The role of tranexamic acid in breast and body contouring surgery: a literature review

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Keywords: breast surgery, plastic and reconstructive surgery, tranexamic acid, hematoma, seroma

Submitted: 23 November 2020 AEST. Accepted: 18 January 2021 AEST Published: 2022 March 31 AEST

DOI: https://doi.org/10.34239/ajops.v5n1.277

Australasian Journal of Plastic Surgery
Vol 5, Issue 1, 2022 | March 31 2022 AEST

Background
Postoperative seroma and haematoma are two of the most common complications following large surface area surgeries. The aim of this study is to review the literature to evaluate evidence for the use of tranexamic acid in reducing postoperative seroma and haematoma formation in breast surgery and body contouring surgery.

Method
A literature search was performed using MEDLINE®, the Cochrane Database of Systematic Reviews (CDSR), the Cochrane Central Register of Controlled Trials (CENTRAL), the Database of Abstracts of Reviews of Effect (DARE) and PubMed® in English from 1 Jan 1990–30 Mar 2020. The search terms ‘TXA’, ‘breast reduction’, ‘mammaplasty’, ‘breast implants’, ‘breast implantation’, ‘breast reconstruction’, ‘mastectomy’, ‘tissue expansion’, ‘body contouring’, ‘breast’ and ‘abdominoplasty’ were used alone and in combination.

Results
A total of six articles were found including three randomised controlled trials, two cohort studies and one retrospective study. Two ongoing trials were found on CENTRAL. No systematic reviews were found.

Conclusion
Literature surrounding the use of TXA in breast and body contouring surgery is sparse compared to what is available in other surgical subspecialties. The literature available shows promising results with the use of TXA in controlling haematoma, drainage volume and seroma formation in breast surgery and body contouring surgery with minimal morbidity in these patient groups.

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Introduction
Seroma and haematoma formation are well known complications following large surface area surgeries such as breast surgery and body contouring surgery. The aim of this study is to review the literature on the role of tranexamic acid (TXA) in reducing the risk of postoperative seroma and haematoma in surgical procedures of the breast and body contouring surgeries.

The seroma rate for breast surgeries varies greatly from 2.5–85 per cent, while haematoma rates range from 1–5 per cent. Similarly, the reported seroma rates following body contouring surgery are wide, ranging from 5–50 per cent. A recent systematic review of 14,061 patients exploring the complication profile of lipoabdominoplasty and abdominoplasty procedures reported a seroma rate of 4.1 per cent, and a haematoma rate of 0.8–1.3 per cent. Seroma and haematoma formation therefore remain unpredictable, potentially resulting in additional treatment and longer hospital stays.

The use of TXA has been widely reported in orthopaedic surgery, where it has been demonstrated to reduce the likelihood of blood transfusion by 33–37 per cent. Several meta-analyses have established no increased risk of major complications such as death, myocardial infarction, stroke, pulmonary emboli, deep vein thrombosis or renal dysfunction with the use of TXA perioperatively. A similar benefit has been demonstrated in cardiothoracic procedures, such as off pump coronary artery bypass surgery. A recent meta-analysis including multiple surgical disciplines demonstrated that a single preoperative dose of TXA significantly reduced perioperative blood loss and the risk of transfusion without increasing the risk of thromboembolic events.

While sufficient literature exists to support the role of TXA in other surgical subspecialties, the role of TXA in reducing perioperative blood loss, drainage volume and seroma risk in surgical breast procedures and body contouring procedures has yet to be established.

Methods
We performed a literature search using MEDLINE®, the Cochrane Database of Systematic Reviews (CDSR), the Cochrane Central Register of Controlled Trials (CENTRAL), the Database of Abstracts of Reviews of Effect (DARE) and PubMed® in English from 1 Jan 1990–30 Mar 2020. The search terms ‘TXA’, ‘breast reduction’, ‘mammaplasty’, ‘breast implants’, ‘breast implantation’, ‘breast reconstruction’, ‘mastectomy’, ‘tissue expansion’, ‘body contouring’, ‘breast’ and ‘abdominoplasty’ were used alone and in combination.

