EFFICACY OF TRANEXAMIC ACID AND CELL SALVAGE IN CONSERVING BLOOD IN SCOLIOSIS SURGERY

LOOI JI KEON

FACULTY OF MEDICINE
UNIVERSITY OF MALAYA
KUALA LUMPUR

2018

EFFICACY OF TRANEXAMIC ACID AND CELL SALVAGE IN CONSERVING BLOOD IN SCOLIOSIS SURGERY

LOOI JI KEON

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

FACULTY OF MEDICINE
UNIVERSITY OF MALAYA
KUALA LUMPUR

2018

UNIVERSITY OF MALAYA

ORIGINAL LITERARY WORK DECLARATION

Name of Candidate: **LOOI JI KEON**

Matric No: **MGE 150025**

Name of Degree: **Master of Anaesthesiology**

Title of Project Paper/Research Report/Dissertation/Thesis ("this Work"):

Efficacy of Tranexamic Acid and Cell Salvage in Conserving Blood in Scoliosis Surgery

Field of Study: **Anaesthesiology**

I do solemnly and sincerely declare that:

(1) I am the sole author/writer of this Work;
(2) This Work is original;
(3) Any use of any work in which copyright exists was done by way of fair dealing and for permitted purposes and any excerpt or extract from, or reference to or reproduction of any copyright work has been disclosed expressly and sufficiently and the title of the Work and its authorship have been acknowledged in this Work;
(4) I do not have any actual knowledge nor do I ought reasonably to know that the making of this work constitutes an infringement of any copyright work;
(5) I hereby assign all and every rights in the copyright to this Work to the University of Malaya ("UM"), who henceforth shall be owner of the copyright in this Work and that any reproduction or use in any form or by any means whatsoever is prohibited without the written consent of UM having been first had and obtained;
(6) I am fully aware that if in the course of making this Work I have infringed any copyright whether intentionally or otherwise, I may be subject to legal action or any other action as may be determined by UM.

Candidate's Signature Date:

Subscribed and solemnly declared before,

Witness's Signature Date:

Name:

Designation:

EFFICACY OF TRANEXAMIC ACID AND CELL SALVAGE IN CONSERVING BLOOD IN SCOLIOSIS SURGERY

ABSTRACT

Note: The efficacy of tranexamic acid and cell salvage will be considered and analysed separately as the former is used to reduce intraoperative blood loss while the latter technique is used to recover lost blood during surgery. Hence, this dissertation will be divided into two parts under each subsection to accommodate for each blood conservation techniques.

Part A - Tranexamic Acid given as single dose to reduce blood loss in scoliosis surgery – is a higher dose range more superior?

Scoliosis surgery is often associated with long operative times and extensive blood loss. Published studies consistently demonstrate the efficacy of tranexamic acid (TXA) to reduce intraoperative blood loss compared to placebo. However, the optimal dose to maximize its anti-fibrinolytic properties without increasing thrombotic complications remains elusive. This retrospective study compares the efficacy of two dose ranges of TXA in reducing intraoperative blood loss in posterior spinal fusion (PSF) surgery. 173 patients with adolescent idiopathic scoliosis (AIS) who underwent PSF in 2015 and 2016 were retrospectively studied. All patients received 1 gram of intravenous TXA without maintenance. They were divided into two groups – Group A- High dose TXA (>20 mg/kg, n=115) and Group B- Low dose TXA ($\leq$20 mg/kg, n=58). Mean age, weight, blood volume, Cobb's angle and number of levels fused were 15.4 years, 41.8 kg, 2914.8 mls, 66.4^{o}, 11.2 levels and 18.2 years, 57.5 kg, 3652.8 mls, 65.7^{o}, 10.8 levels in Groups A and B respectively. In terms of mean absolute intraoperative blood loss (827.8 vs 909.4mls; p=0.26) and percentage of blood volume loss (28.5 vs 24.9%; p=0.11), the differences between the high and low dose groups did not achieve statistical significance.

Total blood loss per segment (72.2 vs 81.1mls; p=0.08) and per screw (56.8 vs 63.8mls; p=0.14) also did not differ significantly between the groups and so did duration of hospital stay (3.4 days vs 3.4 days, p=0.96). No patients received allogenic blood transfusion and none developed thrombotic complications. Higher dose of TXA (>20 mg/kg), failed to demonstrate superiority in reducing blood loss compared to a lower dose of $\leq$ 20 mg/kg when given as a single dose in PSF for AIS.

Part B - A retrospective review of efficacy of cell salvage to conserve blood in scoliosis surgery

Cell salvage is widely practised in scoliosis surgery to reduce allogenic transfusion. However, evidence is limited with regards to its efficacy. This study aims to determine the efficacy of intraoperative cell salvage in single-staged posterior spinal fusion surgery. 89 patients who underwent single-staged posterior spinal fusion for adolescent idiopathic scoliosis in 2016 were retrospectively studied. All patients received intraoperative cell salvage (ICS) as part of institutional protocol. Mean intraoperative blood loss was 909 mls. They were categorised into two groups – Group C ($\leq$ 900 mls blood loss, n=50) and Group D (> 900 mls blood loss, n=39). The mean age and weight was 16.1 years, 46.8kgs and 17.0 years, 49kgs for Group C and D respectively. Preoperative baseline characteristics such as blood volume (3121 vs 3346 mls), Cobb's angle (57.6^{o} vs 66.8^{o}), number of levels fused (9.7 vs 12.4), number of screws (12.4 vs 15.3) were higher in Group D compared to Group C. Blood volume returned by ICS were 260 mls and 560 mls for Group C and D respectively. For both groups, 47% of total intraoperative blood loss was returned via ICS. Analysis of the pre-and postoperative haemoglobin levels did not show statistical significance between Groups C and D (preop: 13.4 vs 13.7 and postop: 11.1 vs 10.7 g/dL). None of the subjects received perioperative

allogenic blood transfusion or reported complications from the use of cell salvage. Intraoperative cell salvage is effective in conserving blood in posterior spinal fusion surgery. Post-operative haemoglobin levels did not differ significantly between the higher and lower blood loss groups.

Keywords

Scoliosis, Tranexamic acid, cell salvage, blood loss

KEBERKESANAN "TRANEXAMIC ACID" DAN "CELL SALVAGE" UNTUK MENGURANGKAN PENDARAHAN DALAM PEMBEDAHAN SKOLIOSIS

ABSTRAK

Nota: Keberkesanan Tranexamic Acid (TXA) dan Cell Salvage (ICS) akan dianalisa secara berbeza kerana TXA digunakan under mengurangkan pendarahan semasa pembedahan manakala ICS digunakan untuk mengembalikan darah yang hilang kepada pesakit.

Bahagian A: Penggunaan Tranexamic Acid sebagai dos tunggal untuk mengurangkan pendarahan dalam pembedahan skoliosis – adakah dos tinggi lebih berkesan?

