The Efficacy of Chitosan Dressing in Reducing Blood Loss for Harvest Site in Split Thickness Skin Graft: A Randomized Control Trial

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Background: *Split thickness skin grafting (STSG) is common procedure for covering soft tissue defects and causes bleeding due to large raw surface area. Chitosan is a biodegradable, non-toxic, complex carbohydrate derivative extracted from chitin found in the shells of crustaceous animals. Chitosan is a new local hemostatic dressing certified for external use. But there was no study which was conducted in the randomized control trial to prove the efficacy of chitosan in reducing blood loss for harvest site in split thickness skin graft.*

Objective: *To compare the efficacy of chitosan dressing and standard dressings in reducing blood loss at STSG harvest site and observe its complications.*

Material and Method: *A randomized control trial study to compare the efficacy of chitosan dressing and standard dressings in reducing blood loss at STSG harvest site was performed between June 2014 to August 2015 at HRH Princess Maha Chakri Sirindhorn Medical Center, Srinakharinwirot University in Nakhon Nayok province. Demographic data, area of harvest site, blood loss, VAS score at the time of wound dressing and complications were recorded.*

Results: *Twenty patients with skin defect were randomly assigned into 2 groups (Chitosan group n = 10 and Standard dressing group n = 10). No difference of demographic data between the 2 groups. The average area of donor site in the chitosan group was 36.5 cm^2 and standard dressing group was 40.2 cm^2 (p-value = 0.42). Blood loss from the chitosan group was 15.4 gm compared with 26.3 gm from the standard group (p-value = 0.81). Even though chitosan dressing can decrease the amount bleeding by 40% compared to the standard dressing but there was no significant difference between the two groups. No serious complication was detected at the time of follow-up.*

Conclusion: *Chitosan gauze dressing did not decrease blood loss from harvest sites of STSG compared with the standard dressing group and there was no serious complication associated with chitosan was detected.*

Keywords: *Skin graft, Dressing technique, Chitosan*

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Bleeding is a common complication of surgery and it is possible to have complications from surgical bleeding. Normally this can be prevented by stopping the site of bleeding with various methods such as applying pressure the wound to stop ongoing bleed or use hemostatic materials such as oxidized cellulose, microfibrillar collagen, fibrin adhesives which all have hemostatic effects[1].

Chitosan is a biodegradable, non-toxic, complex carbohydrate derivative extracted from chitin found in shells of crustaceans[2-4]. It is produced by deacetylation of chitin resulting in poly-n-acetyl glucosamine[5,6]. The main properties of chitosan are its hemostatic ability by increasing platelet adhesion and aggregation and increasing production[7] and also via direct electrostatic interaction between the negatively charged cell membranes of erythrocytes and the positively charged chitosan[8]. Chitosan also has an antibacterial property to some organisms and stimulates wound healing there have been papers on animal models suggesting that chitosan increases the rate of wounds healing and helps keep the wound moist[9].

Split thickness skin grafting (STSG) is a common procedure in patients with skin defects from various causes. Bleeding is a normal complication of this surgery especially in the site of graft harvest. Some group of patients that were performed STSG surgery

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were concerned such as burned patients with massive burn area, STSG is a technique used extensively in the care of burnt tissues as well as during subsequent reconstructive procedures that is possible to have a lot of bleeding due the extent of the area of the harvest or elderly patients with poor general condition and pediatric patients, they cannot tolerate to minimal or moderate bleeding because poor blood reserves. The other patients, bleeding can require the physician to change the wounds dressing before the planned date leading to pain and other complications such as re-bleeding, delayed wound healing, unpleasant scaring from removing the original dressing before the appropriated time.

This study aims to compare the efficacy of chitosan dressing and other standard dressings in hospitals. In this study, mostly concern is the amount of bleeding reduced when using chitosan in relation to the size of the wound. It can be applied to later studies also. As for the pain score the authors used the visual analog scale (VAS) while removing the dressing 2 weeks after the surgery and recorded its complications that could be associated with chitosan.

Material and Method

This study received permission from the Ethics committee of the Faculty of Medicine, Srinakharinwirot University. The authors collected data from the patients with skin defects from various causes who were performed STSG by orthopedic surgeons at HRH Princess Maha Chakri Sirindhorn Medical Center, Srinakharinwirot University in Nakhon Nayok province between June 2014 to August 2015. The authors aimed to investigate the efficacy of chitosan gauze dressing compare to standard dressings in reducing blood loss and observed its complications that could be associated with chitosan. The patients were given an explanation about the study and the plan of management after STSG surgery including the different types of dressings used and side effects and its managements before applying to this study. The exclusion criteria included patients with underlying diseases that affect coagulation or affect the rate of wound healing such as diabetes mellitus, patients that were on medications that change the coagulability state of the blood such as aspirin and warfarin, patients with infected wounds, patients who cannot co- operate or use the VAS, patients who are allergic to seafood were also excluded from this study.