Results
Six articles were found from the search, of which there were three randomised controlled trials, two cohort studies and one retrospective study. Two current ongoing trials were found on CENTRAL. These trials are exploring the use of TXA in reconstructive and cosmetic breast surgery and its effects on bleeding and seroma formation [NCT02615366 and NCT03738527]. No systematic reviews were found.

Discussion
Tranexamic acid is a synthetic anti-fibrinolytic that reversibly binds to lysine-binding sites on plasminogen preventing its conversion to the active protease plasm. Plasmin aids in the formation of fibrin degradation products to dissolve blood clots. Fibrinolysis is hence inhibited by TXA, preventing the breakdown of clots. Tranexamic acid is inexpensive and simple to administer by various routes.

Dosing regimens are designed based on achieving sustained minimal plasma concentrations to effectively inhibit fibrinolysis. In vitro studies have shown that the minimum plasma concentration to inhibit fibrinolysis is 5 μg/ml in children and 10 μg/ml in adults. A recent meta-analysis including multiple surgical disciplines demonstrated that a single preoperative dose of TXA significantly reduced perioperative blood loss and the risk of transfusion without increasing the risk of thromboembolic events.

The intravenous delivery of TXA during major surgery has been shown to reduce the need for blood transfusions by 32–37 per cent, as well as significantly decrease the rate of postoperative bleeding by 34 per cent. Ausen and colleagues showed that the serum concentration stayed above 10 μg/ml for approximately 2.5 hours after 1 gm of TXA was given intravenously, which is sufficient for the majority of surgeries. Reported dosing regimens vary but a total dose of 1 gm has been found to be sufficient for most adults. There has been no evidence to support the use of higher doses. A recent meta-analysis by Heyns and colleagues demonstrated that a single preoperative intravenous dose of 10–20 mg/kg of TXA reduced perioperative blood loss by 153 mL per procedure and it also reduced the transfusion odds by 72 per cent. Reported regimens for the perioperative use
of intravenous TXA in surgical breast procedures are summarised in Table 1. There were no articles related to body contouring surgery and the use of intravenous TXA.

The role of topical TXA has been reported in multiple surgical disciplines as early as the 1970s. The topical use of TXA has been shown to be just as effective as parenteral administration in trauma and orthopaedic patients. Several recent studies have shown that the topical use of TXA can result in much lower peak serum concentrations. This has the theoretical benefit of minimising the risk of systemic thrombotic complications. Topical TXA will also result in lower cerebrospinal fluid (CSF) concentrations, effectively lowering the risk of seizures in susceptible patients.

Two main methods of topical application have been reported. Firstly, TXA has been delivered via wound drains as a bolus following wound closure. In this technique, serum concentrations ranging from 5–35 mg/ml have been reported. Secondly, TXA can be directly applied to the wound bed prior to wound closure with a 20 mL solution at a concentration of 25 mg/ml. Published regimens for the use of topical TXA in breast and body contouring surgeries are presented in Table 2.

### Postoperative drainage

Although not specific to surgeries of the breast, a systematic review and meta-analysis of 104 trials which compared blood loss with and without the use of TXA in surgical patients spanning multiple surgical subspecialties found a 34 per cent reduction in drainage. There is also consistent evidence to support the perioperative use of TXA to reduce drainage fluid more specifically in surgeries of the breast.

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### Table 1: Intravenous regimens for TXA use in surgical breast procedures

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Surgical specialty</th>
<th>Regime</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oertli D</td>
<td>1994</td>
<td>Oncologic breast</td>
<td>TXA 1 gm intravenous 8 hourly for 24 hours followed by 1 gm 8 hourly orally for a further 4 days (5 days total)</td>
<td>Significant reduction in postoperative drainage volume. Decreased rate (not significant) of seroma formation. Nil change in hematoma formation.</td>
</tr>
<tr>
<td>Knight H</td>
<td>2019</td>
<td>Oncologic breast</td>
<td>TXA 1 gm intravenous on induction</td>
<td>Significant reduction in risk of hematoma.</td>
</tr>
<tr>
<td>Lohani KR</td>
<td>2020</td>
<td>Oncologic breast</td>
<td>TXA single dose on induction (15 mg/kg) followed with 500 mg BD orally for 5 days</td>
<td>Significant reduction in axillary drainage with earlier removal of the drain. No significant change in seroma formation and wound related infection.</td>
</tr>
</tbody>
</table>