Pembedahan skoliosis selalunya melibatkan masa yang panjang and kehilangan darah yang banyak. Kajian telah menunjukkan keberkesanan tranexamic acid (TXA) untuk mengurangkan pendarahan semasa pembedahan apabila dibandingkan dengan placebo. Walaupun sedemikian, dos yang optima untuk mencegah fibrolisis dan mengelakkan masalah pembekuan darah (thrombosis) adalah tidak diketahui pada masa ini. Kajian retrospektif ini membandingkan dua dos TXA untuk mengurangkan kehilangan darah dalam pembedahan "posterior spinal fusion"(PSF). 173 pesakit dengan diagnosa "adolescent idiopathic scoliosis" yang melaksanakan PSF dalam tahun 2015 and 2016 telah dikaji. Semua pesakit diberi 1 gram TXA sahaja tanpa dos sambungan. Pesakit-pesakit dibahagikan kepada dua kumpulan – Kumpulan A – Dos tinggi TXA (>20mg/kg, n=115) dan Kumpulan B – Dos rendah TXA ($\leq$20mg/kg, n=58). Umur, berat badan, isipadu darah, sudut Cobb dan jumlah aras tulang belakang yang disambung ialah 15.4 tahun, 41.8kg, 2914.8 mls, 66.4^{o}, 11.2 aras dan 18.2 tahun, 57.5 kg, 3652.8 mls, 65.7^{o}, 10.8 aras dalam kumpulan A and B masing-masing. Dalam konteks isipadu pendarahan semasa pembedahan ((827.8 vs 909.4mls; p=0.26) and peratusan isipadu pendarahan

berbanding dengan jumlah isipadu darah pesakit (28.5 vs 24.9%; p=0.11), perbezaan untuk dua kumpulan tidak mencapai "statistical significance". Kehilangan darah dibahagikan dengan bilangan aras (72.2 vs 81.1mls; p=0.08), dibahagikan dengan bilangan skrew (56.8 vs 63.8mls; p=0.14) dan bilangan hari masuk wad (3.4 hari vs 3.4 hari, p=0.96), juga tidak mencapai "statistical significance" jika membandingkan kumpulan A dengan kumpulan B. Tiada pesakit yang menerima darah allogenik atau mendapat komplikasi pembekuan darah. Kajian ini menunjukkan dos tunggal TXA yang lebih tinggi (>20mg/kg) tidak berkesan untuk mengurangkan pendarahan dalam pembedahan PSF jika dibandingkan dengan dos yang lebih rendah (≤20 mg/kg).

Bahagian B – Kajian retrospektif tentang keberkesanan "Cell Salvage" untuk memelihara kehilangan pendarahan dalam pembedahan skoliosis

"Cell salvage" digunakan secara meluas dalam pembedahan skoliosis untuk mengurangkan tranfusi allogenik. Tetapi, tiada kajian sampai hari ini untuk menunjukkan bukti keberkesanannya dengan kukuh. Oleh yang demikian, kajian ini bertujuan untuk menentukan keberkesanan "intraoperative cell salvage" dalam pembedahan " single-staged posterior spinal fusion surgery". 89 pesakit yang menjalani pembedahan tersebut akan dikaji. Semua pesakit menerima ICS sebagai protokol unit pembedahan. "Mean" isipadu kehilangan darah semasa pembedahan ialah 909 mls. Pesakit-pesakit dibahagikan kepada dua kumpulan – Kumpulan C (≤ 900ml kehilangan darah, n=50) dan Kumpulan D (>900 ml kehilangan darah, n=39). Umur and berat "mean" ialah 16.1 tahun, 46.8kgs dan 17.0tahun, 49 kgs untuk kumpulan C dan D masing-masing. Ciri-ciri pra-pembedahan iaitu isipadu darah (3121 vs 3346 mls), sudut Cobb (57.6^o vs 66.8^o) dan bilangan aras yang dicantum (9.7 vs 12.4), bilangan skrew (12.4 vs 15.3) adalah lebih tinggi untuk Kumpulan D berbanding dengan Kumpulan C. Isipadu darah yang

dikembalikan oleh ICS ialah 260 mls dan 560 mls untuk Kumpulan C dan D masing-masing. Bagi kedua-dua kumpulan, 47% darah yang hilang dapat dikembalikan oleh sistem ICS. Paras hemoglobin sebelum dan selepas pembedahan tidak menunjukkan ketaraan statistic ("statistical significance") apabila dibandingkan antara dua kumpulan C dan D (sebelum 13.4 vs 13.7 dan selepas 11.1 vs 10.7 g/dL). Tiada pesakit menerima transfusi darah allogenik atau melaporkan komplikasi akibat penggunaan ICS. Sebagai kesimpulan, "Intraoperative cell salvage" adalah berkesan untuk memelihara kehilangan darah dalam pembedahan "posterior spinal fusion". Perbezaan paras hemoglobin sebelum dan selepas pembedahan tidak mencapai ketaraan statistik bagi kumpulan yang kehilangan lebih banyak darah apabila dibandingkan dengan kumpulan yang kurang kehilangan darah.

ACKNOWLEDGEMENTS

I would like to thank my supervisor, Associate Prof Dr. Mohd Shahnaz Hasan for being very generous, supportive and encouraging in providing guidance and advice in overseeing the completion of this dissertation despite his busy work schedule.

Much appreciation also directed to Dr Arfah Hanim Mohamad who has laid down the foundation work in the initial part of this research project.

My gratitude also goes to Prof Dr. Kwan Mun Keong and Associate Prof Dr. Chris Chan Yin Wei, the primary surgeons for all patients included in this study. To the Spine Research Unit (SRU, UMMC), especially Ms Josephine Chandran and Ms Nur Sulwana binti Mohamad Hanapi – my heartfelt appreciation for assisting me with the data collection and statistical analysis for this dissertation.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF SYMBOLS AND ABBREVIATIONS

≤	:	Less than or equal to
>	:	More than
AAGBI	:	Association of Anaesthetist of Great Britain and Ireland
AIS	:	Adolescent Idiopathic Scoliosis
ICS	:	Intraoperative Cell Salvage
IV	:	Intravenous
MAP	:	Mean Arterial Pressure
mls	:	mililitres
mmHg	:	milimetre Mercury
n	:	Number
TXA	:	Tranexamic Acid
vs	:	versus
2,3-DPG	:	2,3-diphosphoglycerate
ATP	:	Adenosine triphosphate
ACD	:	Anticoagulant Citrate-Dextrose

