BLOOD CONSERVATION STRATEGIES IN SCOLIOSIS SURGERY

ARFAH HANIM BINTI MOHAMAD

DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTERS IN ANAESTHESIOLOGY

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No. Pendaftaran Penuh MPM 25311
Pensyarah Kanan
Jabatan Anestesiologi
Pusat Perubatan Universiti Malaya

ABSTRACT

BACKGROUND: Posterior spinal fusion for scoliosis surgery requires extensive operative time and may result to significant perioperative blood loss and the need of allogeneic blood transfusion. Allogeneic blood transfusion comes with infective and non-infective complications. To address this issue, multiple methods of blood conservation strategies are introduced and in this study we are reviewing the efficacy of tranexamic acid as a pharmacological approach and cell salvage technique as a non-pharmacological approach in reducing blood loss and requirement of allogeneic blood transfusion in scoliosis surgery

OBJECTIVES: The aim of this study is to calculate and analyse total blood loss and haemoglobin drop following the use of blood conservation therapy. We also analyse the efficacy of different tranexamic acid doses (high and low dose) in reducing blood loss and observe the use of cell salvage technique in relation to total blood loss in affecting the haemoglobin drop postoperatively. Other than that we also observe the incidence of allogeneic blood transfusion and hemodynamic stability following the use of both blood conservation strategies

METHODS: Eighty nine patients who underwent elective single-staged idiopathic scoliosis surgery (posterior repair only) in University Malaya Medical Centre, Federal Territory, Malaysia between 1st January 2016 to 31st August 2016 were retrospectively reviewed. Patients were divided into two groups, the high dose and low dose tranexamic acid group. Total Blood Loss was divided into two groups as well (total blood loss<= 900ml vs >900ml). Outcome measures include preoperative demographics, namely, age, sex, weight, height, blood volume, number of levels fused, radiographic parameters (preoperative Cobb angle) and preoperative haemoglobin; intraoperative data which

includes number of screws inserted, operative time, MAP, fluid requirements (crystalloid/colloid), estimated blood loss (EBL), number of patients requiring blood transfusion; postoperative data which includes drop of haemoglobin (0 hour Hb, 72 hour Post-op Hb) and duration of hospital admission post-surgery. Statistical analysis was done using IBM SPSS software version 24 to derive results and conform conclusions.

RESULTS: There are significant differences in the total blood loss between the 2 groups showing that patients who are in high dose tranexamic acid group have less total blood loss in comparison with the low tranexamic acid group (827.1ml vs 1041.7ml respectively) (p= 0.016). There are no significant differences elicited between haemoglobin drop (p= 0.260), post op 72 hours haemoglobin (p= 0.16) with the total blood loss. All patients received cell salvage blood transfusion and no patient required allogeneic blood products.

CONCLUSION: In this study, we established that high dose tranexamic acid is effective and beneficial in reducing blood loss and avoiding allogeneic blood transfusion in scoliosis surgery. All patients received cell salvage blood transfusion regardless of amount of blood loss and it is deem to be beneficial as there is similar haemoglobin drop and haemoglobin level 72 hours postoperatively in patients with blood loss of more than 900mls as compared to those with lower amount of blood loss. Both blood conservation strategies had effectively reduce blood loss, haemoglobin drop and avoid allogeneic blood transfusion following scoliosis surgery in this study.

ABSTRAK

LATARBELAKANG: Pembedahan 'posterior spinal fusion' untuk skoliosis mengambil masa yang lama dan boleh menyebabkan pendarahan yang banyak sepanjang tempoh pembedahan dan ini memerlukan transfusi darah 'allogeneic'. Transfusi darah 'allogeneic' boleh menyebabkan banyak komplikasi. Untuk menangani masalah ini, pelbagai cara seperti 'blood conservation strategies' telah diperkenalkan dan di dalam kajian ini, kami mengkaji keberkesanan tranexamic acid dan teknik 'cell salvage' untuk mengurangkan pendarahan dan juga mengelak atau mengurangkan transfusi darah 'allogeneic' semasa atau selepas pembedahan skoliosis

OBJEKTIF: Matlamat kajian ini adalah untuk mengira dan menganalisis jumlah pendarahan dan kemerosotan hemoglobin (sel darah merah) tiga hari selepas pembedahan setelah mengunakan strategi-strategi ini. Kami juga akan menganalisis kejituan pelbagai dos tranexamic acid (dos tinggi dan dos rendah) dalam mengurangkan pendarahan dan melihat sama ada penggunaan teknik 'cell salvage' berguna dalam mengurangkan kemerosotan kadar haemoglobin selepas pembedahan skoliosis. Selain daripada itu, kami juga mengkaji insiden pengunaan darah 'allogeneic' dan kestabilan hemodinamik selepas perlaksanaan 'blood conservation strategies'.