### Table 2: Topical regimens for TXA use in breast and body contouring surgeries

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Surgical specialty</th>
<th>Regime</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ausen K</td>
<td>2015</td>
<td>Plastic surgery: reduction mammoplasty</td>
<td>Wound moistened with 20 mL of TXA (25 mg/mL) before wound closure</td>
<td>Significant reduction in drain fluid production.</td>
</tr>
<tr>
<td>Ausen K</td>
<td>2019</td>
<td>Plastic surgery: body contouring</td>
<td>Bolus of 200mL (5 mg/mL) into wound cavity post wound closure (via drainage tubes). Moistening wound surface with 20 mL of TXA (25 mg/mL) prior to wound closure</td>
<td>Peak serum concentration approximately 5 µg/mL.</td>
</tr>
<tr>
<td>Ausen K</td>
<td>2020</td>
<td>Oncologic breast</td>
<td>Wound moistening with 20 mL of TXA (25 mg/mL) before wound closure</td>
<td>Significant reduction in drain production and earlier removal of drain. Increased rate of seroma aspiration in those undergoing lymph node clearance, but no increase in chronic seroma.</td>
</tr>
</tbody>
</table>
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The role of TXA in the reduction of post-surgical seroma is limited. The delineation between postoperative drainage, a seroma and a chronic seroma can be confused. For clarity, a seroma has been described as a collection of serum or lymph under skin flaps following drain removal, while a chronic seroma is a seroma still present at three months post-surgery. The evidence for the use of TXA in reducing the rate of seroma formation is limited. In their randomised controlled trial of 160 patients undergoing lumpectomy or mastectomy with axillary clearance, Oertli and colleagues conducted a second randomised controlled trial on the use of topical TXA in 202 mastectomy patients. Both studies showed a reduction in drainage volume after 24 hours by 39 per cent and 34 per cent respectively. The second larger trial of 202 mastectomy patients demonstrated an earlier removal of drains with the use of TXA. Finally, a randomised control trial by Oertli and colleagues of 160 patients undergoing lumpectomy or mastectomy with axillary clearance found a significant reduction in overall postoperative drainage volume of 35 per cent. These patients received three doses of 1 gm of TXA intravenously eight hourly followed by 1 gm eight hourly orally for a further four days. Although limited, this evidence would support the role of TXA in reducing post-surgical drain output in surgeries of the breast.

Seroma

The role of TXA in the reduction of post-surgical seroma is limited. The delineation between postoperative drainage, a seroma and a chronic seroma can be confused. For clarity, a seroma has been described as a collection of serum or lymph under skin flaps following drain removal, while a chronic seroma is a seroma still present at three months post-surgery. The evidence for the use of TXA in reducing the rate of seroma formation is limited. In their randomised controlled trial of 160 patients undergoing lumpectomy or mastectomy with axillary clearance, Oertli and colleagues found a significant reduction in the rate of seroma formation from 37 per cent to 27 per cent. Lohani and colleagues conducted a prospective double-armed non-randomised cohort study with 93 patients. They also found a reduction in seroma formation in the TXA group (19.1% vs 32.6%), however this was not statistically significant. In contrast, Ausen and colleagues published their randomised control trial of 202 mastectomy patients comparing topical moistening with TXA versus placebo. They found that in the subgroup of patients undergoing axillary lymph node dissection, the use of TXA paradoxically increased the cumulative seroma volume and these patients were more likely to require seroma aspiration. This, however, did not correlate with an increase in chronic seroma rates. The authors proposed that TXA could delay tissue adhesion and the healing of lymphatic vessels, resulting in these findings. Another potential explanation is that TXA is only given in the immediate perioperative period. The seroma-genic period for surgical wounds is likely to surpass this limited perioperative use of TXA. For patients prone to seroma production, the early use of TXA may simply mask early drainage volumes. This raises the question of the potential role of a more prolonged course of TXA in some surgical patients. The evidence to support the use of TXA to reduce seroma rates in surgeries of the breast is therefore mixed.