CHAPTER 1: GENERAL INTRODUCTION

Scoliosis surgery are complex undertakings which require meticulous planning and careful execution of both the surgical and anaesthetic team to ensure a satisfactory outcome. It is invariably associated with prolonged operative time and extensive blood loss. Acute massive intraoperative bleeding leads to haemodynamic instability, shock, disseminated intravascular coagulopathy and inadequate delivery to organs and tissue. (Stainsby, 2000) Various blood conservation techniques have been developed and used to limit blood loss and reduce allogenic blood transfusion in the face of massive blood loss. They can be broadly divided into pharmacological and non-pharmacological methods. The former includes the use of tranexamic acid, aprotinin, desmopressin, and preoperative erythropoietin while the latter comprises techniques such as cell salvage, acute normovolaemic or hypervolaemic haemodilution, preoperative autologous donation and modification of surgical techniques. (Thomas, 2010)

The use of tranexamic acid has becoming popular in trauma and many surgical fields to contain blood loss and reduce allogenic blood transfusion with good evidence emerging in the literature. However, the timing, dose and frequency of intravenous tranexamic acid to optimize its anti-fibrinolytic effects while averting thrombo-embolic complications have not been concretely established. We aim to investigate whether a higher dose range of intravenous tranexamic acid is more effective to decrease intraoperative blood loss compared to a lower dose range when administered as a single dose in posterior spinal fusion surgery.

On the other hand, the opinions in the current literature with regards to the efficacy of intraoperative cell salvage to reduce allogenic blood transfusion remain mixed. As the use of cell salvage requires expertise and involves a steep cost, some authors felt that its use is not justified compared to the traditional way of transfusing allogenic blood to

correct exsanguinative hypotension and anaemia. (Stainsby, 2006) As part of the institutional protocol, intraoperative cell salvage is used for all posterior spinal fusion. Hence, this paper seeks to establish the effectiveness of ICS use in the face of extensive blood loss.

CHAPTER 2: LITERATURE REVIEW

Posterior spinal fusion (PSF) for adolescent idiopathic scoliosis (AIS) involved extensive blood loss, ranging from 16 to 30% of total blood volume. (Shapiro et al, 2004) Ridgeway et al (2003) reported that up to 89% of patients required allogenic blood transfusion without the practise of pre-donated blood. While adverse effects associated with allogenic blood transfusion are fortunately rare, the patients are still exposed to small risk of significant and at times life-threatening complications, such as acute lung injury, viral and bacterial transmission, post-operative infections, transfusion errors, and increased mortality. By reducing the need for allogenic blood transfusion, such unwanted risks are averted to attain a better surgical outcome for the patients.

Two common practices as part of conserving blood during PSF surgery at the local setting will be reviewed, namely tranexamic acid and intraoperative cell salvage.

2.1 TRANEXAMIC ACID IN SCOLIOSIS SURGERY

Tranexamic acid (trans-4-aminomethyl cyclohexane carboxylic acid) is a synthetic analogue of the amino acid lysine and is acts as an antifibrinolytic by reversibly blocking the lysine binding sites on plasminogen and plasmin. By doing so, it prevents fibrin degradation and maintains the framework of fibrin's matrix structure and clot integrity. (Fan, 2014) It can be administered in various ways such as via oral, intravenous and topical routes on bleeding surface.

By avoiding clot breakdown, it is used to reduce bleeding in various settings which include trauma, menorrhagia, cardiac surgery, craniosynotosis surgery, total joint arthroplasty, urological and obstetric procedures. (Faraoni, 2013; Goobie, 2011) It is also

used in spine surgery to decrease blood loss and consequently the need of blood transfusion.

Hiipala et al (1997) showed a significant decrease in the total blood loss (689±289 vs 1509±643 ml) and reduction in the red cell transfusion (1.0±1.2 vs 3.1±1.6 units) when tranexamic acid (TXA) was used in total knee arthroplasty compared to placebo. In their study, an intravenous bolus dose of 15 mg/kg was administered prior to tourniquet deflation followed by two extra doses of 10mg/kg postoperatively.

In the paediatric population undergoing posterior spinal fusion, Neilipovitz et al (2001) demonstrated that a 10mg/kg intravenous loading dose of TXA followed by 1mg/kg/hour infusion throughout surgical period significantly lowered the need for red cell transfusion in the perioperative period while compared to saline placebo.

Furthermore, a recent meta-analysis of six randomized controlled trials concluded that intravenous TXA can significantly decrease the amount of blood loss and subsequently the requirement of blood transfusion in major spinal surgery. (Zhang et al, 2014) The authors also managed to assert the safety of TXA in view no patients in the TXA group developed deep venous thrombosis or myocardial infarction. However, those studies were heterogenous in terms of surgical intervention, threshold for blood transfusion and most importantly the dosing of TXA. The loading dose for TXA ranged from 10mg/kg to 100mg/kg while maintenance dose 1 to 10mg/kg.

While single perioperative dose of intravenous TXA ranging from 10 – 30 mg/kg has been used successfully in primary total hip and knee arthroplasty to reduce blood loss perioperatively (Ralley et al, 2010; Sukeik et al 2011; Hourlier, 2014; George et al, 2015), the evidence for such single dose in spinal surgery was very limited. To our knowledge, the closest evidence in spine surgery for single dose intraoperative intravenous TXA was

conducted by Tsutsumimoto et al (2011). It was a prospective randomized study done in patients undergoing cervical laminoplasty. They received 15mg/kg of IV TXA prior skin incision, compared to placebo group. Of note, they found that IV TXA significantly decrease blood loss postoperatively, but not intraoperatively. This is interesting given the relatively short half-life of intravenous TXA of 1.5 to 2 hours.

To our knowledge, there were no published data in the literature examining the efficacy of different dose ranges of single dose intravenous TXA to limit blood loss in scoliosis surgery. We aim to fill the gap of this knowledge and evidence in the literature via this retrospective study.

2.2 CELL SALVAGE IN SCOLIOSIS SURGERY

Intraoperative cell salvage (ICS) is a technique constituting of three phases – collect, wash and reinfuse red blood cells from the operative site back to the patient via a specialized machine. (AAGBI, 2009) By receiving own's lost blood during the surgery, ICS offers the opportunity to mitigate the need for allogenic blood transfusion in the face of massive blood loss and avoid its associated complications. Furthermore, salvaged blood is touted to have higher mean erythrocyte viability, elevated 2,3-DPG and ATP levels, maintains its deformability to travel across the capillary beds, and beneficial immune-stimulatory effects, as compared to stored allogenic red cells. (Munoz, 1999; Schmidt, 1995) Meanwhile, cell salvage is associated with complications such as non-immune hemolysis, air embolus, coagulation, drug contamination and microaggregates. (Ashworth, 2010) However, their occurrences are rare, making its use appealing by many practitioners.

Weiss et al (2007) reviewed 95 children who underwent PSF and found that cell saver failed to reduce the transfusion requirement in scoliosis surgery. They concluded that cell saver was of no benefit in their patient population. On the other hand, a retrospective review on adults with lumbar fusion surgery demonstrated fewer post-operative transfusions in the cell saver group with less-than-expected difference. (Reitman, 2004) The authors concluded that blood requirements can be met with pre-donation of autologous blood without the need for cell saver in most elective lumbar fusions. They also found the recovery rate of blood by the cell saver was 38%.

