The Thai Journal of Orthopaedic Surgery

The Official Journal of the Royal College of Orthopaedic Surgeons of Thailand

The Official Journal of Thai Hip & Knee Society
The Official Journal of Spine Society of Thailand
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ISSN 0125-7552

Volume 40 / Number 1-2 January-April 2016

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ISSN 0125-7552

Volume 40 / Number 1-2 January-April 2016

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The Thai Journal of Orthopaedic Surgery

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The Journal is free online at http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST

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สารบัญ

Editorial

The current editorial board of the Royal College of Orthopaedic Surgeons of Thailand (RCOST) has been working since May, 2013. One of our main policy is to improve our journal to the national level (cited in Thai Journal Citation Index (TCI)) and to international level (cited in international database of Scopus and PubMed). The Thai Journal of Orthopaedic Surgery is an official journal of RCOST. TCI has started accredited all Thai scientific journals and classified them into three categories. The first category is the journals that have been approved by TCI and and are listed in the TCI database. The second category is the journals that are in the reaccreditation process but are currently listed in the TCI database. The last category includes the journals which quality does not reach the TCI requirement and yet listed in the TCI database.

We are successfully put The Thai Journal of Orthopaedic Surgery into the Thai Journal Citation Index (TCI) as the second category journal. The quality of The Thai Journal of Orthopaedic Surgery is improving and we plan to resubmit our data in order to be approved as the first category journal. As the Thai Journal of Orthopaedic Surgery is currently listed in the second category, TCI allows journals in the second and the third categories to be improved and resubmitted their data every three years.

In this volume, there are four research articles, published:

1. Intraarticular Tranexamic Acid Decreased Transfusion Rates and Blood Loss in Primary Total Hip Arthroplasty: A Prospective Randomized Double-Blind Placebo-Controlled Trial
2. Gentamicin Release from Bone Cement: A Comparative Study between Hand Made Liquid & Powder Gentamicin beads
3. Cost Analysis of Blood Transfusion and Tranexamic acid in Primary Total Knee Arthroplasty
4. Metastasis of cardiac rhabdomyosarcoma at lumbar spine: case report

Once again, we hope that we will receive sufficient high quality articles to obtain a good ranking. In the upcoming volume, which will be distributed in the Royal College of Orthopaedic Surgeons of Thailand and ASEAN Orthopaedic Association (RCOST & AOA) combined meeting during October 6-8, 2016, we assure that more original articles, review articles, and case reports will be included. Lastly, we would like to express our sincere gratitude to all authors, all members of the editorial board, all peer reviewers and editorial office staffs. They all work very hard to improve a high quality and standard for the journal.

Pongsak Yuktanandana, MD
Aree Tanavalee, MD
Sittisak Honsawek, MD

Intraarticular Tranexamic Acid Decreased Transfusion Rates and Blood Loss in Primary Total Hip Arthroplasty: A Prospective Randomized Double-Blind Placebo-Controlled Trial

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Backgrounds: *Total hip arthroplasty (THA) often requires blood transfusion postoperatively. Tranexamic acid (TXA) has been successfully used intravenously to control bleeding. Intraarticular TXA is safe and effective at reducing postoperative bleeding in orthopedic procedures, but there is limited literature regarding its use in THA. The objective of this prospective randomized study was to determine if intraarticular TXA decreased postoperative transfusion rates and bleeding after primary THA.*

Propose: *To study the efficacy of intraarticular tranexamic acid to decrease postoperative transfusion rates and blood loss after primary total hip arthroplasty.*

Methods: *A prospective double-blinded, randomized controlled trial of 135 primary THA of 118 patients investigated the efficacy of intraarticular application of TXA on blood loss compared with a placebo in Maharat Nakhon Ratchasima Hospital during the period from September 2013 to March 2015. Intraarticular TXA (750 mg) was applied after acetabular and femoral canal preparation. The primary outcome was blood transfusion rate, the mean drain blood loss, and total blood loss by Gross formula. Secondary outcomes include the units of blood transfusion, nadir post-operative hemoglobin and hematocrit, hemoglobin and hematocrit concentration change, visual analog scales (VAS), length of hospital stay, and up to 12 weeks follow-up for surveillance complications.*

Results: *Patients in the TXA group insignificantly improved in reduction of transfusion rates (TXA group = 39.7%, Placebo = 55.2%; P-value = 0.07), drain blood loss (TXA group = 535 mL, Placebo = 540mL; P-value = 0.45), and total blood loss by Gross formula (TXA group = 771 mL, Placebo = 757 mL; P-value = 0.59) compared with the placebo. However, the units of blood transfused decreased significantly in the TXA group cases compared to the placebo (TXA = 0.53 units per case, Placebo = 0.88 units per case; P-value=0.035). Visual analog scales (VAS) also reduced significantly in the TXA group (TXA = 3.9, Placebo = 4.7; P-value=0.001). There were three complications in the tranexamic acid group (two acute febrile illness and one dislocation) and five in the placebo group (one superficial infection, two acute febrile illness and two dislocation). There was no sciatic nerve irritation from the diluted dose of tranexamic acid used in the study.*

Conclusions: *The use of 750mg intraarticular tranexamic acid in patients undergoing THA does not effectively reduce postoperative blood transfusion rates and bleeding. However, the units of transfusion (units per case) and visual analog scale could be declined statistically significantly.*

Keywords*: Tranexamic acid, Intraarticular, Total hip arthroplasty, Transfusion rate, Blood loss*

The Thai Journal of Orthopaedic Surgery: 40 No.1-2: 3-12
Full text. e journal: *http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST*

Introduction

Total joint replacement surgery may produce large amounts of perioperative blood loss and significant rates of transfusions. Patients undergoing total hip arthroplasty (THA) are transfused at rates of 16–37%.[1] However, such transfusions are associated with a risk of microbial infection, viral transmission, fluid overload, and high costs.[2]

A variety of blood-conserving techniques has been developed to reduce blood loss and postoperative transfusion rates, including controlled hypotension, regional anesthesia, autologous blood transfusion, intraoperative blood salvage, and the use of erythropoietin and antifibrinolytic agents.[3-4]

In recent years, there have been several studies on the effectiveness of tranexamic acid (TXA), a fibrinolytic inhibitor, for reducing intraoperative and postoperative blood loss.[5-8] Tranexamic acid is a synthetic derivative of the

amino acid lysine that inhibits fibrinolysis by blocking the lysine-binding sites on plasminogen.[9] The coagulation and fibrinolytic systems remain in a state of dynamic balance, which maintains an intact vascular system.[10]

Tranexamic acid, as an antifibrinolytic agents, have been used in orthopedics surgery via an intravenous (IV) route, resulting in a 50% reduction in the rate of transfusions.[11-13] However, there are isolated case reports of thrombus formation, which has generated concerns over the risk of thromboembolic complications in patient populations already at high risk for deep vein thrombosis and pulmonary embolism. These have prevented the widespread acceptance of the use of IV antifibrinolytics in total joint replacement surgery.[14-15]

Topical application of antifibrinolytic agents may produce the same efficacy, but lower systemic absorption and thus a lower risk for thromboembolic complications. Prior studies have suggested that topical tranexamic acid is safe and effective at reducing postoperative bleeding in orthopedic procedures.[16-17] These studies are small and limited to screw fixation of the lumbar spine and total knee arthroplasty (TKA).[18-20] The objective of this prospective randomized study was to determine if intraarticular tranexamic acid decreased postoperative transfusion rates and bleeding after primary total hip arthroplasty (THA).

Patients and Methods

After receiving Institutional Review Board (IRB) approval, this study was performed as a prospective, randomized, double-blind, placebo-controlled trial of the effect of intra-articular application of tranexamic acid on transfusion and blood loss requirements following a unilateral total hip arthroplasty at a single tertiary health care provider (Maharat Nakhon Ratchasima Hospital) with a single surgeon.

Patients of the surgeon author, aged 18 years and older, who were scheduled for a primary THA with or without cement were eligible for inclusion in the trial. Patients with known hypersensitivity to TXA or its ingredients, current preoperative coagulopathy or thrombocytopenia, previous history of deep vein thrombosis (DVT) or pulmonary embolism (PE), suspected pathologic fracture from primary or metastasis bone tumor, or those who refused to participate in the research project were excluded from this study. The baseline level of hemoglobin, hematocrit, prothrombin percentage activity (PT), active partial thromboplastin time (APTT), and platelet count were measured in all participants at least a week before the arthroplasty.

The primary outcome was the change in the proportion of patients undergoing blood transfusion during the index procedure. Secondary outcome measures were blood loss, the units of blood transfused, hemoglobin and hematocrit concentration changes, length of stay, and complications.

Postoperative blood loss was determined by measuring the Redivac drain volumes at the time of removal. The total blood loss (ABL) was calculated using the formula of Gross[27,28,36]as follows:

$$ABL = BV \times \frac{[Hct(i) - Hct(f)]}{Hct(m)}$$

$$Blood\ Volume\ (BV) = Body\ weight\ in\ Kgs \times 70\ mlkg^{-1}$$

Where the reduction in hematocrit was the difference between the preoperative and the lowest postoperative hematocrit values. The Hemoglobin level and the hematocrit were recorded preoperatively and on the first and second postoperative days, and anytime when the patient had anemic symptoms.

The total hip arthroplasty was performed with use of a spinal anesthetic or general anesthesia. The patient was positioned semi-lateral decubitus on the operating table. A standard lateral approach (Modified Hardinge's) with navigation was used.

Designated operating room staff prepared either the study drug, 750 mg of tranexamic acid in 100 mL of saline solution, or the placebo, 100 mL of a saline solution with a similar color, smell, and feel. 50 mL of solution was bathed after acetabular preparation the acetabulum, left for 3 minutes, then removed with suction. An uncemented acetabular component was then impacted with or without adjunct screw fixation. After femoral canal broach preparation, the remaining 50 mL of the solution was placed within the femoral canal, left for 3 minutes, and then removed with suction. The femoral stem was then impacted into place followed by reduction of the final hip components. The gluteus medius muscle was repaired. A Redivac drain was placed. Deep fascia, subcutaneous, and skin closure were performed in a standard fashion.

According to the postoperative protocols, serial blood samples were collected from the patients for complete blood count (CBC) at twenty-four and forty-eight hours postoperatively. The drain was inserted and removed in the morning of the second day postoperatively in all cases. After discharge from hospital, the patients were appointed to follow-up at two, four, eight and twelve weeks after surgery.

A transfusion protocol was utilized to standardize the use of blood transfusions. According to the protocol blood transfusion was not indicated when the hemoglobin concentration was >10 g/dL; was indicated when the hemoglobin concentration was <8 g/dL; and was indicated when the hemoglobin concentration was between 8 and

10 g/dL in a patient who developed fatigue, palpitation, pallor, tachycardia, and tachypnea due to anemia.

Patients received standard patient-controlled analgesia involving morphine for the first forty-eight hours and were then transitioned to oral analgesia. No patients received any thromboprophylaxis.

Prior to participating in the trial, all participants provided written informed consent, which was obtained in the physician office by the surgeon preoperatively.