The patients who participated in the study were randomly assigned by blocked randomization using sealed envelopes into standard dressing group or chitosan dressing group. The authors collected information on sex, age, size of injury wound, hematocrit level, underlying diseases and current medications. All the participants were performed STSG surgery using the skin from thigh as the harvest site. The graft was harvested using the electric dermatome with settings for harvest depth of 0.016 inches. The harvest site was measured and taken a photograph which would be used to calculate the total surface area of the wound with the program image J software version 1.47. After that for the chitosan group the bactrigras were placed followed by chitosan (AnsCare ChitoClot Gauze, model name: CG-212-2, 100% pure chitosan, BenQ Materials Corporation Taoyuan Taiwan) and then 4x4 gauze pads. The authors recorded the amount and size of the dressing material and then closed the wound and wrapped the thigh with a 4 inches elastic bandage (Fig. 1, 2). For the standard dressing group, the wound dressing was done with standard technique using the same methods as the chitosan group the only difference was chitosan gauze was not use.

The authors calculated the average weight of the dressing by weighing the material by and found that the dressing weighs 1.1 gram per piece of 4x4 gauze, 0.45 gram per 5x5 cm of bactrigras, a 5x5 cm chitosan weighs 0.28 grams per piece (Fig. 3). 2 weeks after the surgery all the participant's dressings were removed without use of normal saline solution or any liquids that may increase the weight of the dressing used, the

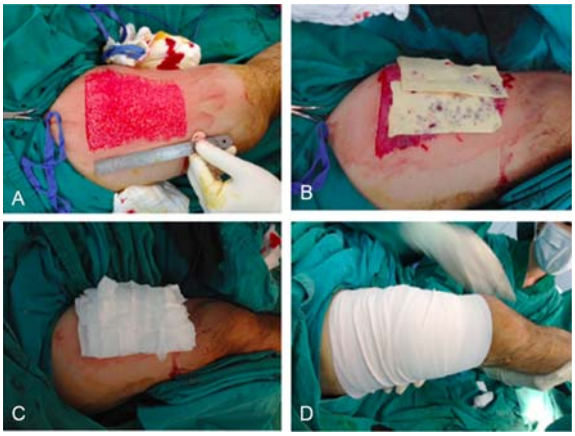

Fig. 1 Dressing techniques in the chitosan group. A) Harvested graft by electric dermatome with thickness of 0.016 inches. B) The chitosan were placed over the bactrigras. C) 4x4 sterile gauzes were placed over the chitosan and bactrigras. D) Elastic bandage 4 inches was used to close the harvest site.

dressing excluding the elastic bandage were collected and weighed. The authors used the weight of the dressing at 2 weeks post-surgery subtracted by the initial weight of the dressing to get the difference in the weight of the dressing which represents the amount of blood accumulated in the dressing material and recorded the results, the authors also recorded the pain score while removing the dressing by using the VAS, and recorded any possible complications that could be associated with the chitosan such as allergic reaction[10]. The data was then compared by using Chi-square and unpaired t-test if the results were lesser than 0.05 it would mean there was a significant statistical difference between the two groups. Previous studies of chitosan dressing have shown that chitosan dressing reduces the bleeding time by 50% compared to the standard dressing[11]. After calculating the size of the population the authors found that this study would require at least 10 participants in each group.

Results

In present study had twenty-two participants but two participants were excluded because one had diabetes mellitus and the other one was on aspirin. In total the study consisted of twenty participants. They were randomized into two groups. Ten were randomized into the chitosan dressing group and the other ten were randomized into the standard dressing group (Fig. 4). There was no loss of follow-up in this study.

In present study average weight of blood accumulated in the chitosan group were 15.4 grams (range 14.5-30.3) compared to the standard dressing group weighing 26.3 grams (range 12.5-32.1) and the VAS score while removing the dressing at 2 weeks post-surgery in both group were 3 (Table 2). Even though the authors found that chitosan dressing can decrease the amount bleeding by 40% compared to the standard dressing but there was no significant difference between the two groups. There was no difference in the pain score when removing the dressing in the two groups and both groups' wounds healed normally and without serious complications such as allergic reaction, wound infection, delayed wound healing or hypertrophic scar.