KAEDAH: Lapan puluh Sembilan pesakit mengalami pembedahan elektif ' posterior spinal fusion' di Pusat Perubatan Universiti Malaya dari 1 Januari 2016 ke 31 Ogos 2016 dikaji secara retrospektif. Pesakit dibahagi kepada dua kumpulan di mana sebahagian pesakit menerima dos tinggi traxemic acid dan sebahagian lagi menerima dos rendah. Jumlah pendarahan juga dibahagi kepada dua kumpulan (pendarahan kurang dan sama dengan 900ml berbanding pendarahan lebih dari 900ml). Demografik pesakit yang dikaji: sebelum pembedahan (umur, berat badan, tinggi, jumlah kandungan darah, jumlah 'levels

fused', sudut Cobb's, kadar haemoglobin); semasa pembedahan (jumlah skru, jangkamasa pembedahan, tekanan darah, pengunaan 'IV fluids', jangkaan pendarahan, jumlah pesakit yang memerlukan tranfusi darah allogeneic); selepas pembedahan (kadar haemoglobin (sejurus selepas pembedahan dan 72 jam selepas pembedahan, dan jumlah hari di dalam wad selepas pembedahan). Analisis statistic dijalankan dengan menggunakan IBM software versi 24.

KEPUTUSAN: Terdapat perbezaan yang ketara (significant differences) dalam jumlah pendarahan di antara kedua –dua kumpulan tranexamic acid di mana penggunaan dos tinggi tranexamic acid adalah lebih berkesan dalam mengurangkan pendarahan berbanding dos rendah (827.1ml berbanding 1041.ml) (p=0.016). Tiada perbezaan yang ketara dilihat Antara kemerosotan kadar haemoglobin (p= 0.260), kadar haemoglobin selepas 72 jam (0.160) berbanding jumlah pendarahan. Semua pesakit menerima transfusi 'cell salvage' manakala tiada pesakit yang memerlukan transfusi darah 'allogeniec'.

RUMUSAN: Dalam kajian ini, kami mendapati dos tinggi tranexamic acid lebih berkesan dalam mengurangkan pendarahan dan keperluan transfusi darah 'allogeneic'. Semua pesakit menerima transfusi 'cell salvage' tanpa megira jumlah pendarahan dan ini menyebabkan tiada perbezaan dalam kemerosotan kadar haemoglobin di antara pesakit yang mengalami pendarahan lebih dari 900ml dan pesakit yang mengalami pendarahan yang kurang daripada itu. Kedua-dua strategi ini telah berjaya dalam mengurangkan pendarahan, kemerosotan kadar haemoglobin dan juga mengelak dari transfusi darah 'allogeneic' di dalam pembedahan skoliosis.

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I would like to extend my gratitude to Prof Shahnaz and Dr,Chloe for their endless support and guidance. I would also like to thank Prof Kwan and Prof Chris, both whom are the primary surgeons for all patients in this study. Besides that I would like to thank Sister Tang for providing the list of subjects for this study and Mrs Sulwana who had assisted me through the statistical analysis of this study. Finally I would like to thank the record office staffs who had provide patient's records and informations.

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LIST OF SYMBOLS/ABBREVATIONS

<=	:	less or equal
>	:	more than
n	:	number
AAGBI	:	Assicoation of Anaesthetist of Great Britain and Ireland
AIS	:	Adolescent idiopathic scoliosis
EBL	:	Estimated blood loss
HIV	:	Human immunodeficiency virus
IV	:	Intravenous fluids
MAP	:	Mean arterial pressure
PTT	:	Partial thromboplastin time
RBC	:	Red blood cell
TXA	:	Tranexamic acid

CHAPTER 1: BACKGROUND

Posterior spinal fusion for scoliosis surgery requires extensive operative time and may result to significant perioperative blood loss and the need of allogeneic blood transfusion. In view of the infective and non-infective complications of allogeneic blood transfusion which will increase the morbidity and mortality of the patients, several blood conservation strategies has been introduced to address this issue. These include pharmacological and non-pharmacological approach. Pharmacological approach involves the use of tranexamic acid, aprotinin or desmopressin in reducing blood loss while non-pharmacological approach includes cell salvage technique, acute normovolemic or hypervolemic hemodilution, preoperative autologous donation, preoperative erythtopoietin.

There are many studies that looked into the efficacy of tranexamic acid of various doses in reducing blood loss and allogeneic blood transfusion requirement and positive results were obtained. Cell salvage on the other hand is more controversial in terms of the effectiveness in reducing allogeneic blood transfusion requirement. In this study we are reviewing the effectiveness of tranexamic acid as a pharmacological approach and cell salvage technique as a non-pharmacological approach in reducing blood loss and requirement of allogeneic blood transfusion in scoliosis surgery.