Randomization was performed by computerization (block of four) and concealed envelopes. Anonymous basic details regarding the patient and surgeon were entered (to allow stratification and subsequent identification), and the staff confirmed this information before randomization. A unique identification number and the allocation group were subsequently assigned. The staff prepared the study medicine and provided it to the surgeons. The surgeons, their team members, and the patient remained blinded to the allocation. The outcomes measures consisted of objective data (transfusion rate, drain blood loss, total blood loss, units of transfusion, nadir post-operative hemoglobin and hematocrit, hemoglobin level change, hematocrit level change, visual analog scale(VAS), length of stay, and complications).

Statistical analysis

Analysis was on the basis of intention to treat. The power calculation was based on the primary outcome measure of the proportion of patients who received blood transfusions 32.1% in placebo group and 12.5% in tranexamic acid group. A one-tailed continuity corrected Chi-squared test with 80% power and a 5% level of significance produced a required sample size which was increased by 20% to allow for drop out, and was 132 cases (66 per groups). Statistical analysis was performed using the STATA, version 12.0 (College Station, TX). Data are reported as mean ± standard deviation (SD). Student t-test and Fisher's exact test were used to compare non-parametric means. Since some continuous data distributions were highly skewed, bootstrapped estimation (10,000 bootstrap samples) was also performed, and was reported when the result differed qualitatively from the parametric findings. The data were analyzed with the use of the Mann-Whitney *U*-test. A *P*-value < 0.05 was considered to be statistically significant.

Results

During the recruitment period from September 2013 to March 2015, 152 cases were scheduled to have a total hip arthroplasty at Maharat Nakhon Ratchasima Hospital. Thirteen cases were excluded due to ineligibility and four cases declined participation. The remaining 135 cases from 118 eligible participants were recruited and formed the study cohort; sixty-seven cases were randomized to the placebo group and sixty-eight, to the tranexamic acid group (Fig. 1). The two groups had similar baseline characteristics (Table 1).

The primary and secondary outcomes are shown in Table 2. The blood transfusion rate tended to be lower in the tranexamic acid group (39.7%) when compared the placebo group (55.2%), but did not show a statistically significant difference (P = 0.07, RR = 0.72) (Fig. 2). The median drain blood loss was 540 mL in the placebo group and 535 mL in the tranexamic acid group (P = 0.45). Total blood loss was estimated with use of the formula developed by Gross[27,28,36]. The mean total blood loss was 757 mL in the placebo group and 771 mL in the tranexamic acid group (P = 0.59). There was no statistically significant difference (Fig. 3). Significantly fewer units of blood were transfused in the tranexamic acid group (0.53 units per case) than the placebo group (0.88 units per case) with a mean difference of 0.35 units per case, P = 0.035 (Fig. 4). Hemoglobin and hematocrit levels were tested on postoperative day two unless there was an earlier clinical need. The nadir postoperative hemoglobin level was higher in the tranexamic acid group (median Hb = 10.2 g/dL) compared with the placebo group (median Hb = 9.6 g/dL), but did not show a statistically significant difference (P = 0.09). Similarly, the nadir postoperative hematocrit level was higher in the tranexamic acid group (median Hct = 30%) compared with the placebo group (median Hct = 29%), but did not show a statistically significant difference (P = 0.15). The change of hemoglobin was lower in the tranexamic acid group compared with the placebo group (median Hb change = 1.7 g/dL vs 1.9 g/dL ; P = 0.33). The change of hematocrit was also lower in the tranexamic acid group compared with the placebo group (median Hct change = 30% vs 29% ; P = 0.33). The mean visual analog scale (VAS) was 3.9 in the tranexamic acid group, significantly less than the 4.7 in the placebo group (mean difference 0.8, P = 0.01). Patients who received the placebo had a mean hospital stay of 5 days compared with 4 days for patients who received tranexamic acid (median difference 1 day; P = 0.18). At the twelve weeks follow-up, there were three complications in the tranexamic acid group (two acute febrile illness and one dislocation) and five in the placebo group (one superficial infection, two acute febrile illness and two dislocation). The frequencies of these complications did not differ significantly between the two arms of the study. There was no sciatic nerve irritation, deep vein thrombosis and venothromboembolism from the diluted dose of tranexamic acid used in the study.

Discussion

THAs may cause considerable blood loss. Postoperative anemia can lead to increased mortality and morbidity, a longer hospital stay, and delayed rehabilitation, especially in patients with vascular disease.[29-32] Blood transfusion is associated with several well-recognized risks and complications, including transfusion-related acute lung injury, hemolytic transfusion reactions, transfusion-associated sepsis, and transmission of infectious agents.[33,34]

In a recent systematic review and meta-analysis[35] of eleven randomized controlled trials, intravenous tranexamic acid reduced blood loss and transfusion needs significantly. However, only one of the included trials had more than fifty participants. Only five studies described a transfusion trigger, which is essential to standardize blood transfusion as an outcome measure. Overall, intravenous tranexamic acid reduced blood transfusion rates by 20% (range, 28% to 34%), comparable with intraarticular tranexamic acid. A similar trend was seen in drain blood loss.

The potential advantages of the intraarticular application of tranexamic acid are direct targeting of the site of bleeding and prevention of systemic side effects. In literature of intraarticular tranexamic acid, there has been only two randomized trials and three retrospective studies evaluating intraarticular tranexamic acid in THA. Although the dosage range used in the literature was 1 to 3g, there are differences in the regiment and technique of administration. However, there is a trend toward reductions in blood transfusion rates and units of blood transfused for tranexamic acid over placebo in all literatures.[21,23,24,25,26] But there is no literature using lower than 1g of intraarticular tranexamic acid.

Our study was carefully designed to minimize error (minimizing bias through use of a randomized design and sampling error through adequate study power). The study design, protocol, and patient information sheets were reviewed by expert research bodies, and the patients receiving care were blinded to the treatment allocation and operated on by a single surgeon. Treatment and placebo solutions had the same color, smell, and feel, maintaining blinding throughout the surgery.

Although visible drain blood loss was not demonstrated to be significantly lower in the tranexamic acid group, it has been known that some blood loss is not clinically visible. Eipe and Ponniah[27] showed that surgical blood loss was underestimated by 64% when clinical methods were used to assess blood-soaked sponges and blood lost to suction bottles and the vacuum drain. They therefore recommended using a biochemical method based on the hematocrit level. In our study, the total blood loss was estimated with use of the Gross formula[27, 28,36]. However, it could be confounded by factors such as patient hydration.

The present study had some limitations. First, the dosage of intraarticular tranexamic acid used in our study (0.75 g) was lower than that used in other studies in which the dosage ranged from 1 to 3g. Inadequate dosage or inadequate bathing time may be the cause of the not statistically significant reduction in transfusion rates and blood loss, thus further study should be performed. Although the dosage of tranexamic acid was low, we may effectively reduce the units for blood transfusion in our patients by using the intraarticular administration route. It implied that intraarticular tranexamic acid may demonstrate cost effectiveness over the placebo. Second, venography or CT scans were not routinely performed to screen for pulmonary embolism or thromboembolic complications. Some asymptomatic venous thromboembolism might have been overlooked. Third, serum concentrations of TXA were not measured. Forth, the study was not adequately powered to detect differences in rare complication such as venothromboembolism. The low incidence rate of their occurrence would necessitate a very large number of participants to detect a small difference precisely. Fifth, the twelve weeks follow-up period was thought to be adequate to identify known adverse events, but it might be inadequate to detect longer-term safety issues, such as accelerated wear of the joint due to exposure to tranexamic acid and functional recovery.

Conclusions

The use of 750mg intraarticular tranexamic acid in patients undergoing THA did not effectively reduced postoperative blood transfusion rates and bleeding. However, the units of transfusion (units per case) and visual analog scale were declined by a statistically significant amount.

Acknowledgements

The authors would like to thank Department of Anesthesiology, Maharat Nakhon Ratchasima Hospital for providing subject to this study

Table 1 Baseline Characteristics of the Study Population			
Demographic Characteristic	Placebo Group (n=67)	Tranexamic Acid Group (n=68)	*P*-value
Age† (yr)	51 ± 14.6	52 ± 14.8	0.55
Gender (n: female/male) % male	17/50 74.6%	24/44 64.7%	0.21
BMI‡ (kg/m^2)	20.8 (18.7-23.4)	21.2 (19.3-24.3)	0.23
Side (n: left/right) % left	40/27 59.7%	35/33 51.5%	0.34
ASA status [n(%)]			0.53
I	14 (20.9%)	11 (16.2%)	
II	31 (46.3%)	38 (55.9%)	
III	22 (32.8%)	19 (27.9%)	
IV	0	0	
Diagnosis [n(%)]			0.6
Osteonecrosis	44 (65.7%)	43 (63.2%)	
DDH	3 (4.5%)	7 (10.3%)	
Osteoarthritis	8 (11.9%)	6 (8.8%)	
Fracture	12 (17.9%)	12 (17.7%)	
Preoperative laboratory values‡			
Hemoglobin (g/dL)	12.1 (10.9-13.3)	12.3 (11.3-13.7)	0.52
Hematocrit (%)	36.4% (33.5%-40.7%)	38.0% (34.2%-41.4%)	0.42
Platelet count (x10^9/L)	265.0 (216.0-349.0)	241.5 (194.5-317.0)	0.13
Preoperative comorbidities [n(%)]			
Coronary arterial disease	1 (3.0%)	0 (0.0%)	0.24
Hypertension	18 (26.9%)	23 (33.8%)	0.38
Dyslipidemia	6 (9.0%)	5 (7.4%)	0.73
Diabetes mellitus	5 (7.5%)	4 (5.9%)	0.74
Obstructive lung disease	3 (4.5%)	2 (2.9%)	0.68
Chronic renal insufficiency	7 (10.5%)	6 (8.8%)	0.75
Cerebrovascular accident	1 (1.5%)	0 (0.0%)	0.49
Liver disease	4 (6.0%)	0 (0.0%)	0.06
Autoimmune disease	7 (10.5%)	10 (14.7%)	0.46
Precaution	4 (6.0%)	1 (1.5%)	0.21
Stem type [n(%)]			0.36
Cementless conventional stem	42 (62.7%)	40 (58.8%)	
Cementless short stem	23 (34.3%)	22 (32.4%)	
Hybrid stem	2 (3.0%)	6 (5.9%)	
Cup size† (mm)	51.5 ± 2.7	51.6 ± 2.7	0.89
General/spinal anesthesia (n)	26/41	19/49	0.18
Operative time‡ (min)	107 (90-135)	113 (90-145)	0.64

† The values are given as the mean and the standard deviation.
‡ The values are given as the median and interquartile range : Non parametric : Mann-Whitney *U*-test
¥ Significantly different.