On the contrary, Liang et al (2013) in their prospective randomized study found that cell saver significantly lowered the perioperative allogenic blood transfusion rate (by 18.2%) in scoliosis surgery. The benefits were even more pronounced in subjects with anaemia and prolonged operation. A recent systematic review by Stone et al (2017)

concluded from 7 studies that cell saver decreased the need for allogenic blood transfusion with cell saver patients received 1.0 fewer unit of allogenic blood versus the control group in scoliosis correction surgery. The benefits were echoed by another recent meta-analysis by Liu et al (2017) which also showed improved haemoglobin and haemotocrit levels on post-operative day 1 in addition to reduced allogenic blood transfusion in scoliosis surgery. Moreover, there was no increase in the incidence of transfusion complications during the surgery associated with cell saver use.

Since the evidence to support the use of ICS in PSF is still inconclusive and subject to debate, we wish to examine in our own local setting if the use of cell salvage is efficacious in conserving blood especially in patients experiencing significant blood loss.

CHAPTER 3: TRANEXAMIC ACID GIVEN AS SINGLE DOSE TO REDUCE BLOOD LOSS IN SCOLIOSIS SURGERY – IS A HIGHER DOSE RANGE MORE SUPERIOR?

3.1 INTRODUCTION

Posterior spinal fusion (PSF) surgery to treat adolescent idiopathic scoliosis often involves extensive operative time and may lead to massive intra- and postoperative blood loss. (Florentino, 2004) In the past, such blood losses are replaced by allogenic blood to restore the oxygen carrying capacity. Allogenic blood transfusion is associated with both infective and non-infective complications which may hinder the surgical outcomes and patient's recovery. (Duffy, 2006; Vamvakas, 2002)

Tranexamic acid (TXA) is an antifibrinolytic agent. It works by reversibly binding to plasminogen and plasmin and thus inhibiting their action of dissolving the fibrin plug. (Neilipovitz, 2004) This synthetic analogue of lysine has been proven effective in various surgical settings to reduce blood loss and transfusion. (Ker, 2012)

However, there appears to be a large dose range for tranexamic acid used with different dosing regimens. (Sethna 2005; Wong, 2008) There is still a paucity of evidence regarding the optimal dose of tranexamic acid used in scoliosis surgery. To our knowledge, there are no published studies to date examining the efficacy of different dose-range of TXA given as a single dose in scoliosis surgery.

This study compares the efficacy of two dose ranges of tranexamic acid in posterior spinal fusion surgery for adolescent idiopathic scoliosis, given as a bolus dose at the start of the surgery in reducing intraoperative blood loss.

3.2 METHODS

This is a retrospective study involving 173 patients diagnosed with AIS who underwent single staged posterior spinal fusion from January 2015 to August 2016 at University Malaya Medical Centre (UMMC), Malaysia. Medical records for the patients were reviewed. All patients had normal renal and coagulation profiles prior to surgery. The surgeries were performed by the same team of senior orthopaedic spine surgeons and a consultant anaesthesiologist. Similar surgical and standard anaesthetic techniques were employed for all patients. No patients donated autologous blood prior to surgery and cell salvage blood recovery system was utilised for all subjects. As this is a retrospective study and all subjects were anonymised, no written informed consent was obtained.

During the study period, a standard bolus dose of 1 gram tranexamic acid was given intravenously to all patients following induction of general anaesthesia. After adjusting for patient's weight, this yields a dose range between 10 – 35 mg/kg. This is not followed by any maintenance infusion intra- or post-operatively.

Patient demographics such as age, gender, preoperative weight and height, preoperative Cobb's angles were recorded. Blood volume was calculated using the Nadler's formula (Nadler, 1962). Intraoperative data such as number of screws inserted, operative time, estimated blood loss (EBL) were also analysed. The EBL was calculated from the cell salvage system and the weight differences between dry and blood-soaked gauzes, excluding blood lost to the floor, surgical gowns and drapes; giving the formula:

Estimated blood loss, EBL (ml)
= final volume accumulated in the reservoir
– total volume of Anticoagulant Citrate-Dextrose (ACD)
– total irrigation fluid used intraoperatively
+ total unfiltered blood

The perfusionist calculated the total volume of ACD used and total unfiltered blood (weight differences between dry and used reservoir). Meanwhile, the nurses measured the total irrigation fluid before being used intraoperatively. (Hasan, 2017)

Data analysis was performed using IBM SPSS software version 24. The patient's basic demographic data, surgical statistics, blood loss were compared by independent T-test. The results were expressed as mean ± SD (standard deviation). A p value of < 0.05 was considered statistically significant.

3.3 RESULTS

A total of 173 patients were included in this retrospective cohort study. They were divided into two groups based on the bolus dose of tranexamic acid received at the start of surgery over their body weight. There were 115 patients who received more than 20 mg/kg of tranexamic acid (Group A) while 58 patients received 20 mg/kg or less of tranexamic acid (Group B).

Table 3.1 Baseline Characteristics of patients in high and low dose tranexamic acid groups in posterior spinal fusion surgery

Baseline Demographics	**Group A (TXA > 20 mg/kg) (n=115)**	**Group B (TXA ≤ 20 mg/kg) (n=58)**	***p* value**
Age	15.4±4.28	18.2±6.35	0.004
Weight (kg)	41.8±4.41	57.5±7.89	<0.001
Blood Volume (mls)	2914.8±315	3653.8±405	<0.001
Cobb's Angle (º)	66.4±19.90	65.7±13.94	0.79
Number of levels fused	11.2±2.4	10.8±2.3	0.29
Number of screws	14.1±2.3	13.7±7.6	0.31
Surgical Duration (mins)	135.0±36.3	144.2±30.4	0.08

The mean age, weight and blood volume were 15.4 vs 18.2 years (p=0.004), 41.8 vs 57.5 kg (p<0.001), and 2914.8 vs 3652.8 mls (p<0.001) for Group A and B respectively. In contrast, baseline surgical factors such as Cobb's Angle (66.4 vs 65.7^{o}), number of levels fused (11.2 vs 10.8), number of screws inserted (14.1 vs 13.7) as well as duration of surgery (135 vs 144 minutes) did not achieve statistical significance for Group A and B respectively with p values of 0.79, 0.29, 0.31 and 0.08 for each parameter compared.