1.1: RATIONALE OF THIS STUDY

We aim to conclude the effectiveness and benefit of both blood conservation strategies, namely, tranexamic acid as the pharmacological approach and cell salvage technique as the non-pharmacological approach in reducing blood loss and allogeneic blood transfusion requirement. We will calculate and analyse total blood loss and haemoglobin drop following the use of blood conservation therapy. We also analyse the efficacy of different tranexamic acid doses (high and low dose) in reducing blood loss and observe the use of cell salvage technique in relation to total blood loss in affecting the haemoglobin drop postoperatively and subsequently avoid allogeneic blood transfusion. Other than that we also observe the incidence of allogeneic blood transfusion and hemodynamic stability following the use of both blood conservation strategies

CHAPTER 2: LITERATURE REVIEW

Scoliosis is a lateral curvature and rotation of the thoraco-lumbar vertebrae resulting rib cage deformity. The cause may be idiopathic or secondary to neuromuscular disease, infection, tumour or injury. Posterior spinal fusion is indicated and the aim of spinal deformity surgery is to correct the curve and fuse the spine, improving posture and halting the progression of pulmonary dysfunction.[1]

These operations may require prolonged operative times with extensive soft tissue dissection and significant perioperative blood loss. [2,3] There are many factors contributes to massive blood loss, namely, neuromuscular etiology, weight and height of the patient, poor nutritional status, severity of spinal deformity, number of spinal segments fused, surgical complexity including reoperation and more complex anterior or posterior approach, intraoperative arterial blood pressure control and dilutional coagulopathy.[4]

In order to address significant blood loss, allogeneic blood transfusions is needed and in extreme cases requires multiple units of allogeneic blood products. Despite significant improvements in the safety of allogeneic RBC transfusion, there still remains underlying risks such as allergic reactions and the risks of bacterial, malarial, HIV and hepatitis infections.[5] It is also associated with increased risk of tumour recurrence[6-8], postoperative infection[9-13], transfusion associated circulatory overload, acute lung injury[14], perioperative myocardial infarction[15], postoperative low-output cardiac failure[16], hypothermia, coagulopathy and increased mortality[17].

There are a lot of studies on multiple methods of reducing blood loss and the need of allogenic blood transfusion hence eliminate risks listed above. Examples of blood conservation strategies include non-pharmacological and pharmacological methods, namely, cell salvage technique, acute normovolemic or hypervolemic hemodilution, preoperative autologous donation, preoperative erythtopoietin[18] and the use of

pharmacological drug to reduce blood loss such as desmopressin,[19] aprotonin,[20] aminocaproic acid[21] or tranexamic acid.[19-20,22]

Cell salvage technique and autologous transfusion has been introduced dated back in 1818 and the first 'modern' cell saver was produced in the 1970s. The aim of cell salvage is to reduce or eliminate the need for allogeneic blood transfusion and the associated risks of infectious and non-infectious complications. The 2009 AAGBI guidelines identified indications for the use of intraoperative cell salvage, which includes anticipated blood loss of >1000 ml or >20% estimated blood volume, patients with a low haemoglobin or at increased risk of bleeding, patients with multiple antibodies or rare blood types, and patients with objections to receiving allogeneic blood such as Jehovah's witness.[23]

There are many potential complications in cell salvage technique, namely, non-immune haemolysis, air embolus, febrile non-haemolytic transfusion reactions, mistransfusion, coagulopathy, contamination with drugs, cleansing solutions and infectious agents, and incomplete washing leading to contamination with activated leucocytes, cytokines, and other microaggregates.[24] However, the risks of such complications have decreased with technical advances, staff training, and increasing experience with cell salvage.

There are multiple studies done to see the benefit of cell salvage technique in reducing the need of allogeneic blood transfusion. Many studies concluded the benefit of cell savage technique however, there is substantial amount studies which says otherwise. Siller et al. [25] studies cell salvage technique use in spinal fusion for idiopathic scoliosis and concluded that blood requirements for this procedure can be met less expensively and more reliably by merely donating one's own blood. Lisander et al. [26] and Abildgaard et al [27] also concluded that cell salvage technique is not sufficient to decrease the need for other blood transfusions in hip arthroplasty and major back surgery respectively.

Jeniffer et al [28] are not in favour of cell salvage technique as well and the study noted that if less than 500 cc of blood loss is expected, the cost of cell saver setup and personnel is not justified and the study found no correlation with benefit based on number of levels fused, diagnosis, or patient weight. These criteria are therefore not helpful in aiding the surgeon in planning for cell salvage setup.

On a contrary, Duffy et al [29] demonstrated a prospective study of the cost-effectiveness of cell salvage in a large teaching hospital and found cell salvage to be cost effective as they take into account the financial benefits of autologous transfusion such as reduction in allogeneic blood transfusion, reduced blood transfusion reactions, reduced postoperative infection rates, and shorter hospital length of stay.

A Cochrane Collaboration meta-analysis of studies published in 2006 studied the use of cell salvage for minimizing allogeneic blood transfusion and found that cell salvage was efficacious in reducing the need for allogeneic blood transfusion in adult elective surgery. Overall, the use of cell salvage reduced exposure to allogeneic blood transfusion by 39%, with an average saving of 0.67 units per patient. Cell salvage was found to be the most effective in orthopaedic surgery and had no negative impact on morbidity or mortality.[30]

Multiple studies on orthopaedic surgeries are in favour of cell salvage technique. One of the RCTs enrolled 100 patients, who had undergone total knee replacements and demonstrated that the use of intraoperative cell salvage reduced the requirement for allogeneic blood transfusion from 80% to 16%.[31] There is, however, no evidence that intraoperative cell salvage reduces allogeneic blood transfusion requirements or cost in adult posterior lumbar fusion surgery,[32,33] scoliosis surgery,[34] or operative treatment of acetabular fractures.[35]

Another mode of blood conservation strategy that will be discussed in this study is the use of tranexamic acid as a pharmacological approach in reducing blood loss and

blood transfusion requirement. Tranexamic acid is a lysine analogue antifibrinolytic drug that has been shown to reduce bleeding in cardiac surgery,[36] craniosynostosis surgery,[37] total joint arthroplasty,[38] obstetrical procedures and urologic procedures.[39] Many studies have been done and proven that tranexamic acid are widely used and beneficial in reducing blood loss in spine surgery as well.