Table 2 Primary and Secondary Outcomes

	Placebo Group (n=67)	Tranexamic Acid Group (n=68)	*P*-value
Primary end point			
Transfusion [n(%)]	37 (55.2%)	27 (39.7%)	0.07
Blood loss‡			
Drain blood loss (mL)	540 (320-690)	535 (400-702.5)	0.45
Total blood loss (mL)	757.1 (387.6-1127.5)	771.8 (340.2-1163.2)	0.59
Secondary end point			
Units of transfusion† (unit per case)	0.88 ± 1.12	0.53 ± 0.76	0.035¥
Nadir post-op hemoglobin‡ (g/dL)	9.6 (9.0-10.7)	10.2 (9.0-11.7)	0.09
Nadir post-op hematocrit‡ (%)	29.0 (27.0-32.0)	30.0 (27.0-34.0)	0.15
Change of hemoglobin‡ (g/dL)	1.9 (1.1-2.9)	1.7 (0.8-2.9)	0.33
Change of hematocrit‡ (%)	6.7 (4.0-9.0)	6.35 (3.1-9.7)	0.48
Length of hospital stay‡ (days)	5 (4-7)	4 (4-6)	0.18
Visual Analog Scale†	4.7 ± 1.9	3.9 ± 1.8	0.01¥
Complication [n(%)]	5 (7.5%)	3 (4.4%)	0.49
Subcutaneous hematoma	1	0	
DVT or PE	0	0	
Acute febrile illness	2	2	
Dislocation or Fracture	2	1	

† The values are given as the mean and the standard deviation.
‡ The values are given as the median and interquartile range : Non parametric : Mann-Whitney *U*-test
¥ Significantly different.

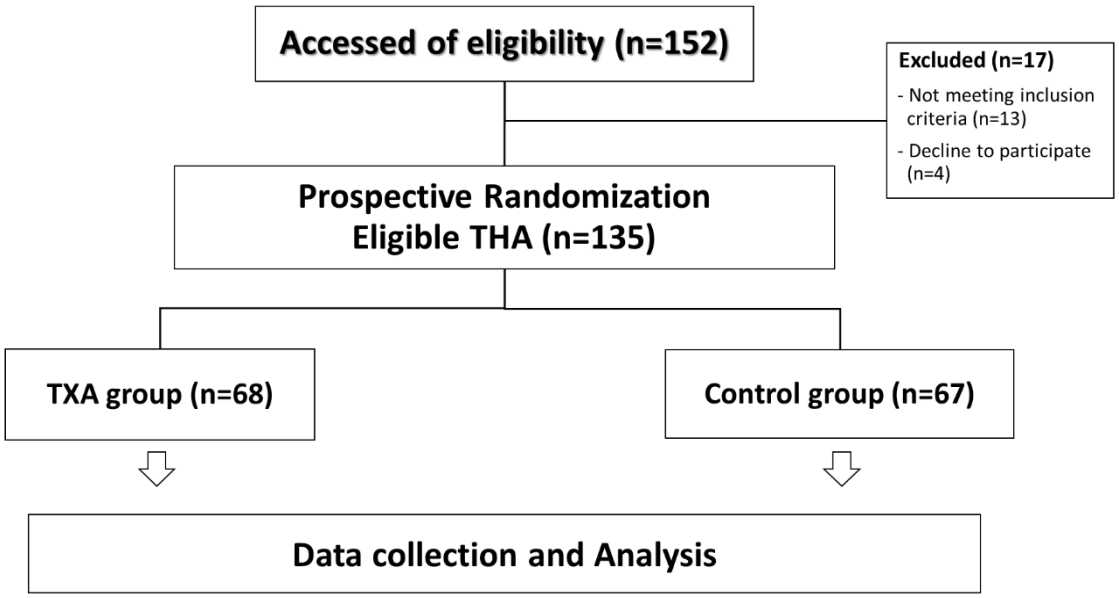

Fig. 1 Flow diagram of patients involved in the trial.

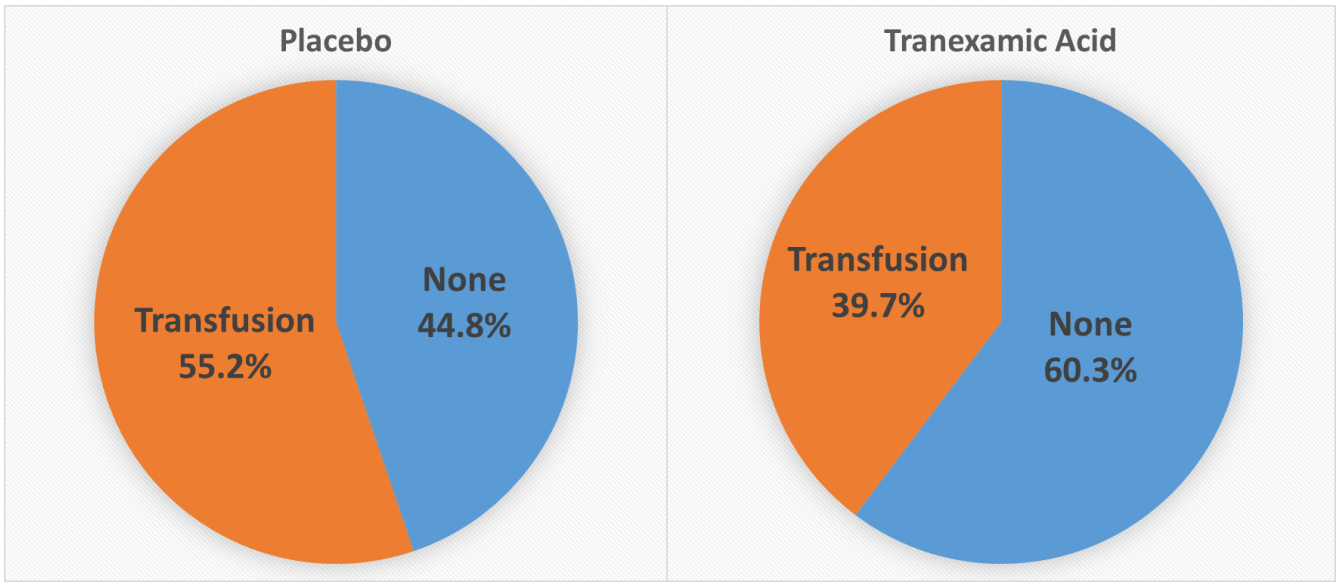

Fig. 2 Flow diagram of primary outcome of blood transfusion rate.

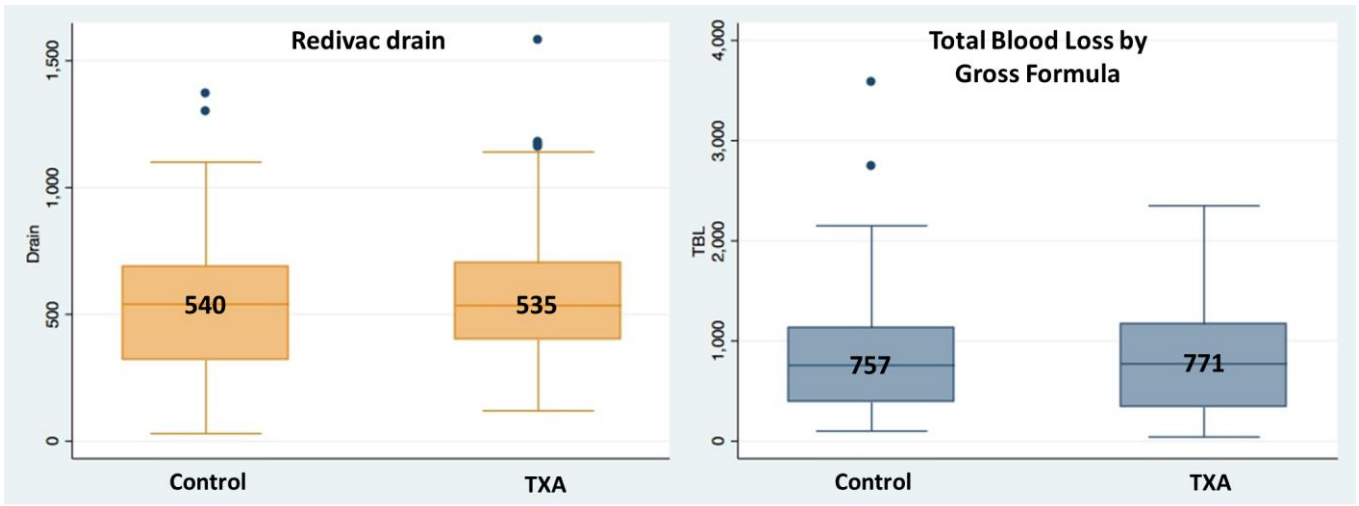

Fig. 3 Flow diagram of primary outcome of blood loss.

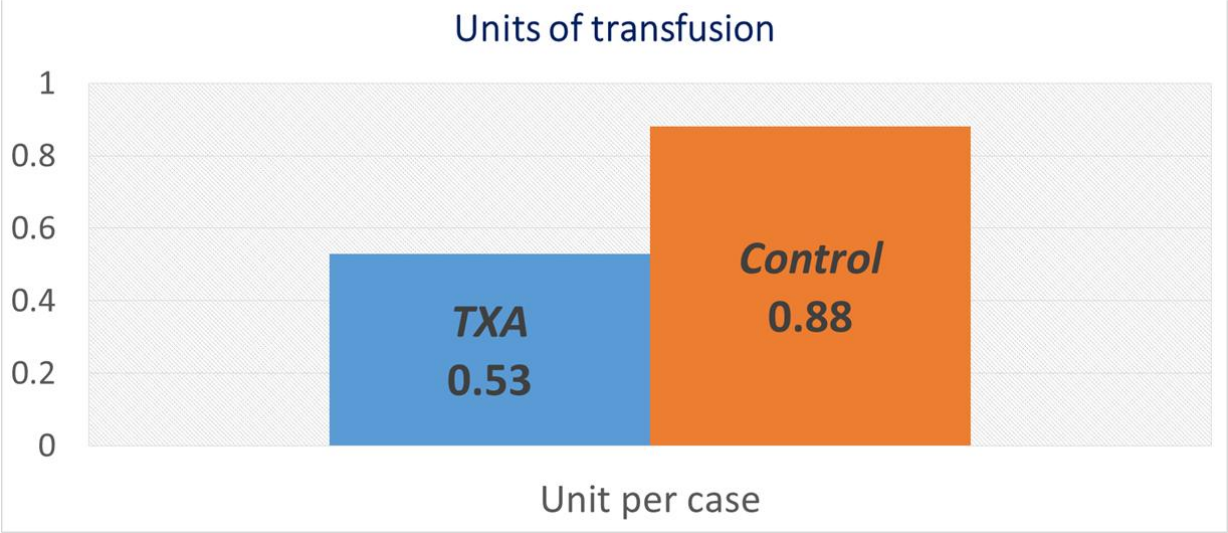

Fig. 4 Flow diagram of secondary outcome of units of blood transfusion.