Table 3.2 Measured outcomes of patients in high and low dose tranexamic acid groups in posterior spinal fusion surgery

Operative Outcomes	**Group A (TXA > 20 mg/kg) (n=115)**	**Group B (TXA ≤ 20 mg/kg) (n=58)**	***p* value**
Total blood loss (mls)	827.8±408.3	909.4±535.0	0.26
% blood loss	28.5±14.0	24.9±14.2	0.106
Total blood loss per segment (ml/segment)	72.2±27.59	81.1±36.5	0.076
Total blood loss per screw (ml/screw)	56.8±22.1	63.8±31.6	0.135
Allogenic blood transfusion	0	0	
Duration of hospital stay	3.4±0.61	3.4±0.49	0.955

With regards to the total blood loss between the high and low dose tranexamic acid groups, the differences did not achieve statistical significance (827.8 vs 909.4 mls, p=0.26). To account for the difference in weight between the groups, analysis based on percentage of blood loss (using total blood loss divided by estimated blood volume) also did not yield statistical significance (28.5 vs 24.9 % blood loss, p=0.106). Blood loss in terms of per levels fused and per screws inserted also did not show statistical differences between the two groups.

The duration of hospital stay also did not differ between the high and low dose tranexamic acid groups (3.4 vs 3.4 days; p=0.955).

All the patients neither received allogenic blood transfusion nor reported any thromboembolic complications throughout their stay till discharge.

3.4 DISCUSSION

Evidence is emerging that tranexamic acid (TXA) is an effective pharmacological intervention to reduce blood loss and transfusion requirement in different settings and types of surgeries such as cardiac, craniosynostosis surgery, total joint arthroplasty, obstetrical and urological procedures (Faraoni, 2013; Goobie, 2011; Hiippala, 2014; Fan, 2014). There is good evidence to support the use of single bolus dose of TXA in reducing intra- and post-operative blood loss in hip and knee arthroplasties as well as coronary artery bypass grafting (George,2015; Ralley, 2010; Pleym, 2003).

In addition, more studies and pooled meta-analyses are showing that TXA is effective in reducing blood loss in spine surgery. (Neilipovitz, 2004; Fan, 2014) However, the data for scoliosis surgery remains scarce and no definitive conclusions could be derived due to the heterogeneity of the procedures, surgical methods and doses of TXA used. A meta-analysis by Fan *et al* (2014) revealed that most of the studies involved initiation of TXA as a loading dose followed by maintenance infusion. In this respect, data regarding single bolus dose of TXA used in posterior spinal fusion is even more lacking.

In a prospective randomised study by Tsutsumimoto et al (2011), TXA was administered intravenously as a single dose of 15 mg/kg compared to placebo in cervical laminoplasty before skin incision. It demonstrated the effectiveness of TXA in reducing postoperative blood loss despite no difference in terms of intraoperative blood loss.

In this retrospective study, all patients received 1g of intravenous TXA following induction of general anaesthesia for scoliosis surgery without maintenance infusion or repeated dosing. The baseline patient's demographics showed significant statistical differences in terms of age, weight and blood volume. This is attributed to the way the subjects were categorised in this study as older age is associated with increased weight and weight correlates positively with blood volume based on Nadler's formula.

This study failed to demonstrate the effectiveness of a higher compared to a lower dose of TXA in reducing intraoperative blood loss in posterior spinal fusion surgery when given as a single bolus at the start of operation. Total intraoperative blood loss was more in the lower dose range group but did not achieve statistical significance. When analysed via percentage blood loss to correct for the weight differences, the difference between the two groups also did not show statistical significance. However, factors which are known to affect intraoperative blood loss such as operating time, surgical techniques, number of vertebral levels fused and Cobb's angle were comparable between the two groups (Fan, 2014; Ng, 2015).

The majority of existing studies which showed positive correlation using high dose TXA in reducing operative blood loss and transfusion requirements practised maintenance dose in addition to a loading dose with large differences in their dosing regimens. (Fan, 2014) Loading doses as high as 100 mg/kg with maintenance of 10 mg/kg/hour have been reported. (Sethna, 2005) Meanwhile, other studies showing effectiveness using single dose TXA used placebo such as normal saline as a comparison. (Tsutsumimoto, 2011) However, the result of our analysis did not demonstrate that a higher single TXA dose is more superior in reducing intraoperative blood loss compared to a lower dose in posterior spinal fusion scoliosis surgery.

Another reason that could account for the above finding is the pharmacokinetics (PK) of TXA itself. In cardiopulmonary bypass surgery, the PK of TXA is found to fit into an open two-compartmental model with linear elimination. Hence, the authors concluded that to maintain effective concentrations throughout the cardiac surgery, a regime encompassing continuous infusion would be most appropriate. (Grassin-Delyle, 2013) In scoliosis surgery, the effect of a single dose of TXA may diminish quickly with prolonged operative time (due to redistribution and excretion in urine), ongoing significant blood loss (due to loss of tranexamic acid in blood) and intraoperative fluid and blood transfusion (due to dilution effect). Further pharmacokinetic studies especially outside cardiac surgery to determine the optimal dosing regimen of tranexamic acid are much desired.

Of course, there are limitations of this study owing to its retrospective design. After categorising the subjects into two groups, it is worthy to note that the number of patients in the high dose group exceeded the comparative group by a large number. This could confound the study findings. Additionally, intraoperative blood loss is an estimated value and its accuracy could be affected by irrigation and hidden blood loss. (Smorgick, 2013) Furthermore, the postoperative drainage was not accounted for into the estimation of the blood loss in this study. The cases were performed in a university hospital setting with high case load by experienced surgeons and skilful anaesthetists. Hence, the findings may not be generalizable to other centres.

3.5 CONCLUSION

In conclusion, higher dose of tranexamic acid (>20 mg/kg) failed to demonstrate superiority in reducing intraoperative blood loss compared to a lower dose of $\leq$ 20 mg/kg when given as a single dose in posterior spinal fusion for adult idiopathic scoliosis.

Prospective studies to investigate the optimal timing, dose range and duration of TXA administration in this setting are much desired.

CHAPTER 4: A RETROSPECTIVE REVIEW OF EFFICACY OF CELL SALVAGE TO CONSERVE BLOOD IN SCOLIOSIS SURGERY

4.1 INTRODUCTION

Scoliosis surgery is often associated with significant intraoperative blood loss. To limit perioperative allogenic blood transfusion, various strategies such as pre-donated autologous blood, hypotensive anaesthesia, proper positioning, haemodilution as well as antifibrinolytics have been used. (Lee, 1998; Copley,1999; Wong, 2008; Hasan, 2017) Intraoperative cell salvage (ICS) is one of the more popular options employed by many centres. (Stone, 2017)

Red cell transfusion in the face of significant blood loss aims to restore the oxygen carrying capacity by haemoglobin. Albeit allogenic blood transfusion is considered safe in current medical practice, there are still risks of unwanted and unacceptable side effects such as haemolysis, allergic reactions, immunosuppression and disease transmission associated with its use. (Ashworth, 2010)

Cell salvage aims to decrease perioperative allogenic blood transfusion and hence the associated risks for infectious and non-infectious complications. Studies have shown compared to allogenic blood, salvaged red cells have increased mean erythrocyte viability and 2,3-diphosphoglycerate (2,3-DPG) and adeno-triphosphate (ATP) levels, maintaining their biconcave disc shape. (Munoz, 1999) These in theory should translate to improvement in oxygen-carrying capacity and oxygen delivery to tissue. (Schmidt, 1995)

The use of ICS is also associated with potential complications such as non-immune haemolysis, air embolus, coagulopathy, contamination with cleaning solutions and drugs

and microaggregates. (Klein, 2008) With technical advancements and increasing experience with ICS use, the complications in reported literature are rare.