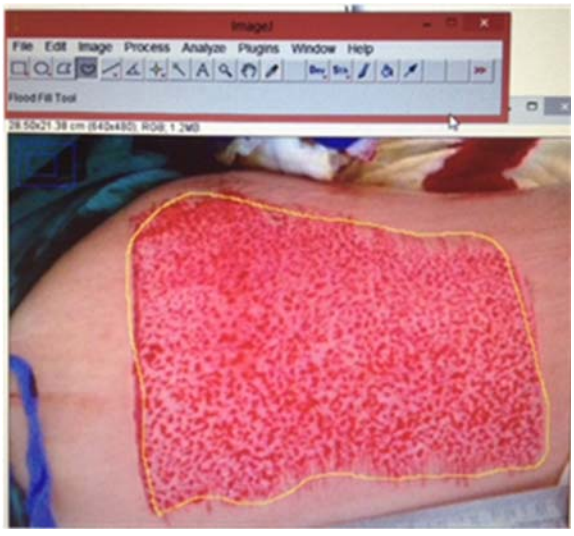

Fig. 2 The calculation of total surface area of the wound with the program image J software version 1.47.

Fig. 3 A 5x5 cm chitosan weighs 0.28 grams per piece.

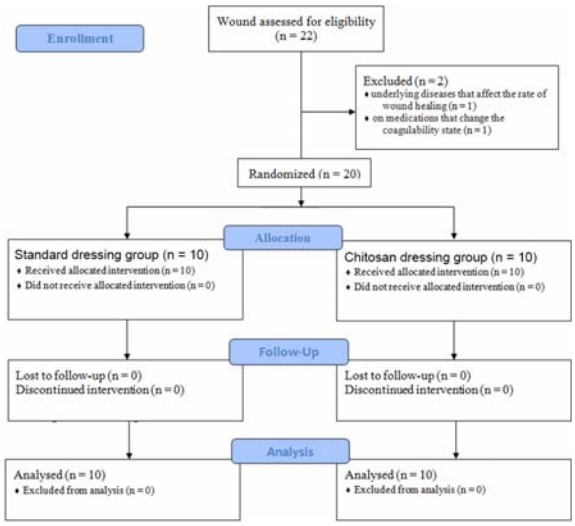

Fig. 4 CONSORT 2010 Flow Diagram.

Discussion

Chitosan dressing was first used on humans in the army in the Iraq war and Afghanistan war reports showed 69 soldiers were wounded and were bleeding from the wound received chitosan dressing to stop the bleed results showed 97% success rate in stopping the bleed initially before the patients were transported to hospital for further treatment[12,13]. Brown MA[14] reported that using chitosan dressing for road traffic accidents on bleeding wounds by applying pressure could stop bleeding by 79% where 74% the bleeding was controlled by 3 minutes. The authors of that paper concluded that chitosan dressing was useful in patients which could not control their bleeding by normal measures. Arbel J[15] found that chitosan reduced bleeding time and reduced hematoma of femoral artery after coronary angiography compared to the standard dressing. Jain Y[11] found that use of chitosan after intervention in pediatric patients with congenital cardiac conditions could reduce clotting time compared to the standard dressing by as much as 50%.

Many clinical case reports revealed that chitosan dressing had strong trends toward faster hemostasis onset and less total blood loss in patients with trauma scenarios or arterial bleeding compared to standard dressing but it's efficacy has not been tested and proven in superficial wound as STSG harvest site.

The present study is the first randomized control study to compare two groups between Chitosan and Standard dressing in wound dressing with a superficial raw surface area in split thickness skin grafting with accurate statistics which is the strong point of this study. The authors found that the chitosan dressing decreased the amount bleeding by 40% compared to the standard dressing but there was no significant difference. It might be because split thickness skin graft harvest site is a superficial wound and slowly bleed so the interaction of chitosan with red blood cells forms an adherent membrane which temponades the wound[16] may not effective in this type of wound and the pressure bandage was applied on STSG harvest site postoperatively in present study that could reduce bleeding from harvest site. There was no serious complication associated with chitosan was detected.

The limit of this study is the numbers of participants were quite low and also harvest site areas in present study were not very large leading to a not significant statistics different result in the groups of amount of blood in the dressing material and the VAS score when removing the dressing at 2 weeks post-surgery and the pressure from bandage that was applied postoperatively could not be exactly controlled.

Conclusion

In present study found the chitosan dressing did not decrease the amount of blood loss in split thickness skin graft harvest sites when compared to standard dressing. However, there was no serious complication associated with chitosan was detected.

Table 1. Demographic data

Topic	Chitosan (n = 10)	Standard (n = 10)	*p*-value
Gender			0.18
Male	4	7	
Female	6	3	
Mean age (years) (SD = 13.47)	45.5 (34-60)	42.1 (30-55)	0.61
Donor site area (cm^2) (SD = 14.11)	36.5 (23.3-56.2)	40.2 (35.1-58.7)	0.42
Hematocrit (%) (SD = 3.71)	36.7 (33-41)	35.3 (30-42)	0.11

Table 2. Blood volume and VAS

	Treatment		*p*-value
	Chitosan	Standard	
Blood weight (g) (SD = 10.35)	15.4 (14.5-30.3)	26.3 (12.5-32.1)	0.81
VAS dressing (IQR, 2 to 5)	3 (3-5)	3 (2-5)	0.62

The authors believed that further studies on this topic should prove to be useful.