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การศึกษาการใช้ยาต้านการสลายไฟบริน (ทรานซามีน) แบบเฉพาะที่ ในผู้ป่วยผ่าตัดเปลี่ยนข้อสะโพกเทียม เพื่อลดการเสียเลือด และอัตราการรับเลือดหลังผ่าตัด

จิธายุทธ เสือจุ้ย, พบ, ณัฐวุฒิ ชนะฤทธิชัย, พบ, อุรวิศ ปิยะพรมดี พบ, ยิ่งยง สุขเสถียร, พบ

วัตถุประสงค์: *เพื่อศึกษาการใช้ทรานซามีนแบบในข้อ ในการผ่าตัดข้อสะโพกเทียมชนิดทั้งหมด เพื่อการลดปริมาณการรับส่วนประกอบของเลือด และลดการเสียเลือด*

วิธีการศึกษา: *การศึกษาประสิทธิภาพของยาต้านการสลายไฟบริน (ทรานซามีน) แบบเฉพาะที่ โดยศึกษาไปข้างหน้า มีการทดลองแบบสุ่มและปกปิดสองทางเทียบกับยาหลอก ในการผ่าตัดข้อสะโพกเทียมชนิดทั้งหมด ณ โรงพยาบาลมหาราชนครราชสีมา ระหว่างเดือนกันยายน พ.ศ. 2556 ถึง เดือนมีนาคม พ.ศ. 2558 มีจำนวนการผ่าตัดที่เข้าร่วมศึกษาทั้งสิ้น 135 ครั้ง จากผู้ป่วย 118 ราย โดยการใช้ยาต้านการสลายไฟบริน ในขนาด 750 มก. แบ่งครึ่งสารละลาย และนำไปแช่หลังการเตรียมเบ้าสะโพก และหลังจากการเตรียมโพรงกระดูกก่อนใส่ข้อสะโพกเทียม นาน 3 นาที ทั้งสองที่โดยผลลัพธ์หลักที่ทำการศึกษาคือร้อยละของผู้ป่วยที่ได้รับส่วนประกอบของเลือด และปริมาณการสูญเสียเลือด ทั้งจากสายระบายเลือด และจากการคำนวณด้วยสูตรของ Gross และผลลัพธ์รอง ได้แก่ ค่าเฉลี่ยจำนวนถุงเลือดที่ได้ต่อคน ค่าฮีโมโกลบิน และฮีมาโตคริตที่ต่ำที่สุดหลังผ่าตัด ค่าฮีโมโกลบิน และฮีมาโตคริตที่ลดลง ค่าความเจ็บปวด ระยะเวลาการนอน รพ.หลังผ่าตัด และติดตามผู้ป่วยในสัปดาห์ที่ 2, 4, 8, 12 หลังการผ่าตัดเพื่อศึกษาผลข้างเคียงต่างๆของการใช้ยาต้านการสลายไฟบริน เฉพาะที่*

ผลการศึกษา: *ผู้ป่วยในกลุ่มที่ได้รับยาต้านการสลายไฟบริน (ทรานซามีน) มีอัตราการรับเลือดที่ไม่แตกต่างจากกลุ่มควบคุม (TXA group = 39.7%, Placebo = 55.2%; P-value = 0.07), มีปริมาณการเสียเลือดทางสายระบายเลือดไม่แตกต่าง (TXA group = 535 มล., Placebo = 540 มล.; P-value = 0.45) และปริมาณการสูญเสียเลือดจากการคำนวณด้วยสูตรของ Gross ไม่แตกต่างเมื่อเทียบกับกลุ่มควบคุม (TXA group = 771 มล., Placebo = 757 มล.; P-value = 0.59) แต่พบว่าผู้ป่วยในกลุ่มที่ได้รับยาทรานซามีนมีปริมาณการใช้ส่วนประกอบของเลือดลดลงอย่างมีนัยสำคัญทางสถิติ เมื่อเทียบกับกลุ่มควบคุม (TXA = 0.53 units per case, Placebo = 0.88 units per case; P-value=0.035). ด้านความเจ็บปวด visual analog scales (VAS) พบว่าลดลงอย่างมีนัยสำคัญทางสถิติเช่นกัน (TXA = 3.9, Placebo = 4.7; P-value=0.001) และด้านผลข้างเคียงจากการใช้ยา พบว่ามี 3 รายในกลุ่มที่ได้รับยาทรานซามีน (ไข้ 2ราย และข้อสะโพกเทียมหลุดเคลื่อน 1 ราย) และ 5 รายในกลุ่มควบคุม (แผลติดเชื้อชั้นตื้น 1 ราย, ไข้ 2 ราย และข้อสะโพกหลุดเคลื่อน 2 ราย) และไม่พบการระคายเคืองต่อเส้นประสาทไซอาติก จากการใช้ยา ในการศึกษานี้*

สรุป : *การใช้ยาต้านการสลายไฟบริน (ทรานซามีน) ในขนาด 750 มิลลิกรัม แบบเฉพาะที่ในการผ่าตัดเปลี่ยนข้อสะโพกเทียมไม่มีประสิทธิภาพในการลดอัตราการรับเลือด และลดปริมาณการเสียเลือดได้อย่างมีนัยสำคัญทางสถิติ ซึ่งอาจเกิดจากปริมาณยาที่ไม่เพียงพอ หรือจากการแช่ที่ไม่นานเพียงพอ อย่างไรก็ตามพบว่าสามารถลดปริมาณการรับสารประกอบของเลือดในผู้ป่วย และคะแนนความเจ็บปวดหลังผ่าตัดได้อย่างมีนัยสำคัญทางสถิติ โดยไม่พบความแตกต่างในเรื่องของผลข้างเคียงจากการใช้ยา*

Gentamicin Release from Bone Cement: A Comparative Study between Hand Made Liquid & Powder Gentamicin beads

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Background and Purpose: *Gentamicin beads are widely used in treatment of bone and joint infections. The commercial form is expensive and may be unavailable in most hospitals in Thailand. Most orthopaedic surgeons make them from gentamicin and powdered bone cement, but this still has high costs. In this study, the author used liquid gentamicin, which was used regularly in intravenous route, to mix in bone cement and compare gentamicin release between handmade liquid and powder gentamicin beads.*

Methods: *A prospective randomized clinical trial in patients with bone and joint infections from bacterial causes in Hatyai Hospital. Patients were divided into liquid gentamicin and powder gentamicin groups. Gentamicin concentration in surgical areas were collected, compared, and analyzed.*

Results: *Thirty patients in each group who had bacterial bone and joint infections were treated with bone debridement and gentamicin beads were placed in surgical area. The liquid gentamicin group resulted in significantly higher levels than in the powder group. Both groups had gentamicin levels many times higher than the minimal inhibitory concentration (MIC) and persisted for at least 28 days. Clinical results of both groups were excellent and no renal toxicity was observed.*

Conclusions: *The liquid gentamicin group had more antibiotic released to the surgical area than the powder group, no renal toxicity detected, and appears to be cost-effective in the treatment of bacterial bone and joint infections.*

Key words: *Liquid gentamicin, Gentamicin release from bone cement, Handmade bone cement, Gentamicin-impregnated polymethymethacrylate.*

The Thai Journal of Orthopaedic Surgery: 40 No.1-2: 13-20
Full text. e journal: *http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST*

Introduction

The use of antibiotic impregnated polymethymethacrylate (PMMA) for the treatment of bone and joint infections has been widely used since the 1970s[6,11,12,14].Various antibiotics have been mixed with bone cement including gentamicin. Gentamicin was proved to be the antibiotic of choice to add into polymethymethacrylate to create antibiotic beads because it is has a low minimal inhibitory and bactericidal concentration (MIC), a low rate of allergy, free solubility in water, and is stable in high temperatures. Commercial gentamicin beads are expensive and may be unavailable in most hospitals in Thailand. Most orthopaedic surgeons make beads and chains themselves from bone cement and powder gentamicin, but still at a rather high cost. Liquid gentamicin is the other preferred choice and is cheaper than the powder form[1,5]. The purpose of this study is to compare the releasing of gentamicin from bone cement between the liquid and powder forms.

Patients and Methods

A prospective randomized controlled trial was performed from 2011 to 2014, and included 60 patients with bacterial bone and joint infections treated at Hatyai Hospital.

Inclusion criteria for this study were as follows: (a) Chronic osteomyelitis of a long bone, defined by one or more foci in the bone contained purulent material, infected granulation tissue, and sinus tract from bone or sequestrum, (b) Infected fracture of long bone, defined by purulent discharge from the surgical wound after bone debridement and / or fixation in the acute or subacute period within 6 weeks, (c) Hip or knee joint infections, defined by bacterial infective arthritis of hip or knee joints that need surgical debridement, and (d) Infection after spinal surgery, defined by purulent discharge from the surgical wound after thoracolumbar spine surgery, either disease or trauma, within 6 weeks.

Exclusion criteria were as follows: (a) Infection other than bacterial causes, (b) Infection in sarcoma, (c) Wound that were unable to be closed into closed space, and (d) Cases with insufficient space to insert chains of 6 beads of

gentamicin beads. A pilot study was performed after permission from the ethics committee of Hatyai hospital was granted. The pilot study had 5 patients in each group and calculated for sample size. The process of this study is divided into 4 steps:

1. Preoperative period: Every patient was informed by the surgeon, and they gave their consent and agreed to be included in this study. Ward nurses randomly picked a number from 4 envelopes. If the number was 1 or 2 that patient was put in the liquid gentamicin group, and if the number was 3 or 4 they were put into the powder group. Essential preoperative laboratory tests including creatinine were done in every case.
2. Procedure in operating room: Prophylactic antibiotics (1 gram of cefazolin) were administered 30 minutes before bone debridement. In cases of allergy to cefazolin, ciprofloxacin (500 milligrams) was used instead. No post-operative antibiotics were used. Liquid Gentamicin beads were made case by case using 480 mg of liquid gentamicin (NIDA pharma incorporation company limited, 80 milligrams /ampule, 2 ml/ ampule) and 40 grams of bone cement (Zimmer ^{R}). Liquid gentamicin was mixed with the liquid monomer first, then cement powder was added. The mix was put into a 50 mL syringe and injected to a polyethylene mold with a core wire (Fig. 1). For powder gentamicin bead preparation, 40 grams of antibiotic cement (Zimmer ^{R}) which contained 500 milligrams of powder gentamicin, was put into the liquid monomer and beads and chain created in the same manner as the liquid gentamicin beads. Six chains of 30 beads per chain were made from 40 grams of cement. After performing bone debridement, bacterial cultures were collected and placement of gentamicin beads in the surgical area was done. The wound was then closed. Suction drainage was placed and clamped. Postoperative film was examined after placement gentamicin beads present (Fig. 2).
3. Process after gentamicin beads placement: After 24 hours, 5 ml of fluids was taken from drain tube for gentamicin level assessment and then clamped again. Specimens were collected daily for 7 days and sent to the laboratory department to measure for gentamicin concentrations by the VITROS 4600 Enzymatic instrument multiple-point Immuno-rate Test (Johnson & Johnson Thailand. LTD.).
4. Removal of gentamicin beads were performed at the twenty eighth day after bead placement. Fluid was taken again for gentamicin concentration measurements. Gentamicin concentrations were analyzed between the 2 groups using Independent Sample *t*-tests.

Results

There were 60 patients in the present study, 30 per group, with an average age of about 30 years in both groups. Sex, creatinine levels, diagnosis, and pathogens are shown in Table 1.