To date, there is a paucity of evidence with regards to the efficacy of cell salvage in reducing allogenic blood transfusion and cost effectiveness. (Weiss, 2007) The purpose of this retrospective review is to determine the efficacy of cell salvage in single-staged posterior spinal fusion surgery.

4.2 METHODS

This retrospective study included 89 patients who underwent posterior spinal fusion for idiopathic scoliosis from January 2016 to August 2016 at University Malaya Medical Centre. All patients have normal haematological and coagulation profile prior to surgery. The operative procedures were performed by a team of experienced senior surgeons and a consultant anaesthesiologist. Standard surgical and anaesthetic techniques were used for all patients. No patients donated autologous blood prior to surgery. Cell saver was employed for all patients. As this is a retrospective study and all subjects were anonymised, no written informed consent was obtained.

The total intraoperative estimated blood loss (EBL) was calculated from the cell salvage system and the weight differences between dry and blood-soaked gauzes, excluding blood lost to the floor, surgical gowns and drapes. EBL is estimated as follows:

Estimated blood loss, EBL (ml)
= final volume accumulated in the reservoir
– total volume of Anticoagulant Citrate-Dextrose (ACD)
– total irrigation fluid used intraoperatively
+ total unfiltered blood

The perfusionist derived the total volume of ACD used and total unfiltered blood (weight differences between dry and used reservoir). Meanwhile, the nurses measured the total irrigation fluid before being used intraoperatively. (Hasan, 2017)

Patient demographics such as age, gender, preoperative weight and height, preoperative Cobb's angles and haemoglobin levels were recorded. Blood volume of each subject was estimated using the Nadler's formula. (Nadler, 1962) Intraoperative data such as number of screws inserted, operative time and mean arterial pressure, amount of blood salvaged were also analysed. Haemoglobin levels sampled at 48 – 72 hours post-procedure were examined.

The mean blood loss for all patients will be derived and based on this parameter, the patients will be categorised into two groups – Group C with less than or equal to mean blood loss, and Group D with more than mean blood loss.

Data analysis was performed using IBM SPSS software version 24. The patient's basic demographic data, surgical statistics, blood loss were compared by independent T-test. The results were expressed as mean $\pm$ SD (standard deviation). A p value of < 0.05 was considered statistically significant.

4.3 RESULTS

Mean intraoperative blood loss was 909.6 $\pm$ 471.9 mls. The patients were categorised into two groups – Group C ($\leq$ 900 mls blood loss, n=50) and Group D (> 900 mls blood loss, n=39).

The mean age and weight were comparable for Group C and D; 16.1 vs 17.0 years (p=0.412) and vs 46.8 vs 49 kgs (p=0.287) respectively. Preoperative baseline

characteristics such as blood volume (3121 vs 3346 mls), Cobb's angle (57.6^{o} vs 66.8^{o}), number of levels fused (9.7 vs 12.4), number of screws (12.4 vs 15.3) were higher in Group D compared to Group C.

Table 4.1 Baseline demographics of patients in low and high blood loss groups in posterior spinal fusion surgery

Baseline Characteristics	**Group C (Blood loss ≤ 900 mls)(n=50)**	**Group D (Blood loss >900 mls) (n=39)**	***p* value**
Age (years)	16.1±6.0	17.0±4.6	0.412
Weight (kg)	46.8±9.7	49.0±8.9	0.287
Blood Volume (mls)	3121.1±410.3	3346.9±534.4	0.032
Cobb's Angle (^{o})	57.6±8.9	66.8±18.1	0.005
Number of levels fused	9.7±2.6	12.4±1.4	<0.001
Number of screws	12.4±2.1	15.3±1.3	<0.001
Surgical Duration (mins)	120.1±28.3	156.7±30.9	<0.001

Mean arterial pressure between the Groups C and D (72.5 vs 71.9 mmHg; p=0.548) did not differ significantly. Blood volume returned by cell saver were 260 mls and 560 mls for Group C and D respectively, achieving statistical significance. For both groups, about 47% of total intraoperative blood loss was returned via cell saver. Analysis of the pre-and postoperative (48 – 72 hours) haemoglobin levels did not demonstrate statistical significance between Groups C and D (preop: 13.4 vs 13.7 and postop: 11.1 vs 10.7 g/dL).

Table 4.2 Measured operative data for patients in low and high blood loss groups in posterior spinal fusion surgery

Operative Data	Group C (Blood loss ≤ 900 mls) (n=50)	Group D (Blood loss >900 mls) (n=39)	*p* value
Pre-op Hb (g/dL)	13.4±1.1	13.7±1.3	0.3
Post-op Hb (g/dL)	11.1±1.5	10.7±1.3	0.187
Blood saved by cell saver (mls)	260.8±105.8	560.2±217.9	<0.001
Blood saved by cell saver (mls/kg)	5.8±2.6	11.5±4.1	<0.001
% of blood loss saved by cell saver	47.1±6.9	47.0±4.0	0.861
Mean arterial pressure (mmHg)	72.5±2.3	71.9±2.5	0.548
Allogenic blood transfusion	0	0	
Duration of hospital stay	3.5±0.5	3.6±0.8	0.438

None of the subjects received perioperative allogenic blood transfusion or reported complications from the use of cell salvage.

4.4 DISCUSSION

The AAGBI guidelines published in 2009 recommended the use of intraoperative cell salvage (ICS) for anticipated blood loss of > 1000mls (or >20% estimated blood volume), patient population with pre-operative anaemia or at increased risk of bleeding, patients with rare blood types or multiple antibodies and those who refuse allogenic blood transfusion. (AAGBI, 2009) Since the complexity of scoliosis surgery involves prolonged operative times and significant blood loss, the use of ICS is popular in many centres. It was reported in the literature that the cost of a unit of allogenic blood ranges from $386 to $2400 while using Cell Saver costs between $240 to $512 per case. (Hannon, 2006; Reitman, 2004; Miao, 2014; Siller, 1996))

Despite their popularity, there is insufficient evidence at present to support the routine use of ICS in scoliosis surgery as the published data are inconsistent, heterogenous and even conflicting in their conclusions with regards to the efficacy and cost effectiveness of ICS. Nonetheless, recent data from randomised trials and meta-analyses suggested that cell saver significantly reduces the transfusion requirement in scoliosis corrective surgery. (Stone, 2017; Liu, 2017; Liang, 2014) In contrast, Weiss et al found that cell saver did not reduce the demand for other transfusion in scoliosis surgery (Weiss, 2007). Meanwhile, Siller *et al* (1996) concluded that pre-donated autologous blood was more cost effective than cell saver usage to meet blood requirements in spinal fusion surgery for idiopathic scoliosis.