A meta-analysis by Zhang et al.[40] done in 2014 elucidates the effectiveness of tranexamic acid in reducing blood loss and also discussed the related thrombotic complications. They concluded that the use of tranexamic acid is effective in reducing amount of blood loss, the volume of blood transfusion, the transfusion rate and postoperative PTT.

Recent retrospective study done by Daniel et al.[41] compared tranexamic acid dose, 10mg/kg loading dose followed by 1mg/kg/hr maintenance versus 50mg/kg loading dose followed by 5mg/kg/hr maintenance. The study concluded that high dose tranexamic acid is more effective than low dose tranexamic acid in reducing blood loss (by 30%), and blood transfusion requirement (by 60%). In terms of complications, both group show no differences in morbid event rates and thrombotic event.

In this study, the data obtained from the record noted tranexamic acid was given in bolus dose of 1g at the beginning of the surgery. When calculated according to weight, the dose ranges between 10mg/kg to 35mg/kg. The dose will be analyse in relation to the haemoglobin drop 72 hours post operatively. The effect of tranexamic acid use of two range of dosages devided as high and low tranexamic dose compounded with cell salvage technique as blood conservation strategy will be evaluated in terms of reducing blood loss and allogenic blood transfusion requirement in this study.

CHAPTER 3: METHODOLOGY

This is a retrospective study comprising of 89 patients diagnosed with AIS (adolescent idiopathic scoliosis) who underwent single staged posterior spinal fusion in the span of eight months between January 2016 to August 2016 and they were retrospectively reviewed. Since this was a retrospective study and the information of the patients was anonymized, no written informed consent was obtained from the participants. Subjects were between the ages of 10 to 35 years old. All patients were screened for renal insufficiency and coagulopathy prior surgery. The correction of AIS were performed by the same senior doctors and applied same surgical technique for all patients. There was no preoperative blood donation from all patients and cell savage autologous blood recovery system was applied in all subjects.

Outcome measures including preoperative demographics, namely, age, sex, weight, height, blood volume, number of levels fused, radiographic parameters (preoperative Cobb angle) and preoperative haemoglobin; intraoperative data which includes number of screws inserted, operative time, mean BP, fluid requirement (crystalloid/colloid), estimated blood loss(EBL), number of patients requiring blood transfusion; postoperative data which includes drop of haemoglobin (0 hour Hb, 72 hour Post-op Hb) and duration of hospital admission post-surgery.

Total blood loss is calculated by summing up estimated blood loss intra operatively and postoperative blood loss in drain. Estimated blood volume was calculated following Nadler's formula as described by Nadler et al.[42] All patients was given cell salvage autologous blood transfusion regardless amount of blood loss intraoperatively.

The standard tranexamic acid dose given was 1g for every patient and deriving various dosages in relation to patient's weight ranging between 10mg/kg to 35mg/kg. Tranexamic acid was given at a bolus dose following induction for all patients, there was

no maintenance infusion dose of tranexamic acid following that. Following the surgery, all patients were managed similarly. Blood sample for haemoglobin level was taken at 0 hour post-surgery through ABG sampling while the 72 hour postoperative hemoglobin blood sample was taken and sent to the biochemistry lab for testing.

Statistical analysis

This study involved 89 patients who underwent scoliosis surgery in UMMC from January 2016 to August 2016. Sample size was based on estimated blood loss (EBL) as an outcome variable of the study. Two means formula was used for sample size estimation since it involved two groups which comprised of high and low dose of tranexamic acid. By using the mean of low dose tranexamic acid group which was 968mls and the high dose tranexamic acid group was 695mls from previous study[41], we obtained effect size of 0.73 and considering 80% as power of study, a statistical power analysis indicated a minimum sample size of 62 subjects were needed. The calculation was performed using G*Power software (version 3.1.9).

Data obtained are tabulated in a computer files and analysed using IBM SPSS software version 24 to derive results and conform conclusions. A descriptive statistics of the socio demographic characteristics were initially done to evaluate the distribution, normality and homogeneity of the data. Descriptive analysis included frequency and percentage distribution for categorical variables and mean and standard deviation for numerical variables. Statistical analysis was followed by independent t-test to determine relationship between two ranges of tranexamic acid (high dose and low dose range) in reducing blood loss, haemoglobin drop and requirement of allogenic blood transfusion. The relationship between cell salvage autologous transfusion with haemoglobin drop and allogenic blood transfusion requirement were analysed through this test. Correlation test were performed to determine the relationship of patient's demographics and tranexamic

acid groups were analysed as well. Results were considered statistically significant with a p value less than 0.05.