The results of gentamicin release in the surgical areas in the two groups showed the highest level on the first day after surgery and decreased with time. The liquid form had a higher level than the powder form. According to the experiments performed, it gave an average gentamicin level in the liquid form of 41.556 mg/L, while the powder form was at 38.093 mg/L, collected on the first day. On day seven, the level of the liquid form dropped to 3.266 mg/L and1.936 mg/L in the powder form. Gentamicin levels at the time of bead removal average 25.973 mg/L in the liquid group and 22.90 mg/L in the powder group (Fig. 3). Analysis of gentamicin levels with Independent Sample T-test showed normal distribution of data in both groups, and that the liquid gentamicin group was significantly different from the powder group (Table 2).

Regarding clinical results, all patients were followed for one year after the gentamicin beads placement and there were no cases of recurrent of purulent discharge, sinus tract, or the need for redebridement in any patient in both groups. The results of the blood tests for inflammation, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) had returned to normal levels.

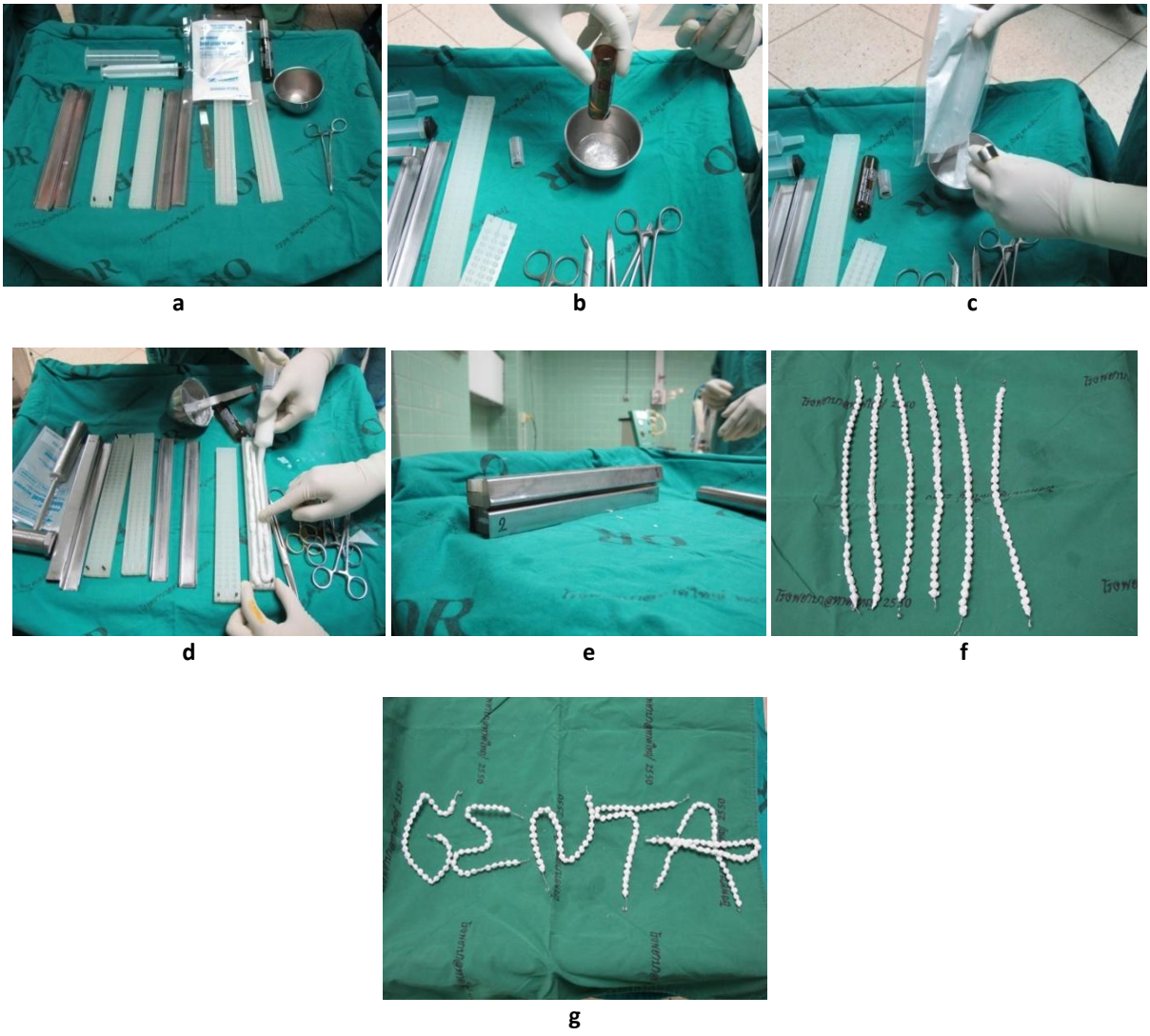

Fig. 1 Handmade Gentamicin Beads
(a) Mold made from polyethylene and cement
(b) Liquid monomer was mixed with liquid gentamicin
(c) Cement powder was added and mixed
(d) Cement was put into syringe and injected to polyethylene mold
(e) Compression of cement with mold compressor
(f) & (g) Beads and chains were made

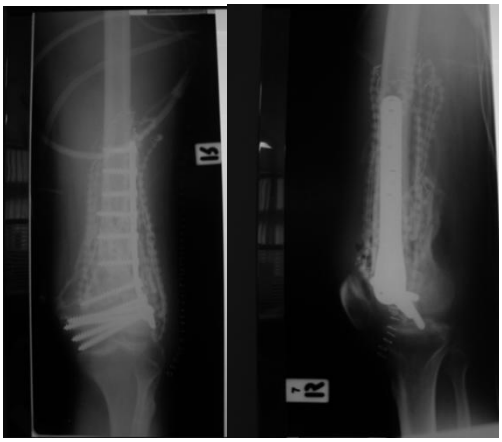

Fig. 2 Postoperative film after placement gentamicin beads

Table 1 Characteristics of patients with bacterial bone and joint infections

Characteristics	**Liquid gentamicin group (N = 30)**	**Powder gentamicin Group (N = 30)**
Age (years)	30.06 (16 - 54)	30.03 (17 – 52)
Sex Male / female	21/9	18/12
Creatinine level at preoperative period Creatinine level at date of removal of gentamicin beads	1.1 (0.8-1.3) 1.0 (0.8-1.2)	1.0 (0.8-1.2) 1.0 (0.9-1.2)
Diagnosis		
- Chronic osteomyelitis of proximal femur	3	5
- Chronic osteomyelitis of femoral shaft	4	6
- Chronic osteomyelitis of distal femur	13	10
- Septic arthritis of the hip	1	0
- Infected fracture of proximal femur	2	1
- Infected fracture of femoral shaft	2	3
- Infected fracture of distal femur	3	4
- Infected fracture of tibia	2	0
- Spinal infection after surgery	0	1
Pathogens		
- Methicillin Resistance Staphylococcus aureus (MRSA)	3	2
- Methicillin Sensitive Staphylococcus aureus	8	5
- *Streptococcus spp.*	6	9
- *Escherichia coli*	3	2
- *Klebsiella pneumonia*	1	0
- Mixed Organisms	9	12

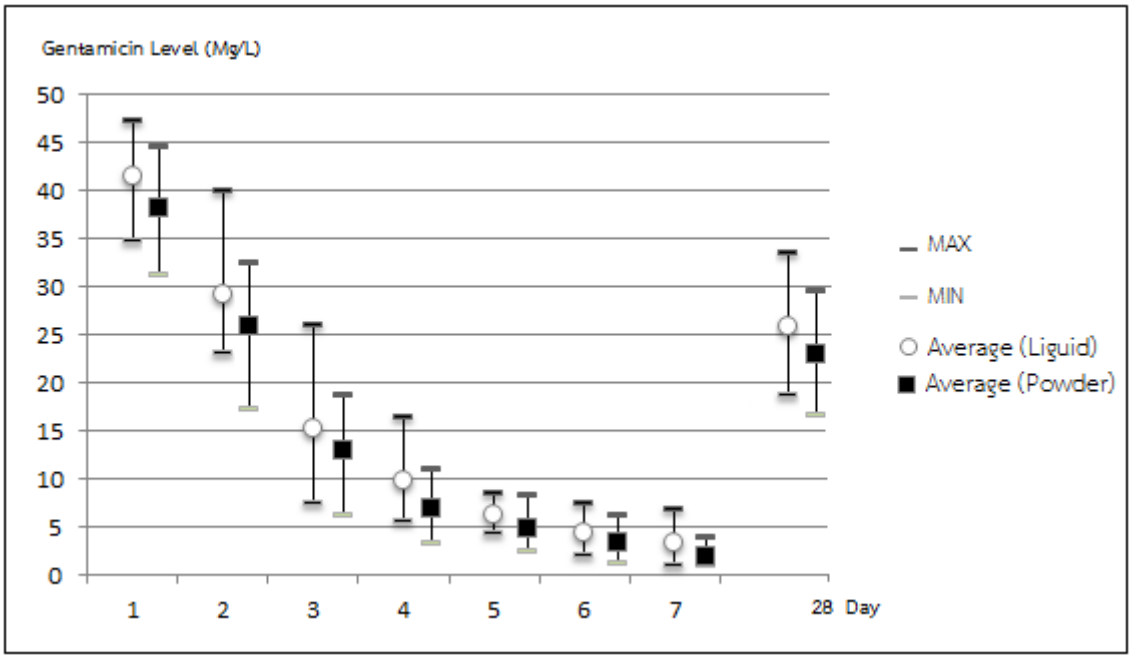

Fig. 3 Comparison of gentamicin levels between liquid and powder groups

Table 2 Analysis of gentamicin levels

Day	Mean Gentamicin Level		Mean Difference	P Value	95% Confident Interval	
	Liquid Group	Powder Group			Lower	Upper
1	41.556	38.093	3.462	0.000	1.7092	5.2155
2	29.243	25.802	3.441	0.001	1.4256	5.4571
3	15.338	12.972	2.365	0.036	1.6323	4.5672
4	9.774	6.871	2.903	0.000	1.6607	4.1453
5	6.310	4.756	1.554	0.000	0.9193	2.1880
6	4.494	3.319	1.174	0.010	0.5130	1.8357
7	3.266	1.936	1.330	0.000	0.7959	1.8641
28	25.973	22.900	3.073	0.020	1.1616	4.9838

Discussion

Gentamicin is a common antibiotic used in the treatment of infections. It is effective against organisms with a low minimal inhibitory and bactericidal concentration (MIC). This antibiotic also has a low rate of allergy, free solubility in water, and is stable at high temperatures[1,6,14]. It has a therapeutic drug level between 0.6- 0.8 mg/L, higher doses or prolonged treatment may lead to renal toxicity. This limitation is one of the problems in treating with gentamicin. Local administration of gentamicin with PMMA is the prefer choice of treatment for bone and joint infections. Gentamicin beads can be used with doses many times higher than standard doses without renal toxicity[1,3]. In this study, antibiotic levels in the liquid gentamicin group were significantly higher than the powder group from the first day after the operation until the seventh day. Antibiotic levels were highest on the first day after operation; the liquid gentamicin group had levels 51.9 times higher than the MIC and 47.6 times higher in the powder group before levels gradually reduced. By the seventh day after operation, the liquid gentamicin group had levels 4 times higher than the MIC and the powder group had levels 2.4 times higher than MIC. By the twenty eighth day, when we removed the gentamicin beads, we collected fluid in the surgical areas for antibiotic level measurements and found that gentamicin

levels in the liquid gentamicin group were 32.46 times higher than the MIC and levels were 28.62 times higher in the powder group. Therefore, both forms of gentamicin beads had high antibiotic levels in the surgical area and which lasted at least 28 days. The gentamicin levels at twenty eighth day were higher than at days 3-7 in the first week (Figure 3). This could be explained by gentamicin infiltration into local tissue around surgical areas. Higher elution of liquid gentamicin from the bone cement results from more porosity in the liquid beads type[1,4]. Liquid gentamicin 480 milligrams (12 ml) were mixed properly with 40 grams of bone cement[2]. However, more fluid was unable to be incorporated with powder cement. 500 milligrams of liquid gentamicin were not used when compared with 500 milligrams gentamicin powder because it may lead to errors in dosages during preparation. There are some limitations of this study such as differences in the size of surgical area which may affect the gentamicin concentration, limit the gentamicin volume to mix with cement, hinder the application in cases with small space to insert the antibiotic beads. Additionally, this study had a short duration of follow up for recurrent infection. Many studies report that gentamicin beads with high antibiotic levels were able to get rid of infections despite the presence of gentamicin resistant organisms identified by laboratory tests [7,11,12]. Gentamicin beads can treat MRSA, as shown in 5 cases of this study, due to the locally high dose of antibiotic bathing the surgical area. Even mixed organisms could be treated with gentamicin beads effectively.