During the study period, all patients received cell salvage technique as part of the institutional protocol. Our data showed that higher Cobb's angle, levels of fusion and number of screws inserted, in addition to longer operative time correlate positively with increased blood loss, achieving statistical significance between the two groups.

The higher the blood loss, the higher amount of blood was salvaged by the system and returned to the patient. Of note, the proportion of blood loss returned to the patients by the ICS system was rather consistent (about 47%) in both high and low blood loss group. On the other hand, Weiss et al (2007) found that a blood loss of 500 mls is likely to be returned by cell saver while a systematic review by Stone et al (2017) suggested that cell saver can decrease the number of allogenic blood transfusions by one unit. Further studies are warranted to identify and risk-score potential patients with increased risk of intraoperative bleeding. Targeting the use of cell salvage in this group of patients may improve its cost effectiveness instead of blanket use for all patients.

The pre- and post-operative haemoglobin levels did not differ significantly between the groups despite their differences in blood loss. It showed that intraoperative cell

salvage is efficacious in conserving blood in subjects who had higher blood loss. Its use is justified as none of the patients, especially those with higher blood loss, were transfused with allogenic blood throughout their admission stay.

There are several limitations to this study. This study is retrospective in nature, and the indications for allogenic blood transfusion were not pre-defined. In addition, intraoperative blood loss is an estimated value and its accuracy could be affected by irrigation and hidden blood loss. (Smorgick, 2013) The cases were performed in a university hospital with high case load by experienced surgeons and skilful anaesthetists. Hence, the findings may not be generalizable. Due to the retrospective design, the timing to sample post-operative haemoglobin could not be standardized to a specific time-point after surgery. This may serve to confound the results as suggested by a study by Grant due to post-operative haemoglobin drift. (Grant, 2014)

4.5 CONCLUSION

Intraoperative cell salvage is effective in conserving blood in posterior spinal fusion surgery, especially in patients with higher blood loss. Post-operative haemoglobin levels did not differ significantly between the higher and lower blood loss groups with no patients received allogenic blood transfusion in the perioperative period. In this study, cell salvage managed to recover about 47% of intraoperative blood loss in both the groups.

CHAPTER 5: CONCLUSION

Scoliosis surgery can be associated with significant blood loss. Tranexamic acid, when administered as a single intravenous dose, a higher dose range of more than 20 mg/kg did not appear to be superior to lower dose range of 20 mg/kg or less in decreasing intraoperative blood loss in posterior spinal fusion for adolescent idiopathic scoliosis correction. No patients reported hematological or neurological complications with the use of tranexamic acid. Hence, optimal timing, dose range and duration of tranexamic acid administration need to be examined in future studies.

On the other hand, this retrospective study showed that surgery with higher blood loos benefit from intraoperative cell salvage in limiting blood loss and alleviating the need for allogenic blood transfusion. Post-operative haemoglobin levels did not differ significantly between the higher and lower blood loss groups. No patients received allogenic blood transfusion in the perioperative period even in the higher blood loss group. Cell salvage managed to recover approximately 47% of intraoperative blood loss in this study.

Meticulous surgical technique and anaesthetic management including the use of tranexamic acid and cell salvage eliminated the need of allogenic blood transfusion for all patients examined in the study period. This represent good medical practice as allogenic blood is considered as rare commodity in many healthcare systems and its transfusion is associated with a remote but realistic potential for adverse transfusion reactions.

REFERENCES

Ashworth A, Klein AA. (2010) Cell salvage as part of a blood conservation strategy in anaesthesia. *BJA*; *105(4)*: 401-416

Association of Anaesthetists of Great Britain and Ireland Safety Guideline. Blood Transfusion and the Anaesthetist: Intra-operative Cell Salvage. (2009)

Copley LA, Richards BS, Safavi FZ et al. (1999) Hemodilution as a method to reduce transfusion requirements in adolescent spine fusion surgery. *Spine;24* :219-222

Duffy G, Neal KR et al (1996) Differences in postoperative infection rates between patients receiving autologous and allogenic blood transfision: a meta-analysis of published randomised and non-randomised studies. *Tranfus Med; 6*: 325-8 14.

Fan Z, Kun W, Feng-Ning L, Xuan H et al. (2014) Effectiveness of tranexamic acid in reducing blood loss in spinal surgery: a meta-analysis. *BMC Musculoskeletal Disorders*; *15*: 448

Faraoni D, Goobie SM et al. (2013) New insights about the use of tranexamic acid in children undergoing cardiac surgery: from pharmacokinetics to pharmacodynamics. *Anesth Analg; 117*:760-762.

Florentino-Pineda I, Thompson GH, Poe—Kochert C et al (2004) The effect of amicar on perioperative blood loss in idiopathic scoliosis: the results of a prospective, randomised double-blind study. *Spine 29(3)*: 233-238 8

George DA, Sarraf KM, Nwaboku H. (2015) Single perioperative dose of tranexamic acid in primary hip and knee arthroplasty. *Eur J Orthop Surg Traumatol; 25(1)*: 129-133

Goobie SM, Meier PM, Pereira LM et al. (2011) Efficacy of tranexamic acid in pediatric craniosynostosis surgery: a double-blind, placebo controlled trial. *Anesthesiology; 114*: 862-71

Grant MC, Whitman GJ, Savage WJ, Ness PM, et al. (2014) Clinical predictors of postoperative haemoglobin drift. *Transfusion; 54*: 1460-1468.

Grassin-Delyle S, Tremey B, Abe E, Fischler M et al. (2013) Population pharmacokinetics of tranexamic acid in adults undergoing cardiac surgery with cardiopulmonary bypass. *BJA; 111 (6)*: 916-924

Hannon TJ, Gjerde KP (2006) The contemporary economics of transfusions. *Perioperative Transfusion Medicine 2nd Edn*; 130-138

Hasan MS, Ng CC, Chan CYW, Kwan MK. (2017) Effect of intraoperative autologous transfusion techniques on perioperative hemoglobin level in idiopathic scoliosis patients undergoing posterior spinal fusion: A prospective randomized trial. *Journal of Orthopaedic Surgery; 25(2)*: 1-7

Hiippala ST, Strid LJ, Wennerstrand MI, et al (2014) Medical advances in the treatment of postpartum haemorrhage. *Anesth Analg; 119*: 1140-47

Hourlier H, Fennema P (2014) Single tranexamic acid dose to reduce perioperative morbidity in primary total hip replacement: a randomized clinical trial. *Hip Int*; 24(1): 63-68.