What is already known on this topic?

Chitosan has been widely accepted as the newer material used for dressing the wound to stop ongoing bleed. But there was no study which was conducted in the randomized control trial to prove the efficacy of chitosan in reducing blood loss and the complications associate with chitosan are still the concern.

What this study adds?

The chitosan dressing did not decrease blood loss in split thickness skin graft harvest sites compared to the standard dressing and there was no serious complication associated with chitosan was detected.

Acknowledgements

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Potential conflicts of interest

None.

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การศึกษาเกี่ยวกับประสิทธิภาพของการใช้วัสดุปิดแผลไคโตซานเพื่อลดปริมาณเลือดออกในผู้ป่วยที่ทำการผ่าตัดปลูกถ่ายผิวหนังชั้นนอก: งานวิจัยแบบสุ่มและมีกลุ่มควบคุม

ฐิติณัฐ ดิลกหัตถการ, ภรัณยู วิไล, วิศิษฏ์ รังษิฌาภรณ์

ภูมิหลัง: *การผ่าตัดปลูกถ่ายผิวหนังชั้นนอกเป็นหัตถการที่ทำในผู้ป่วยที่สูญเสียผิวหนังชั้นนอกไป ซึ่งทำให้เกิดภาวะเลือดออกมากในบริเวณที่ย้ายผิวหนังมา เนื่องจากมีพื้นผิวดิบบริเวณกว้างทำให้ต้องเปลี่ยนวัสดุปิดแผลก่อนถึงเวลาอันควร ทำให้ผู้ป่วยเกิดความเจ็บปวดขณะเปลี่ยนวัสดุปิดแผล และอาจทำให้เกิดแผลเป็นที่ไม่พึงประสงค์ ไคโตซานเป็นวัสดุปิดแผลที่สกัดจากเปลือกแข็งของสัตว์ทะเล มีคุณสมบัติทำให้เลือดหยุดเร็วขึ้น สามารถช่วยลดปริมาณเลือดออกจากแผลผ่าตัดได้*

วัตถุประสงค์: *เพื่อศึกษาการใช้ไคโตซานเปรียบเทียบกับการใช้วัสดุแบบมาตรฐานในการปิดแผล ผู้ป่วยที่ทำการผ่าตัดปลูกถ่ายผิวหนังชั้นนอก ในการช่วยลดปริมาณเลือดออกจากแผลผ่าตัด รวมถึงศึกษาภาวะแทรกซ้อนจากการใช้ไคโตซาน*

วัสดุและวิธีการ: *ผู้นิพนธ์ได้ดำเนินการศึกษาแบบสุ่มและมีกลุ่มควบคุมในผู้ป่วยที่เข้ารับการผ่าตัดปลูกถ่ายผิวหนังชั้นนอก ตั้งแต่เดือนมิถุนายน พ.ศ. 2557 ถึงเดือนสิงหาคม พ.ศ. 2558 จำนวน 20 ราย ที่ศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดาฯ สยามบรมราชกุมารี คณะแพทยศาสตร์ มหาวิทยาลัยศรีนครินทรวิโรฒ จังหวัดนครนายก โดยแบ่งเป็น กลุ่มทดลอง คือ ผู้ที่ได้รับการปิดแผลด้วยไคโตซาน 10 ราย และกลุ่มควบคุม คือ ผู้ที่รับการปิดแผลด้วยวิธีมาตรฐาน 10 ราย โดยมีการเก็บข้อมูล ได้แก่ข้อมูลพื้นฐานของผู้เข้าร่วมงานวิจัย ขนาดของแผล น้ำหนักของวัสดุปิดแผล คะแนนความปวด และภาวะแทรกซ้อนที่เกิดขึ้นภายในระยะเวลา 2 สัปดาห์ หลังการผ่าตัด*

ผลการศึกษา: *ไม่มีความแตกต่างกันใน 2 กลุ่มประชากร ปริมาณเลือดออกโดยเฉลี่ยจากกลุ่มที่ใช้ไคโตซานเท่ากับ 15.4 กรัม มีปริมาณน้อยกว่า ปริมาณเลือดออกจากกลุ่มที่ปิดแผลโดยวิธีมาตรฐานซึ่งมีปริมาณเท่ากับ 26.3 กรัม แต่ไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติ และไม่พบภาวะแทรกซ้อน จากการใช้ไคโตซานเป็นวัสดุปิดแผล*

สรุป: *การศึกษานี้พบว่าไคโตซานไม่สามารถลดปริมาณเลือดออกจากแผลผ่าตัดย้ายผิวหนังเมื่อเปรียบเทียบกับการปิดแผลด้วยวิธีมาตรฐาน*