Liquid gentamicin may lead to weakening of the bone cement due to the higher porosity than powder forms [4,8], but this did not affect the treatment of infection, except in cement spacers for infected total joint arthroplasty. With regards to safety, none of the patients had renal toxicity in this study. This was because of the local action with no systemic effect[1,3]. Handmade liquid gentamicin beads are cheaper than handmade powder gentamicin beads by about 55 percent, and four times cheaper than the commercial form.

Conclusions

Liquid gentamicin in bone cement has significantly higher antibiotic levels than powder gentamicin form. They are safe and cost-effective for the treatment of bacterial bone and joint infections.

Acknowledgements

The author is grateful and would like to sincerely give special thanks to the Hatyai Hospital who have financially supported the gentamicin level laboratory.

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การปลดปล่อยยาเจนตาไมซินจากซีเมนต์กระดูก: การศึกษาเปรียบเทียบระหว่างเจนตาไมซินแบบน้ำและแบบผง

สุรสิทธิ์ ปานมณี, พบ.

หลักการและวัตถุประสงค์ : *การใช้เม็ดยา gentamicin (เจนตาไมซิน) รักษาการติดเชื้อของกระดูกและข้อได้ผลดี แต่ยาแบบสำเร็จรูปมีราคาแพงและหาซื้อได้ยากไม่สอดคล้องกับการใช้งานจริง ศัลยแพทย์ออร์โธปิดิกส์มักจำเป็นต้องทำขึ้นใช้เองจาก bone cement (ซีเมนต์กระดูก) ที่มียาเจนตาไมซินแบบผง ผสมอยู่ แต่ก็ยังมีต้นทุนการผลิตสูงระดับหนึ่ง ผู้วิจัยจึงศึกษาการใช้ยาเจนตาไมซินแบบน้ำที่ใช้ฉีดในโรงพยาบาล มีราคาถูกกว่ามาใช้ทดแทน การศึกษานี้จะทำการเปรียบเทียบการปลดปล่อยยาเจนตาไมซินจากซีเมนต์กระดูกระหว่างยาแบบน้ำและแบบผง*

วิธีการศึกษา : *เป็นการศึกษาทดลองเปรียบเทียบแบบสุ่ม โดยศึกษาในผู้ป่วยติดเชื้อแบคทีเรียในกระดูกและข้อจำนวน 60 รายที่มารักษาที่โรงพยาบาลหาดใหญ่ จับฉลากแบ่งผู้ป่วยเป็น 2 กลุ่ม กลุ่มที่ 1 ใช้ยาเจนตาไมซินแบบน้ำ กลุ่มที่ 2 ใช้ยาเจนตาไมซินแบบผง ผสมในซีเมนต์กระดูกวัดระดับยาที่ถูกปลดปล่อยออกมาในบริเวณที่ฝังยานำมาเปรียบเทียบกัน*

ผลการศึกษา: *การศึกษานี้ทำในผู้ป่วยติดเชื้อในกระดูกและข้อกลุ่มละ 30 ราย พบว่าการผสมยาเจนตาไมซินแบบน้ำมีระดับยาในบริเวณฝังยาสูงกว่าแบบผงอย่างมีนัยสำคัญ ระดับยาทั้ง 2 กลุ่มสูงกว่าระดับยาขั้นต่ำที่สามารถฆ่าเชื้อโรคได้หลายเท่าและคงอยู่จนถึง 28 วันเป็นอย่างน้อย ให้ผลการรักษาทางคลินิกดีเท่าเทียมกันทั้ง 2 กลุ่มและปลอดภัยต่อการทำงานของไต*

สรุป: *การผสมยาเจนตาไมซินแบบน้ำในซีเมนต์กระดูกสามารถปลดปล่อยยาออกฤทธิ์เฉพาะที่ได้สูงกว่าแบบผง มีความปลอดภัย ไม่เป็นพิษต่อไต ให้ผลการรักษาทางคลินิกที่ดี และมีต้นทุนที่ถูกกว่า ทำให้สามารถประหยัดค่าใช้จ่ายในการรักษาผู้ป่วยกลุ่มนี้ได้*

Cost Analysis of Blood Transfusion and Tranexamic acid in Primary Total Knee Arthroplasty

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Purpose: *To determine transfusion rates and trends of allogenic blood transfusion in total knee arthroplasty patients and to analyze the cost of blood transfusions in TKA.*
Methods: *This study was a non-randomized retrospective study that included 342 osteoarthritis knees which underwent unilateral primary TKA from June, 2012 through June, 2014. The patients were categorized into 2 groups; group 1 were treated with tranexamic acid and group 2 received no treatment with tranexamic acid. All surgeries were performed in the Department of Orthopedics, Police General Hospital. The data of blood transfusion was collected from blood bank by software "BloodTrans" and the cost of blood transfusions were collected from the Pharmaceutical and Financial Department, Police General Hospital.*
Results: *342 total knee arthroplasty patients were included. The male:female ratio was 80:262. The average age was 68.74 (50-84) years. The average weight was 67.0 (58-90) kilograms. The average height was 163 (160-172) cm. The average BMI was 25.21(22.2-28.5) kg/m^2, the number of knees (right:left) were 216:126. The average level of preoperative Hct in group 1 was 36.40 % (30-44.5) and in group 2 was 38.7 % (30-43.5). The average level of postoperative Hct in group 1 was 31.4 % (26-40.5) and group 2 was 30.1 % (23-38.5). The overall number of patients who received blood transfusions was 164 (48%): in the tranexamic group 54 patients (36%) and 110 patients (58%) in the non-tranexamic acid group. The total number of blood units transfused was 233 units, and the overall average number of units received per patient was 0.68 units: in group 1 the average was 0.47 units and 0.85 units in group 2. The total cost of blood transfusions was 174,300 baht. The average cost of per blood transfusion was 530 baht per TKA: in the tranexamic group 463 baht (12% lower than average costs) and 584 baht (10% higher than average costs) in the non-tranexamic acid group.*
Conclusions: *The average number of units of blood transfused was lower than standard blood transfusions. But, the transfusion rate was higher than the standard treatment. The tranexamic group had lower transfusion rates and costs of blood transfusions compared to the non-tranexamic acid group. The use of tranexamic acid continues to rise and shows positive results. The indication of blood transfusions need to be evaluated with the appropriate criteria.*

Keywords*: Cost Analysis, Blood Transfusion, Tranexamic acid, Total knee arthroplasty*

The Thai Journal of Orthopaedic Surgery: 40 No.1-2: 21-26
Full text. e journal: *http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST*

Introduction

Blood management involves the evaluation and optimization of the circulating blood volume prior to surgery. As we all know, the number of total knee arthroplasty (TKA) is going to increase in the future. However, the limitation of blood product is in the opposite direction of annual numbers of knee joint replacements. Even though the transfusion is simple, the risks of blood transfusions have led to the establishment of blood conservation programs in orthopedic surgery that have become more desirable[1,2]. The transfusion rate was historically 50% with the development in all technical aspects in total knee arthroplasty. However, nowadays, the transfusion rate is between 8% and 13%. Allogenic blood transfusion is of concern because of its cost, its potentials for disease reactions, its lack of religious tolerance and acceptance, its immunomodulation with the increased susceptibility for post-operative infection, its increased length of stay, its perception of illness, and its interference with PT/ambulation[3]. In conventional TKA, the average blood loss is between 600-1200 cc. Tranexamic acid use in bilateral TKA was associated with a significant reduction in perioperative serum hemoglobin drop, and a reduced need for allogeneic blood transfusion from 50% to 11% of patients. No autologous blood donation or drains were used and there were no venous thromboembolic events reported[13]. The concept of modern knee replacement with minimally invasive surgery (minimidvastus, subvastus) will preserve blood loss and decrease blood transfusions. Although tranexamic acid is used for the prevention of bleeding in TKA, a

cost analysis still needs to be investigated. The role of tranexamic acid in TKA has been confirmed in several studies, so cost-utility analysis should be studied prior to proposing it as a general recommendation.

Materials and Methods

Institutional Review Board approval was obtained from our institution for a retrospective chart review. This study was a non-randomized retrospective study that included 342 osteoarthritis knees which underwent unilateral primary TKA from June, 2012 through June, 2014. The patients were categorized into 2 groups; group 1 treated with tranexamic acid and group 2 received no treatment with tranexamic acid. All surgeries were performed in the Department of Orthopedics, Police General Hospital. The data of blood transfusions was collected from the blood bank by ”BloodTrans” software and the costs of blood transfusions were collected from the Pharmaceutical and Financial Department, Police General Hospital. The cost of cross matching, which was done for all patients, was 150 baht in each case and 750 baht for each bag of blood transfusion.

This was a cost analysis study considering the total costs of the treatment from the retrospective data in Police General Hospital from June, 2012 - June, 2014. The total cost of the treatment consisted of the direct medical costs including group matching, and the cost of blood transfusion. No indirect or disability costs were included for this analysis. The average cost per person and per knee (Baht) were analyzed. Statistical analysis and demographic data are shown as the mean.

Results

342 total knee arthroplasty patients were included. The male:female ratio was 80:264. The average age was 68.7 (50-84) years. The average weight was 67.0 (58-106) kg. The average height was 163 (160-172) cm. The average BMI was 25.2 (22.2-28.5) kg/m^2. The number of knees (right:left) included was 216:126. Baseline patient characteristics are summarized in Table 1. The total number of patients that received blood transfusions was 164 patients (48%): 54 patients (36%) in the tranexamic group and 110 patients (58%) in the non-tranexamic acid group. Comparing the average percentage of patients receiving blood transfusions, the tranexamic group had a lower percentage of about 31.43 percent compared to the non-tranexamic group of which about 21.2 percent received transfusions. The number of blood transfusions was 233 units, the total number of patients who received blood transfusion was 0.68 units: in the tranexamic group 0.47 units, and in the non-tranexamic acid group was 0.85 units.

