extent of mastectomy (Hashemi *et al.,* 2004) extent of lymphnode dissection and method of raising the skin flap such as electrocautery or knife (Porter *et al.,* 1998). Drains are placed under the flaps to remove this seroma postoperatively which usually persist for few days but in certain patients it continuous for many days and drain are kept for longer periods. In some patients the seroma is collected under the flaps even after removal of drains, which needs repeated aspirations by syringe or some times by tube drainage. Thus seroma can be categorized as postoperative "total wound drainage" and delayed flap collection after removal of drains which is called "seroma". The incidence of seroma formation is 30% (Bland *et al.,* 2005).

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Fibrinolytic activity of the plasmin system in serum and lymph may contribute to fluid accumulation in the dead space under the skin flap and in the axillary fossa. Fibrin complexes already formed within and around vessels may be degraded, resulting in further leakage of blood and lymph from the vessels. Tranexamic acid (trans-4 aminomethylcyclohexanecarboxylic acid, of molecular weight 157.2 Da) is a synthetic antifibrinolytic agent. Structurally it resembles ε-aminocaproic acid but is ten times more portent. Fibrinolysis is inhibited by blockade of plasminogen activation. Tranexamic acid also has a direct antiplasmin action, inhibiting fibrin degradation.

Patients and Methods

The present study was conducted to evaluate the perioperative and postoperative use of tranexamic acid on total wound drainage after modified radical mastectomy. This study included 50 patients of MRM performed in the department of Surgery and Oncosurgery, Pt. B.D. Sharma PGIMS, Rohtak. They were divided into two groups of 25 cases each. In Group-I (study group) received tranexamic acid in perioperative and postoperative period while Group II (control group) patient did not receive tranexamic acid. Patients were excluded who had any history of thromboembolic events, severe varicose veins, coagulation disorders or are receiving anticoagulant drugs.

MATERIALS AND METHODS

Group-I- Tranexamic acid (1gm 8 hourly) was given perioperatively and continued in the postoperative period upto 5th postoperative day. Initially it was given intravenously (1gm 5 ml / 8 hourly). First dose was given initially on the induction of anaesthesia and continued until the 5th day after surgery.
Group-II (Control) all the modified radical mastectomy cases not receiving tranexamic acid.

Surgical Technique

All the modified radical mastectomy were done by same oncosurgeon using electrosurgical cautery. Amount of blood loss and blood transfusion given during surgery were recorded. Two drains were placed, anterior one under the skin flaps and posterior one in axillary fossa. Anterior drain was removed on 4th postoperative day and posterior drain was removed when wound drainage was less than 30ml/24 hours. The amount of seroma fluid in the form of total wound drain was recorded daily. Patients were followed up for 1 month after drain removal to observe any post drain seroma formation. Patients who developed post drain seroma were aspirated. Number of aspirations and amount of fluid was recorded every time. Patients who required any surgical management were also recorded. All the patients were also observed for wound infection, wound dehiscence and flap necrosis during postoperative period and follow up.

RESULTS

Patient's age, tumor size, neoadjuvant chemotherapy status and total number of lymph nodes isolated were similar in study group and treatment group (Table I). The mean (±S.D) duration of surgery in study group was significantly lower than in control group (57.76±12.69 minutes versus 65.36±6.42 minutes; p<0.001). The mean (±S.D.) amount of wound drainage was significantly lower in study group as compared to control group (781.4±248.64 versus 1023±146.3 ml; p<0.001). The mean (±S.D.) duration of drainage was also lower in study group as compared to control group (10.2±2.12 versus 13.72±2.40 days; p<0.001), this difference was significant (Table II).

Table I. Comparing both groups with regard to patient and tumor characterstics

Patient's characteristics	Group I (n=25) Study group	Group II (n=25) Control group
Total number of patients	25	25
Mean (±S.D.) age (years)	46.96±9.69	46.08±10.38
Tumour size (T_2-T_3)	20 (80%)	22 (88%)
Received neoadjuvant chemotherapy	7 (28%)	9 (36%)
Total number of lymph nodes isolated	15.36±3.77	14.32±3.97

Table II. Comparision of surgical variables in both groups

	Group I (n=25) Study group	Group II (n=25) Control group	P value
Mean duration of surgery (minutes)	57.76±12.69	65.36±6.42	<0.01
Mean amount of blood loss (ml)	70.64±14.56	88.72±13.26	<0.001
Mean amount of wound drainage (ml)	781.4±248.64	1023±196.3	<0.001
Mean duration of wound drainage (days)	10.2±2.12	13.72±2.40	<0.001

In our study there was no significant difference in study and control group in relation to amount of wound drainage in patient those received neoadjuvant chemotherapy and those who did not received neoadjuvant chemotherapy (Table III). In the present study it was also observed that there is no significant reduction in wound drainage in relation to number of lymph nodes isolated in both the groups (Table IV).