CHAPTER 4: RESULTS

There were 89 patients who were diagnosed with AIS underwent posterior spinal fusion in between 1st January 2016 to 31st August 2016 and all were reviewed in this study. All patients obtained normal renal function test, coagulation profile and platelet concentration prior operation. All patients was given general anaesthesia with standard monitoring and goal mean arterial pressure of 60-75mmHg and postoperative patient controlled analgesia morphine (PCAM) for pain management. There was no major complications sustained intraoperatively or postoperatively in all patients. The patients were divided into two groups, there were 55 patients in high dose tranexamic acid group (20.1mg/kg to 35mg/kg) and 34 patients in low dose tranexamic acid group (10mg/kg to 20mg/kg).

There were significant differences between age, weight and blood volume in between the two groups, whereas there is no significant differences in the other demographics of patients (Cobb's angle, number of levels fused, Pre op haemoglobin, post op haemoglobin at 72 hours, surgical durations) in the two groups. The mean age group in the TXA high and low dose group are 15 and 18 respectively, while the mean weight is 42kg and 57kg respectively ($p = <0.001$). There are significant differences between the two groups as dose between the two groups are calculated according to patient's weight. Age and blood volume is associated with weight, hence both demographics has significant relationship with both groups as well ($p = 0.009$ and $p < 0.001$ respectively). Surgical demographics of patients exhibit similar means between the 2 groups, including Cobb's angle ($p = 0.192$), number of levels fused ($p = 0.523$), preoperative haemoglobin ($p = 0.260$), post op 72 hours haemoglobin ($p = 0.176$) and surgical duration ($p=0.154$) (Table 4.1).

Table 4.1: Mean demographics data of patients in both groups (TXA high and low dose group)

Data	TXA (high dose) group (n=55)	TXA (low dose) group (n=34)	*p* value
Age (years)	15.3 ± 4.0	18.4 ± 6.8	0.009
Weight (kg)	42.0 ± 4.3	57.2 ± 7.7	<0.001
Blood volume (mls)	2950.7 ± 275.1	3655.8 ± 415.0	<0.001
Cobb's angle (°)	60.1 ± 14.3	64.2 ± 14.4	0.192
Number of levels fused	11.0 ± 2.4	10.6 ± 2.7	0.523
Pre op Hemoglobin (g/dL)	13.3 ± 1.2	13.9 ± 1.18	0.260
Hemoglobin 72 hours (g/dL)	10.7± 1.31	11.2 ± 1.5	0.176
Surgical duration (minutes)	132.1 ± 35.8	142.8 ± 31.8	0.154

Table 4.2 exhibits that there is a significant differences in total blood loss between the 2 groups showing that patients who are in high dose tranexamic acid group have less total blood loss in comparison with the low tranexamic acid group (827.1ml vs 1041.7ml respectively) (p= 0.016). No patients received allogeneic transfusion in this study. No significant differences elicited in terms of mean MAP (p= 0.628) haemoglobin drop (p= 0.07), post op 72 hours haemoglobin (0.196), surgical duration (p= 0.303) and hospital stay (p= 0.427).

Table 4.2: Measured outcomes of patients in both groups (TXA high and low dose group)

Data	TXA (high dose) group (n=55)	TXA (low dose) group (n=34)	*p* value
Mean MAP (mmHg)	72.1 ± 2.3	72.6 ± 2.5	0.628
Allogenic blood transfusion	0	0	<0.001
Total blood loss (mls)	827.9 ± 372.7	1041.7 ± 580.9	0. 016
Hb drop (g/dL)	2.5 ± 0.9	2.7 ± 1.4	0.070
Post op Hb 72 hours (g/dL)	11.2 ± 1.5	10.8 ± 1.2	0.196
Surgical duration (minutes)	132.1 ± 35.8	142.8 ± 31.8	0.303
Hospital stay (nights)	3.5 ± 0.7	3.5 ± 0.7	0.427

The differences in total blood loss between the low and high TXA dose group are shown in Table 4.3. The low dose group had a mean total blood loss of 1041.7mls compared with the high dose group which was 827.1mls, showing a 20.5% decrease in total blood loss when high dose regimen was used (p= 0.016). This decrease in total blood loss was significant when assessed with number of levels fused (p= 0.030), however, no significant differences of total blood loss with weight in both group (p= 0.286).