Table 1 Baseline characteristics of patients

Characteristic	TXA	Non-TXA	Total
Number of patients (Male:Female)	52(50:102)	190(65:125)	342(80:264)
Mean (range) age (years)	66(50-82)	68(55-84)	68(50-84)
Mean (range) bodyweight (kg)	65.0(60-90)	67.5(58-85)	67.0(58-90)
Mean height (cm)	161(160-168)	162(161-172)	163(160-172)
Number of knees (Right:Left)	152(100:52)	190(116:74)	342(216:126)

Table 2 Prevalence of blood transfusion in TKR

Group	TXA	Non-TXA	Total
No. of patients	152	190	342
Mean Preop. Hct	36.4 (30.0-44.5)	38.7(30.0-43.5)	
Mean Postop.Hct	31.4(26.0-40.5)	30.1(23.0-38..5)	
No blood transfusion	98	80	178
Blood transfusion	54	110	164
Blood transfusion (%)	36	58	48
No. of unit transfusion	71	162	233
Average pt. No transfused	0.64	0.42	0.52
Average unit of transfusion	0.47	0.85	0.68

The total cost of blood transfusions was 174,300 baht. The average cost of a blood transfusion was 530 baht per TKA: in the tranexamic group 463 baht (12% lower than the average cost) and in the non-tranexamic acid group 584 baht (10% higher than the average cost)**.** *The total saving cost of tranexamic acid was about 22%*.

Table 3 Average costs of blood transfusions

Average	TXA	Non-TXA	Total (Baht)
Cost of cross matching	22,800	28,500	51,300
Cost of blood transfusion	40,500	82,500	123,000
Blood expense in TKA	63,300	111,000	174,300
Cost TXA	7,080	-	7,080
Total blood expense	70,380	111,000	181,380
Average cost of transfusion	463	584	530

Discussion

As we all know, the number of TKAs is going to increase in the future. However, the availability of blood is decreasing compared to the annual numbers of knee joint replacements in ageing societies.. Even though the transfusion is simple, the risks of blood transfusion have been established. The risks associated with blood transfusion include the potential for blood-borne infection, allergic reaction, and transfusion reactions. Furthermore, red blood cell (RBC) transfusions add significant cost to the healthcare system which will likely increase as demand continues to grow. Programs of blood conservation in orthopedic surgery have become more desirable.

The transfusion rate was historically 50% with the developments in all technical aspects in total knee arthroplasty. However, nowadays, the transfusion rate is between 8% and 13%. The average volume of blood transfused is 2.2 units. The concept of modern knee replacement with minimally invasive surgery (minimidvastus, subvastus) preserves blood loss and decreases blood transfusion. In our study, the average number of units of blood transfused is lower than standard blood transfusions. But the blood transfusion rate is higher than the standard treatment. The total number of patients who received blood transfusions was 164 (48%): 54 patients (36%) in the tranexamic group and 110 patients (58%) in the non-tranexamic acid group. Tranexamic Acid (TXA), a plasminogen-activator inhibitor, has been employed to reduce perioperative blood loss and prevent the need for post-operative transfusion. The reasons for lower numbers of units of blood transfused are improvements to and better understanding of the surgical techniques, and non-pharmacologic and pharmacologic agents, such as tranexamic acid. Blood Management has to be focused on pre-operatively, which includes medical

anemia evaluations and optimizations, and intra-operatively which includes modifications to anesthesia and surgical techniques, such as soft tissue techniques including exposure that should be quadriceps preservation, and handling soft tissue with MIS (minimally invasive surgery). Technique is recommended, tissue hemostasis during and after releasing the tourniquet electrocautery, especially the lateral inferior genicular artery at the posterolateral corner and the lateral superior genicular artery in lateral release or perforating branch in the subvastus approach. The bone techniques are precise bone cuts and the medullary canal technique. The medullary canal technique can be non-reaming by using an extra medullary guide and navigator or the conventional technique that generally is used with a bone plug, and post-operative which include blood salvage, standardization of hemoglobin, fluid management.

Health care costs are of concern. Tranexamic acid has been shown to be cost effective with reduced blood loss and transfusions, as well as its low cost compared to other anti-fibrinolytics. Chimento et al. compared the cost savings of TXA compared to a placebo group and reported higher pharmacy costs with use of TXA, but the savings from decreased blood transfusions and shorter hospital stays more than offset these higher pharmacy costs. Despite the significant literature support for the use of TXA in TKA, many common medical conditions, including renal insufficiency, history of previous DVT, and cardiac and cerebrovascular disease may contraindicate the use of intravenous tranexamic acid at the time of surgery. In our study, the total cost of blood transfusions was 174,300 baht. The average cost of a blood transfusion was 530 baht per TKA, 463 baht in the tranexamic group (12% lower than the average cost) and 584 baht in the non-tranexamic acid group (10% higher than the average cost). The overall cost saving is 22 percent. The tranexamic group had lower transfusion rates and costs of blood transfusion. Because of the increasing incidence of TKA in the future, there are rising concerns regarding the supply, cost, and excessive or inappropriate use of blood transfusions, to save medical costs.

Conclusions

The average number of units of blood transfused is lower in TKA patients than standard blood transfusions, but the transfusion rate is higher than the standard treatment. The tranexamic group had lower transfusion rates and costs of blood transfusions compared to the non-tranexamic acid group. The use of tranexamic acid continues to rise and shows positive results. The the administration of a blood transfusion needs to be evaluated using the appropriate criteria. This study compared the cost of blood transfusions and evaluated the cost analysis of tranexamic acid. The limitation of this study is that it is retrospective. The study suggests that further investigation and improvement of new surgical techniques and proven technologies, are required for improving the effectiveness of blood management.

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การวิเคราะห์ความคุ้มค่าของการให้เลือดและการใช้ Tranexamic acid ในการผ่าตัดข้อเข่าเทียม

ธนา ธุระเจน, พบ, ชัชวาลย์ วิเศษศิริพงษ์,พบ

วัตถุประสงค์: *เพื่อวิเคราะห์อัตราการให้เลือดหลังการผ่าตัดข้อเข่าเทียมและวิเคราะห์ถึงความคุ้มค่าของการให้เลือดในการผ่าตัดข้อเข่าเทียม*

วิธีการศึกษา: *การศึกษานี้เป็นการศึกษาย้อนหลังในผู้ป่วยจำนวน 342 ราย ที่ได้รับการผ่าตัดข้อเข่าเทียมข้างเดียวในโรงพยาบาลตำรวจ ระหว่างเดือนมิถุนายน 2555 ถึง เดือนมิถุนายน 2557 โดยแบ่งผู้ป่วยออกเป็นสองกลุ่ม กลุ่มแรกได้รับยา tranexamic acid ส่วนในกลุ่มที่สอง ผู้ป่วยไม่ได้รับยา tranexamic acid โดยผู้ป่วยทั้งสองกลุ่มได้เข้ารับการดูแลรักษา ในภาควิชาออร์โธปิดิกส์ โรงพยาบาลตำรวจ ข้อมูลในการให้เลือดได้รับการเก็บโดยโปรแกรมของธนาคารเลือด "BloodTrans" และค่าใช้จ่ายจากการให้เลือดเก็บข้อมูลจากห้องยาผู้ป่วยในและแผนกการเงินของโรงพยาบาลตำรวจ*

ผลการศึกษา: *ผู้ป่วยจำนวน 342 ราย ที่ได้รับการผ่าตัดข้อเข่าเทียม เป็นผู้ป่วยเพศชาย 80 ราย เพศหญิง 262 ราย อายุเฉลี่ย 68.7 (50-84) ปี น้ำหนักตัวเฉลี่ย 67.0 (58-90) กิโลกรัม ส่วนสูงเฉลี่ย 163.0 (160-172) เซนติเมตร ดัชนีมวลกาย 25.2 (22.2-28.5) กิโลกรัมต่อตารางเมตร จำนวนเข่าขวา 216 ราย เข่าซ้าย 126 ราย ความเข้มข้นของเลือดก่อนการผ่าตัดเฉลี่ยในกลุ่มที่หนึ่งร้อยละ 36.4 (30.0-44.5) กลุ่มที่สองร้อยละ 30.1 (30.0-43.5) ค่าความเข้มข้นหลังการผ่าตัดในผู้ป่วยกลุ่มที่หนึ่งร้อยละ 31.4 (26.0-40.5) และกลุ่มที่สองร้อยละ 30.1 (23.0-38.5) ผู้ป่วยจำนวน 164 รายได้รับเลือดหลังการผ่าตัดข้อเข่าเทียมคิดเป็นร้อยละ 48 ของผู้ป่วยทั้งหมด โดยในผู้ป่วยจำนวนนี้เป็นผู้ป่วยในกลุ่มที่หนึ่งจำนวน 54 ราย (ร้อยละ 36) และผู้ป่วยกลุ่มที่สองจำนวน 110 ราย (ร้อยละ 58) และจำนวนเลือดที่ใช้ไปทั้งหมดเป็น 233 ยูนิต ค่าเฉลี่ยของจำนวนเลือดที่ใช้ต่อผู้ป่วยทั้งหมดเท่ากับ 0.68 ยูนิตต่อคน โดยในผู้ป่วยกลุ่มที่หนึ่งค่าเฉลี่ยเท่ากับ 0.48 ยูนิตต่อคนและในกลุ่มที่สองเท่ากับ 0.85 ยูนิตต่อคน ราคาของเลือดที่ให้ผู้ป่วยทั้งหมดคือ 174,300 บาท โดยมีค่าใช้จ่ายเฉลี่ยของการให้เลือดต่อการผ่าตัดข้อเข่าเทียมทั้งหมดคือ 530 บาท ค่าใช้จ่ายเฉลี่ยของการให้เลือดต่อกลุ่มผู้ป่วยกลุ่มที่หนึ่งคือ 463 บาท (น้อยกว่าค่าใช้จ่ายเฉลี่ยรวมร้อยละ 12) และต่อผู้ป่วยกลุ่มที่สองคือ 584 บาท (สูงกว่าค่าเฉลี่ยรวมร้อยละ 10) โดยสามารถลดค่าใช้จ่ายของการให้เลือดโดยการใช้ยา tranexamic acid ไปได้ประมาณร้อยละ 22*

สรุป: *จำนวนปริมาณเลือดที่ให้ผู้ป่วยในการศึกษาน้อยกว่าการให้เลือดในมาตรฐานทั่วไปของการผ่าตัดข้อเข่าเทียม แต่อัตราการให้เลือดกับผู้ป่วยสูงกว่ามาตรฐานทั่วไป การใช้ยา tranexamic acid ทำให้อัตราการให้เลือดลดลงและค่าใช้จ่ายจากการให้เลือดลดลงด้วยเมื่อเทียบกับกลุ่มที่ไม่ได้ให้ยา ซึ่งจากการศึกษาพบว่าการใช้ยา tranexamic acid มีผลดีต่อการรักษาโดยข้อบ่งชี้ในการให้เลือดแก่ผู้ป่วยหลังการผ่าตัดข้อเข่าเสื่อมควรจะต้องมีการพิจารณาในการศึกษาต่อไป*

Metastasis of cardiac rhabdomyosarcoma at lumbar spine: case report

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We report a case and review literatures of a 78-year-old man presenting with progressive dyspnea for 1 month. A diagnosis of cardiac pleomorphic rhabdomyosarcoma with lung and scalp metastasis was made then surgical tumor removal was performed. One month later the patient complained of severe low back pain. After complete investigation, he was diagnosed with metastatic rhabdomyosarcoma at lumbar spine and adjacent paravertebral soft-tissue. He underwent a second operation resulting in a satisfactory early postoperative outcome. He passed away approximately 6 weeks later as a result of severe congestive heart failure and irreversible respiratory failure.