Table III. Comparison of Amount of wound drainage (Early Seroma) in Relation To neoadjuvant chemotherapy

	Mean amount of wound drainage	
	Group I (n=25) Study group	Group II (n=25) Control group
Neoadjuvant chemotherapy	872.85±193.88	1023.33±141.42
No neoadjuvant chemotherapy	705.33±305.36	1023.75±153.61

Table IV. Comparison of total Wound Drainage in Relation to Lymph Nodes Dissection

Number of lymph nodes	Mean amount of wound drain (ml)	
	Study	Control
<5	0	0
6-10	803.75±235.04	932.5±103.72
11-15	865±334.25	1041.25±162.81
16-20	894±229.77	1060.90±121.52

Table V. Other Postoperative Complications

	Group I (n=25) Study group	Group II (n=25) Control group
Seroma formation (post drain)	11	5
Within 14 days	6	5
After 14 days	5	0
Haematoma	0	0
Flap necrosis	0	0
Wound infection	3	0
Wound dehiscence	2	1

Postoperative complications as shown in Table V none of the patients in study group and control group had flap necrosis or haematoma. 11 (44%) patients in study group had seroma formation after removal of drains as compared to 5 (20%) patients in control group. Three patients of study group had wound infection compared to none in control group wound was managed by local drainage and antibiotics. Two patients of study group had wound dehiscence compared to 1 in the control group. As shown in Table V, five patients developed seroma within 14 days of removal of drains. All patients were managed by single aspiration.

In study group six patients developed seroma within 14 days of removal of drain which were managed by aspiration of seroma. Two patients required only single aspiration while one patient required aspirations twice. One patient needed corrugated tube drainage and the remaining two patients were managed by reinsertion of negative suction drainage. Among five patients who had seroma formation even after 14 days of drain removal, two patients needed only single aspiration while one patient needed two aspirations and one patient was aspirated three times. The fifth patient was managed by corrugated drainage. Tranexamic acid well tolerated during intravenous and oral administration without any side effects.

DISCUSSION

Seroma formation is the most frequent complication of MRM. The exact etiology of seroma formation remains controversial but certain factors like extent of mastectomy, extent of lymph node dissection and methods of surgical dissection influence the amount and duration of seroma formation. Several intervention have been reported with the aim to reduce seroma formation such as use of compression bandage, suction drains (Divino *et al.,* 2000), flap fixation with sutures (O'Dwyer *et al.,* 1991), sclerotherapy (Sitzmann *et al.,* 1983) and fibrin glue (Jain *et al.,* 2004; Moore *et al.,* 2001; Johnson *et al.,* 2005; Dinsmore *et al.,* 2000) to obliterate the dead space. However none of the them proved effective in controlling the seroma formation absolutely. Suction drains may not control the seroma formation but effectively drain it out and helps in fixing the flap and therefore it is a standard practiced to put close suction drains instead of simple drains after MRM. Recently tranexamic acid has been used systemically for controlling seroma formation by inhibiting the fibrinolytic action of plasmin system in serum and lymph and has shown promising results (Oertli *et al.,* 1994).

In the present study the amount of blood loss during surgery was significantly less in study group as compared to control group ($p<0.001$), so also the duration of surgery ($p<0.001$). Amount of seroma formation was also significantly less in study group as compared to control group and the closed suction drains were also removed early in study group as compared to control group ($p<0.001$). The stage of breast carcinoma, neoadjuvant chemotherapy, total number of nodes dissected and number of lymph nodes positive for metastatic diseases does not effect the seroma formation. Though the amount and duration of drain output was less in study group as compared to control group. But the late seroma formation after removal of drains was more in study group as compared to control group (44% vs. 20%). Also the patient in study group required repeated aspiration and even tube drainage for this late seroma. While the late seroma formation was treated by single aspiration in control group. None of the patients in both groups had either flap necrosis or haematoma. Three patients (12%) developed wound infection in study group and all these 3 patients required repeated aspiration for seroma which lead to infection of the wound. Two patients in study group had wound dehiscence, who also required repeated aspiration for their seroma, which resulted in wound dehiscence after wound infection. It is therefore concluded that tranexamic acid is effective in controlling the seroma formation when used perioperatively and postoperatively. The total wound drainage is reduced and drains can be removed early but there is increase in the incidence of late seroma formation, which was resistant to simple aspiration due to which the overall complication rate were higher in study group.

The possible explanation is that tranexamic acid was used only for 5 days, which resulted in less amount of seroma formation in early postoperative period but there was increase in late seroma formation when drug was stopped and by that time drains have been removed.

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