Ker K, Edwards P, Perel P, Shakur H et al. (2012) Effect of tranexamic acid on surgical bleeding: systematic review and cumulative meta-analysis. *BMJ; 344*: e3054.

Klein AA, Nashef SA, Sharples L et al. (2008) A randomised controlled trial of cell salvage in routine cardiac surgery. *Anesth Analg; 107*:1787-1495

Lee TC, Yang LC, Chen HJ. (1998) Effect of patient position and hypotensive anaesthesia on inferior vena cava pressure. *Spine; 23*: 941-947

Liang J, Shen J, Chua S, Fan Y et al. (2014) Does intraoperative cell salvage system effectively decrease the need for allogenic transfusions in scoliotic patients undergoing posterior spinal fusion? A prospective randomised study. *Eur Spine J; 24(2)*: 270-275

Liu JM, Fu BQ, Chen WZ, Huang SH et al. (2017) Cell salvage used in scoliosis surgery: is it really effective? *World Neurosurgery; 101*: 568-576

Miao YL, Ma HS, Guo WZ, et al. (2014) The efficacy and cost-effectiveness of cell saver use in instrumented posterior correction and fusion surgery for scoliosis in school-aged children and adolescents. *PLoS One 2014;9*: e92997

Munoz GM, Sanchez AY, Garcia VJJ, Merida FJ et al. (1999) Pre and post-operative autotransfusion. A comparative study of hematology, biochemistry and red cell metabolism in pre-donated blood and blood from post-operative surgical drainage. *Sangre; 44*: 443–50

Nadler SB, Hidalgo JU, Bloch T. (1962) Prediction of blood volume in normal human adults. *Surgery; 51 (2)*: 224-32

Neilipovitz D (2004) Tranexamic acid for major spinal surgery. *Eur Spine J; 13*: S62-S65.

Ng BKW, Chau WW, Hung ALH, Hui CAN (2015) Use of tranexamic acid (TXA) on reducing blood loss during scoliosis surgery in Chinese adolescents. *Scoliosis; 10*: 28

Pleym H, Stenseth R, Wahba A, Bjella L et al. (2003) Single-Dose Tranexamic acid reduces postoperative bleeding after coronary surgery in patients treated with aspirin until surgery. *Anesth Analg; 96(4)*: 923-928.

Ralley F, Berta D, Binns V, Howard J (2010) One intraoperative dose of tranexamic acid for patients having primary hip or knee arthroplasty. *Clin Orthop Relat Res; 468(7)*: 1905-1911

Reitman CA, Watter WC, Sassard WR. (2004) The cell saver in adult lumbar fusion surgery- A cost-benefit outcomes study. *Spine; 29(14)*: 1580-1584

Ridgeway S, Tai C, Alton P, et al. (2003) Pre-donated autologous blood transfusion in scoliosis surgery. *J Bone Joint Surg Br*; 85: 1032–1036.

Schmidt H, Kongsgaard U, Kofstad J, Geiran O et al. (1995) Autotransfusion after open heart surgery: the oxygen delivery capacity of shed mediastinal blood is maintained. *Acta Anaesthesiol Scand; 39*: 754–8

Sethna NF, Zurakowski D, Brustowicz RM, Bacsik J et al. (2005) Tranexamic acid reduces intraoperative blood loss in pediatric patients undergoing scoliosis surgery. *Anesthesiology; 102*: 727-732.

Shapiro F, Sethna N (2004) Blood loss in pediatric spine surgery. *Eur Spine J*;13(1): S6–S17.

Siller TA, Dickson JH, Erwin WD. (1996) Efficacy and cost considerations of intraoperative autologous transfusion in spinal fusion for idiopathic scoliosis with predeposited blood. *Spine; 21*: 848-852

Smorgick Y, Baker KC, Bachison CC, Herkowitz HN et al. (2013) Hidden blood loss during posterior spine fusion surgery. *Spine J; 13 (8)*: 877-881

Stainsby D, MacLennan S, Hamilton PJ (2000) Management of massive blood loss: a template guideline. *BJA*; 85(3): 487-491

Stainsby D, MacLennan S, Thomas D, Isaac J, Hamilton PJ (2006) Guidelines on the management of massive blood loss. *BJH*; 135 (5): 634-641.

Stone N, Sardana V, Missiuna P (2017) Indications and outcomes of cell saver in adolescent scoliosis correction surgery- a systematic review. *Spine; 42(6)*: e363-370

Sukeik M, Alshryda S, Haddad FS, Mason J (2011) Systematic review and meta-analysis of the use of traxenamic acid in total hip replacement. *J Bone Joint Surg Br*; 93-B: 39-46.

Thomas D, Wee M, Clyburn P, Walker I, Brohi K, et al (2010) Blood transfusion and the anaesthetist: management of massive haemorrhage. *Journal of the AAGBI*; 65 (11): 1153-1161

Tsutsumimoto T, Shimogata M, Ohta H, Yui M et al. (2011) Tranexamic acid reduces perioperative blood loss in cervical laminoplasty: a prospective randomized study. *Spine; 36*: 1913-1918.

Vamvakas EC et al. (2002) Meta-analysis of randomised controlled trials investigating the risk of postoperative infection in association with while blood cell-containing allogenic blood transfusion: the effects of the type of transfused red blood cell product and surgical setting. *Tranfus Med Rev; 16*: 304-14 15.

Weiss J, Skaggs D, Tanner J, Tolo V. (2007) Cell Saver: is it beneficial in scoliosis surgery? *J Child Orthop; 1*: 221-227

Wong J, El Beheiry H, Rampersaud YR, Lewis S et al. (2008) Tranexamic acid reduces perioperative blood loss in adult patients having spinal fusion surgery. *Anesth Analg; 107*: 1479-1486

LIST OF PUBLICATIONS AND PAPERS PRESENTED

"Is a higher dose range of tranexamic acid more superior in reducing blood loss in scoliosis surgery?" – (BP-CO7) was presented at the *Asia Pacific Spine Society (APSS) Annual Meeting* in Taiwan 8th to 9th June 2018 (by Associate Prof. Dr. Chris Chan Yin Wei) and accorded the **"Best Clinical Research Award".**

(Authors: Looi Ji Keon, Mohd Shahnaz Hasan, Arfah Hanim Mohamad, Chris Chan Yin Wei, Kwan Mun Keong)

"Efficacy of cell salvage as blood conservation technique in scoliosis surgery" was accepted for a 2-minute presentation during the *Asia Pacific Spine Society (APSS) Annual Meeting* in Taiwan dated 8th to 9th June 2018.

(Authors: Arfah Hanim Mohamad, Mohd Shahnaz Hasan, Looi Ji Keon, Chris Chan Yin Wei, Kwan Mun Keong)