Table 4.3: Measured outcomes of total blood loss in both groups (TXA high and low group)

Data	TXA (high dose) group (n= 55)	TXA (low dose) group (n= 34)	*p* value
Total blood loss (ml)	827.9 ± 372.7	1041.7 ± 580.9	0.016
Total blood loss/ number of level fused	73.7 ± 25.8	94.1 ± 37.4	0.030
Total blood loss/ Cobb's angle	13.8 ± 5.6	16.3 ± 8.8	0.024
Total blood loss/ weight	19.8 ± 8.58	18.6 ± 10.7	0.286

This study also looked into cell salvage technique contributing as blood conservation strategy in scoliosis surgery. The mean total blood loss obtained was 909.6ml ± 471.9ml. All patients, regardless of amount of blood loss intraoperatively received cell salvage blood transfusion. Table 4.4 shows the patient's demographics in relation to total blood loss of less and equal to 900mls and another group which comprised of blood loss more than 900mls. There are significant differences in blood volume (p= 0.031), Cobb's angle (p< 0.001) and number of levels fused (p< 0.001) in which a higher amount of each respective parameters causes blood loss of more than 900mls. Other demographics, namely, the age (p= 0.857), weight (p= 0.894), pre op haemoglobin (p= 0.594), post op 72 hours haemoglobin (p= 0.166) and surgical duration (p= 0.840) elicited no significant differences in both groups.

Table 4.4: Mean total blood loss in relation to patient's demographics

Mean blood loss (ml) = 909.6 ± 471.9

Data	Total blood loss (<=900mls) (n=50)	Total blood loss (>900mls) (n=39)	*p* value
Age	16.1 ± 6.0	17.0 ± 4.6	0.857
Weight (kg)	46.8 ± 9.7	49.0 ± 8.9	0.894
Blood volume (mls)	3121.1 ± 410.3	3346.9 ± 534.4	0.031
Cobb's angle (^{0})	57.6 ± 8.9	66.8 ± 18.1	<0.001
Number of levels fused	9.7 ± 2.6	12.4 ± 1.4	<0.001
Pre op Hb (g/dL)	13.4 ± 1.1	13.7 ± 1.3	0.594
Post op Hb 72 hours (g/dL)	11.1 ± 1.5	10.7 ± 1.3	0.166
Surgical duration (minutes)	120.1 ± 28.3	156.7 ± 30.9	0.840

There are no significant differences elicited between mean MAP (p= 0.548), haemoglobin drop (p= 0.260), post op 72 hours haemoglobin (p= 0.16), surgical duration (p= 0.840) and hospital stay (p= 0.227) in both groups. All patients received cell salvage and no allogeneic blood transfusion was given in all patients. The insignificant difference between haemoglobin drop and post op 72 hours haemoglobin and both groups shows that giving cell salvage is beneficial in reducing haemoglobin drop and allogeneic blood transfusion requirements (Table 4.5).

Table 4.5: Measured outcomes of haemoglobin drop in relation of total blood loss

Data	Total blood loss (<=900mls) (n= 50)	Total blood loss (>900mls) (n= 39)	*p* value
Mean MAP (mmHg)	72.5 ± 2.3	71.9 ± 2.5	0.548
Allogenic blood transfusion	0	0	<0.001
Hemoglobin drop (g/dL)	2.3 ±1.1	2.9 ± 1.0	0.260
Post op Hb 72 hours (g/dL)	11.1 ± 1.5	10.7 ± 1.3	0.166
Surgical duration (minutes)	120.1 ± 28.3	156.7 ± 30.9	0.840
Hospital stay (nights)	3.5 ±0.5	3.6 ± 0.8	0.227

We compared both total blood groups with tranexamic acid dose groups (high vs low dose) and the mean number of patients which was given tranexamic acid doses (high vs low dose) was similar in both total blood loss groups. There are slightly more patients in high dose tranexamic acid group who had total blood loss of <= 900mls (n=33, 60%), however, we elicited that there were no significant differences between total blood loss groups (<=900mls vs >900mls) and trranexamic acid groups (high vs low dose) (p= 0.386). (Table 4.6)

Table 4.6: Comparison between tranexamic acid groups (high vs low dose) and total blood loss groups (<=900mls vs >900mls)

Data	Total blood loss (<=900mls) (n= 50)	Total blood loss (>900mls) (n= 39)	*p* value
TXA (low dose) group (n= 34)	17 (50%)	17 (50%)	0.386
TXA (high dose) group (n= 55)	33 (60%)	22 (40%)	

CHAPTER 5: DISCUSSION

Major orthopaedic surgery such as posterior spinal fusion for scoliosis surgery may result in significant blood loss and the requirement for allogeneic blood transfusion. The major concerns about adverse effects of allogeneic blood transfusion have encouraged the review of transfusion practice and the search for transfusion alternatives to decrease or avoid the use of allogeneic blood transfusion. These strategies include the correction of perioperative anaemia, pharmacological and non-pharmacologic measures to reduce blood loss such as preoperative autologous blood donation and perioperative red blood cell salvage technique[43]. In this study we looked into the use of tranexamic acid as a pharmacological measure and cell salvage technique as a non-pharmacological approach to be deem beneficial in reducing blood loss and avoid allogeneic blood transfusion in scoliosis surgery.

Tranexamic acid (TXA) is a synthetic lysine analogue antifibrinolytic agent which acts as a competitive blockade of lysine binding sites of plasminogen, plasmin, and tissue plasminogen activator.[44] Tranexamic acid has been shown to reduce bleeding in cardiac surgery[36], craniosynostosis surgery[37], total joint arthroplasty[38], obstetrical procedures and urologic procedures[39]. Many studies have been done and proven that tranexamic acid are widely used and beneficial in reducing blood loss in spine surgery as well.