Haematoma

There is evidence to support the use of perioperative TXA to reduce the rate of haematoma formation in surgical patients. Although the evidence is limited, this is also true for surgeries of the breast. In their retrospective cohort study of 304 patients undergoing mastectomy with and without reconstructive procedures, Knight and colleagues demonstrated a significant reduction in haematoma formation. In this study, patients who received a single intravenous dose of 1 gm of TXA on induction of anaesthesia, had a post-surgical haematoma rate of 2.1 per cent compared to 7.5 per cent for patients who did not receive TXA. In 2015, Ausen and colleagues published their randomised controlled trial on the use of topical TXA in 30 reduction mammoplasty patients. In this study they recorded two haematomas in patients who did not receive TXA54 compared to no haematomas in the treatment group. This study was too underpowered to make this finding significant. However, later in 2020, Ausen and colleagues conducted a second randomised controlled trial of the use of topical TXA in 202 mastectomy patients. In the treatment arm there was a one per cent haematoma rate compared to seven per cent in the placebo arm. In contrast, Oertli and colleagues found no significant difference in the...
rate of postoperative haematoma with the use of TXA in their prospective randomised trial of 180 patients undergoing lumpectomy or mastectomy with axillary clearance. This study showed that haematoma formation was infrequent and similar in both groups, being unaffected by the use of TXA. 43 Although the literature appears to support the role of TXA in moderating the risk of haematoma formation in the breast surgery group, the evidence is limited and will require further research to establish a more accurate measure of the role of TXA in this context.

Safety of tranexamic acid

Among clinicians there remain reservations over the use TXA due to concerns of thrombotic complications, such as deep vein thrombosis (DVT), pulmonary emboli (PE), cerebrovascular accidents (CVA) and myocardial infarction (MI). There is sufficient evidence to demonstrate that there is no increased risk of DVT, PE or MI with the perioperative use of TXA. 32,57–60 For patients with recent MI, percutaneous coronary angioplasty or stent implantation, the use of TXA perioperatively should be used with caution and only after individual risk assessment.

There is, however, an increased risk of non-ischemic convulsive seizures with the use of TXA. 35 This occurs as TXA can cross the blood-brain barrier and cause hyperexcitability through its antagonistic action on y-aminobutyric acid type A receptors in the brain. 34 This effect has been shown to be dose-dependent with a significantly higher incidence of seizures occurring at higher doses of TXA. 55,61,62 In patients at risk of seizures, caution should be exercised with the use of TXA. In these patients, consideration should also be given to the use of topical TXA as this results in much lower plasma serum concentrations and similarly much lower cerebrospinal fluid (CSF) concentrations.

Conclusion

The perioperative use of TXA offers the promise of prevention of some of our most common surgical and post-surgical dilemmas, such as haematoma, prolonged drainage and seroma formation. The literature surrounding the use of TXA in the breast surgery and body contouring patient groups is sparse when compared to the available literature for the use of TXA in other surgical sub-specialities. Our search has demonstrated only six articles specific to the use of TXA in breast surgery and body contouring surgery. There are current trials seeking to help clarify this situation, however, the current use of TXA in the setting of breast surgery and body contouring surgery should be guided by the larger pool of evidence in other surgical subspecialties. Even still, the current literature shows promising results with the use of TXA in controlling haematoma, drainage volume and seroma formation, with minimal morbidity in the breast surgery and body contouring patient groups.

Although further research is required to substantiate its use, consideration should be given to the preferential delivery of TXA topically over other means as current literature would support its efficacy, while achieving lower plasma and CSF concentrations and effectively reducing the risk of complications.

Conflict of interest

The authors have no conflicts of interest to disclose.

Funding declaration

The authors received no financial support for the research, authorship, and/or publication of this article.
References


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