A meta-analysis by Zhang et al. [40] done in 2014 elucidates the effectiveness of tranexamic acid in reducing blood loss and also discussed the related thrombotic complications. They concluded that the use of tranexamic acid is effective in reducing amount of blood loss, the volume of blood transfusion, the transfusion rate and postoperative PTT.

Another meta-analysis published in 2015 by Cheriyan et al.[45] measures the efficacy of tranexamic acid in reducing blood loss in spine surgery and noted that tranexamic acid reduced intraoperative, postoperative and total blood loss by an average of 219ml and the proportion of patients who received blood transfusion reduced as well.

Numerous studies were done to elicit the effectiveness and efficacy of tranexamic acid to be deem beneficial and safe to be used in spine surgery. Various range of doses were applied, the lowest starting from loading dose of 10mg/kg continued with maintenance 1mg/kg/hr[3,46-48] to the highest loading dose of 100mg/kg followed by maintenance 10mg/kg/hr[49]. However, no proper pharmacokinetic modelling study in scoliosis surgery to ascertain the optimal dose to achieve adequate inhibition of fibrinolysis, as well as to dose which related to complications such as seizures and thromboembolic event. The safety and efficacy of TXA for scoliosis surgery remains controversial.

Recent retrospective study done by Daniel et al.[41] compared tranexamic acid dose, 10mg/kg loading dose followed by 1mg/kg/hr maintenance versus 50mg/kg loading dose followed by 5mg/kg/hr maintenance. The study concluded that high dose tranexamic acid is more effective than low dose tranexamic acid in reducing blood loss (by 30%), and blood transfusion requirement (by 60%). In terms of complications, both group show no differences in morbid event rates and thrombotic event.

In another setting, two doses of tranexamic acid in adults undergoing cardiac surgery with cardiopulmonary bypass is compared, 10mg/kg loading dose followed by 1mg/kg/hr (low dose) versus 30mg/kg loading dose followed by 16mg/kg/hr (high dose) respectively[50]. The results exhibit no significant difference between both groups in terms of reducing the incidence of blood product transfusion up to 7 days, however, high dose

tranexamic acid is more effective than low dose to decrease transfusion needs, blood loss, and repeat surgery. Both groups exhibit no differences in terms of adverse events such as renal dysfunction, thromboembolic event and seizures.

In this retrospective study, all patients were given bolus dose of 1g TXA following induction in scoliosis surgery. When elucidated according to patient's weight, we derived two ranges of TXA dose in which 10-20mg/kg signifies low dose TXA group and 20.1-35mg/kg implies high dose TXA group. There were no maintenance dose of TXA given in all patients. In our study, the high dose TXA group had significantly less intraoperative blood loss and post op blood drainage (total blood loss) by 20.5% when compared to low dose TXA group. Total blood loss in relation to Cobb's angle and number of level fused show significant differences in both group. Larger curve magnitudes were positively correlated with longer fusion segments, increased operative time and greater estimated intraoperative blood loss[51]. Results exhibit no significant differences in terms of haemoglobin drop at day three post-surgery and the post op 72 hours haemoglobin level between the two groups. These results may be associated with the usage of cell salvage technique intraoperatively for all patients.

The use of intraoperative cell salvage technique and autologous blood transfusion has become an integral method of blood conservation. The main benefit of autologous transfusion is to reduce the requirement of allogeneic blood transfusion and avoid its associated complications. Allogeneic blood transfusion has been associated with infectious and non-infectious complications namely risks of bacterial, malarial, HIV, hepatitis infections and postoperative infection[5], increased risk of allergic reaction, tumour recurrence[6-8], transfusion associated circulatory overload, acute lung injury[14], perioperative myocardial infarction[15], postoperative low-output cardiac failure[16], hypothermia, coagulopathy and increased mortality[17].

The cell salvage technique has been used clinically for decades and widely applied in spine surgery, however, there are conflicting points of view regarding the efficacy and cost effectiveness of its use.

A Cochrane Collaboration meta-analysis of studies published in 2006 studied the use of cell salvage for minimizing allogeneic blood transfusion and found that cell salvage was efficacious in reducing the need for allogeneic blood transfusion in adult elective surgery. Overall, the use of cell salvage reduced exposure to allogeneic blood transfusion by 39%, with an average saving of 0.67 units per patient. Cell salvage was found to be the most effective in orthopaedic surgery and had no negative impact on morbidity or mortality[30].

Specifically in spinal fusion surgery, some authors have demonstrated that the cell saver did not decrease allogeneic blood transfusion requirements in spine surgery studies performed in adults. Owens et al [52] demonstrated in adult posterolateral fusion surgery patients that the use of autologous cell saver transfusion did not reduce requirements for intraoperative or postoperative allogeneic blood transfusion. Canan et al [53] indicated that the use of the cell saver for single level posterior lumbar decompression and fusion did not significantly reduce the need for allogeneic blood transfusion and was not cost-effective. Similar findings were reported in Weiss et al[54] which `demonstrated that in patients undergoing spinal fusion for scoliosis, the use of the cell saver did not decrease the rate of allogeneic transfusion.

However, apart from these negative studies suggesting that use of the cell saver is expensive and redundant, there are abundant of other studies which says otherwise. Goulet et al.[55] found that transfusion requirements were decreased when cell salvage technique was used in orthopaedic procedures while Anand et al.[56] showed that the use of cell salvage technique decreased the need for allogeneic blood transfusion in scoliosis surgery. Bowen et al.[57] demonstrated that cell saver use decreased allogeneic transfusion,

particularly in operations 6 hours in duration with an estimated blood loss 30% of the total blood volume in pediatric idiopathic scoliosis patients. Besides that, Ersen et al[58] reported that the cell saver reduced both intraoperative and postoperative blood transfusion in patients undergoing posterior spinal fusion for adolescent idiopathic scoliosis.

In this study, all patients were given cell salvage blood intraoperatively regardless of the amount of estimated blood loss during the surgery. The 2009 AAGBI guidelines identified indications for the use of intraoperative cell salvage, which includes anticipated blood loss of >1000 ml or >20% estimated blood volume, patients with a low haemoglobin or at increased risk of bleeding, patients with multiple antibodies or rare blood types, and patients with objections to receiving allogeneic blood such as Jehovah's witness[23]. There is a study done by Jennifer et.al[28] which concluded that cell salvage technique does not reduce the need for other transfusion in scoliosis and not cost effective if less than 500mls of blood loss is expected, however, it is difficult to predict the estimated blood loss in all patients going for posterior spinal fusion in order to choose which patient might benefit cell salvage technique as scoliosis surgery is categorized in surgery which requires extensive operative times with extensive soft tissue dissection and significant perioperative blood loss.

The mean total blood loss in this study was around 900mls and cell salvage technique was applied to all patients. Results exhibit significant differences in blood loss less or equal than 900mls and more than 900mls with regards patients Cobb's angle and number of level fused which proves that larger curve magnitudes is correlated with longer fusion segments in which will result in increased operative time and leads to greater estimated intraoperative blood loss.

In this study we measured the haemoglobin drop and haemoglobin levels at 72 hours (day 3) postoperatively. In a recent study by Grant et al.[59] who retrospectively

examined data from 11 common surgeries and over 3100 patients to determine the predictors of hemoglobin drift. They concluded that surgeries requiring greater amounts of IV fluid and blood, such as spinal fusions and major pancreatic surgeries had the most post-operative hemoglobin drift, about a 2.5 g/dL downward hemoglobin drift over the first 3 post-operative days, hence in this study we looked into the haemoglobin level and hemoglobin at day three following surgery

There is no significant differences between both groups (blood loss <=900mls and >900mls) in terms of post haemoglobin drop 72 hours (day 3) after surgery and haemoglobin levels at 72 hours postoperatively. Furthermore, when compared both tranexamic acid groups and total blood loss groups the mean of patients were similar and there were no significant differences elicited in both groups. This results prove that it's clinically significant to give cell salvage intraoperatively as the patients who has blood loss of more than 900mls has similar haemoglobin drop and haemoglobin levels at 72 hours post-surgery as compared to patients in the lesser blood loss group. All patients did not require allogeneic blood transfusion intra- and postoperatively.

There are certain limitations that should be recognized in our study. First, many studies delineate tranexamic acid dose comparing high and low dose with a specific amounts such as loading dose of 10mg/kg (low dose) vs 50mg/kg (high dose) and these will be followed by maintenance dose ranging from 1-10mg/kg/hr whereas in this study patients were given tranexamic acid 1g bolus dose at the beginning of the surgery in all subject, hence, instead of a specific dose to be recommended, we can only conclude a range of doses from 20.1-35mg/kg (high dose group) to be deem beneficial. The limitations of this study are innate to its retrospective designed and the indications for transfusion were not defined with objective parameters. Another drawback will be the part where the intraoperative blood loss is truly an estimated value and can be inaccurate due to irrigation and unaccounted blood loss.

CHAPTER 6: CONCLUSION

In posterior spinal fusion surgery for scoliosis, extensive operation time and massive blood loss may be expected, therefore, it is apt to apply blood conservation strategies to address this issue. The use of tranexamic acid has been proven beneficial in reducing blood loss and allogeneic blood transfusion requirement in many studies. In our study, we established that high dose tranexamic acid is effective and beneficial in reducing blood loss and allogeneic blood transfusion in scoliosis surgery. While some studies are not agreeable with liberal use of cell salvage technique as it may be costly and ineffective, many studies proved otherwise. In this study, all patients received cell salvage blood transfusion regardless of amount of blood loss and it is deem to be beneficial as there is similar haemoglobin drop and haemoglobin level 72 hours postoperatively in patients with blood loss of more than 900mls as compared to those with lower amount of blood loss. Both blood conservation strategies had successfully reduce blood loss and avoid allogeneic blood transfusion following scoliosis surgery in this study.

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