This is the first case report of metastatic cardiac pleomorphic rhabdomyosarcoma at lumbar spine which is assumed to be a rare and aggressive disease.

Keywords: *Metastasis, cardiac tumor, pleomorphic rhabdomyosarcoma, lumbar spine, case report*

The Thai Journal of Orthopaedic Surgery: 40 No.1-2: 27-32
Full text. e journal: *http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST*

Case report

A 78-year-old man presented with progressive dyspnea for 1 month. The physician detected a 2.0x1.5 cm ulcerative nodule at scalp overlying the left fronto-parietal region without other obvious abnormalities. The radiologist further noticed a 5 cm mass at right paratracheal from a chest x-ray. Chest computed tomography (CT) was then performed and confirmed with computed tomography pulmonary angiography (CTPA) in addition with an echocardiography study revealing a 5.5x3.8x5.0 cm lobulated mass at the posterior segment of the upper lobe along with a 4.2x1.6 cm subpleural nodule at the lower lobe of the right lung and a 3.4x6.0x5.3 cm lobulated mass with inhomogeneous enhancement occupying the right ventricle as well as a 2.7x2.4 cm mass at the left ventricle. (Fig. 1) The initial diagnosis was suspected of cardiac tumor with lung and scalp metastasis. An open thoracotomy with cardiac tumor removal along with tricuspid valve repair was performed simultaneously with scalp tumor excision. Histopathology and special immunohistochemistry studies of both specimens indicated a cardiac pleomorphic rhabdomyosarcoma with scalp metastasis. The patient refused adjuvant chemotherapy and radiation therapy at thoracic and scalp because of personal believes.

One month later the patient gradually felt pain at his lower back. The muscle strength was 4/5 in the lower extremities with intact sensation and negative Babinski sign from physical examination. Plain lumbar x-ray revealed an osteolytic lesion at the body of L3, and magnetic resonance imaging (MRI) of the lumbar spine suspected of bony metastasis at L3 vertebra associated with a 1.5x4.2 cm posterior epidural mass at L2-3 and a bilateral paraspinal mass with extension into the left L2-3 neural foramen causing spinal canal stenosis with compression of cauda equine nerve roots. (Fig. 2A-2D) A diagnosis of suspected metastatic rhabdomyosarcoma at lumbar spine and paravertebral soft-tissue was made. Decompressive laminectomy at L2-3 with pedicular screw fixation from L2 to L4 with vertebroplasty to L3 vertebra was performed 3 days later with satisfactory early postoperative results without any immediate complications. (Fig. 2E-2F) The histopathological features of the lesion showed pleomorphic vesicular-chromatic spindle-shaped and polygonal-shaped cells arranged in fascicular pattern with strong immunoreactivity to desmin and cytokeratin corresponding with metastatic pleomorphic rhabdomyosarcoma. Technitium-99m (Tc-99m) bone scintigraphy was performed later and the finding was increased radiotracer uptake at L2-L3 without bony metastasis elsewhere, however the patient insisted of refusing adjuvant radiation therapy at lumbar spine. Therefore, his lung metastatic condition was getting worse and massive pleural effusion was developed 4 weeks later. The patient passed away approximately 6 weeks postoperatively as a result of severe congestive heart failure and irreversible respiratory failure.

Discussion

Cardiac tumors are considered to be rare diseases with the incidence ranging from 0.0017% to 0.28% in autopsy studies.[1] Primary lesions are

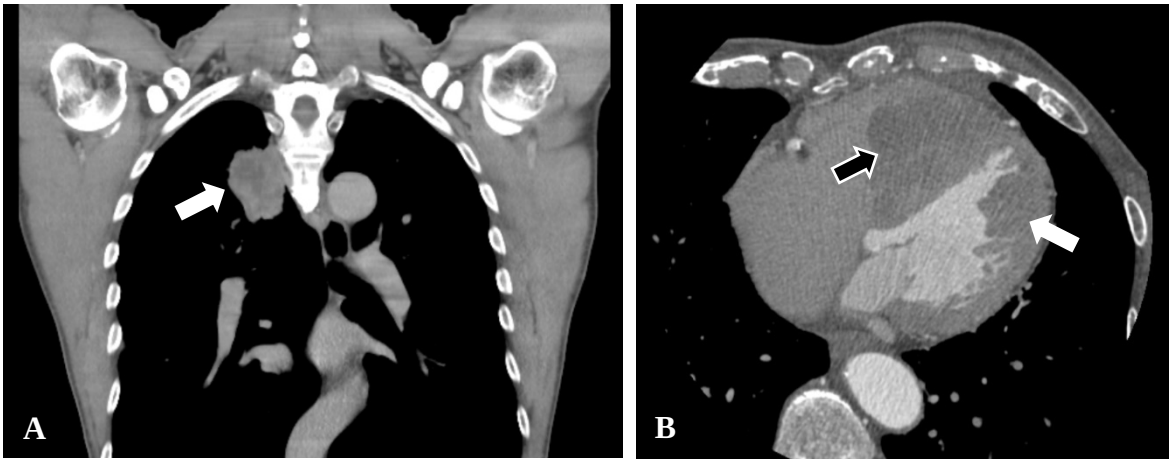

Fig. 1 Chest computed tomography (CT) shows lobulated mass (white arrow) at posterior segment of the right upper lung. (A) Computed tomography pulmonary angiography (CTPA) demonstrates masses at the right ventricle (black arrow) and left ventricle (white arrow). (B)

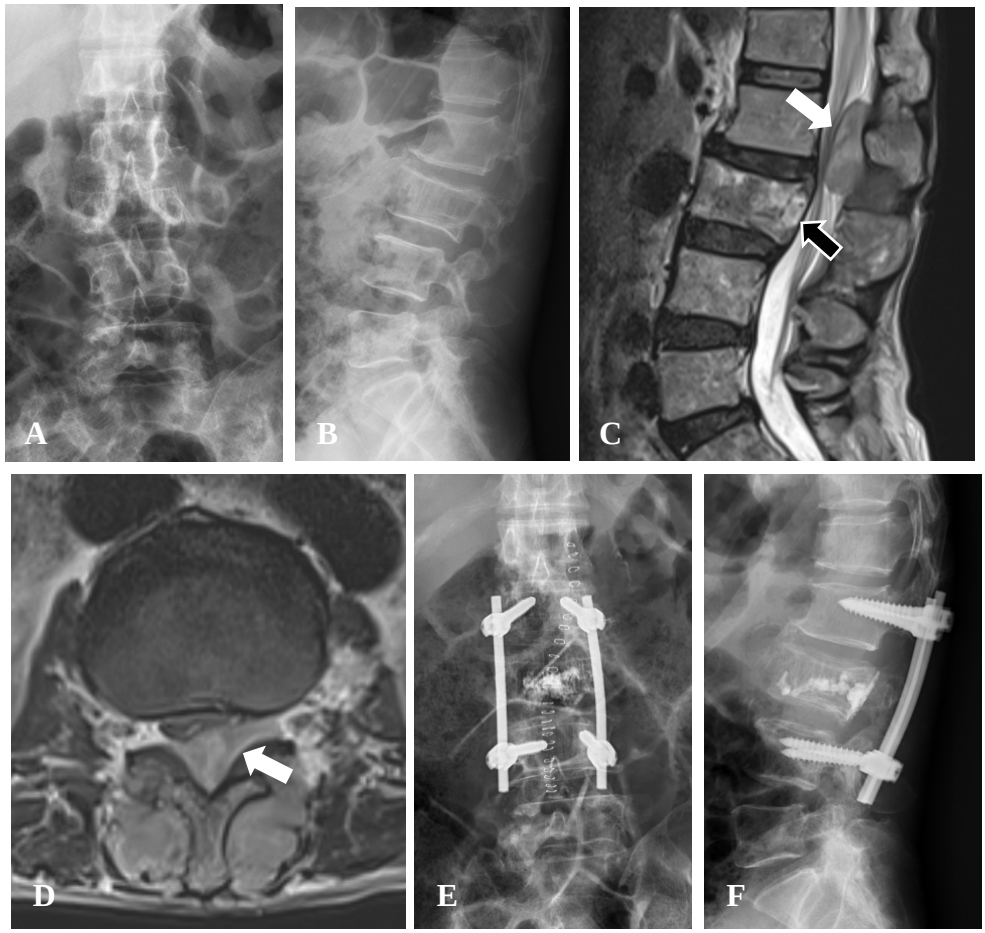

Fig. 2 Plain lumbar x-rays demonstrate an osteolytic lesion at the body of L3. AP view (A), Lateral view (B) Magnetic resonance imagings (MRI) of the lumbar spine depict bony metastasis at L3 vertebra (black arrow) and an epidural mass at L2/3 level (white arrow). Sagittal view (C), Axial view (D) Postoperative x-rays reveal spinal instrumentations at L2-L4 level and vertebroplasty at L3 vertebra. AP view (E), Lateral view (F)

less frequent than metastases to the heart. The majority of cardiac malignant neoplasms in adults are sarcoma, particularly angiosarcoma, which is the most common in adults and has the worst prognosis.[2, 3] Rhabdomyosarcoma is considered to be the second most frequent primary cardiac tumor in adults and the most common in children which makes up approximately 20% of all primary malignant cardiac tumors.[4] Rhabdomyosarcoma can be classified into 3 main types including embryonal, alveolar, and pleomorphic. Even though patients with cardiac rhabdomyosarcoma can present with varieties of cardiac symptoms, they are usually at the advanced stage of the diseases. Tiyapant A., et al. reported the first case of cardiac rhabdomyosarcoma in Thailand with clinical presentation of cardiac tamponade.[5] The patients can also present with skeletal pain and bone lesions from metastases on radiographs without evidence of a primary tumor.[6] Transthoracic echocardiography remains the widely available screening method for the early diagnosis of a cardiac tumor. On the other hand, computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) are demonstrate better soft tissue characterization of the neoplasm.[7]

Surgery is the method of choice for treatment of cardiac rhabdomyosarcoma in order to confirm the diagnosis, relief of cardiac symptoms, and prolongation of life. Heart transplantation can offer long-term survival and can be considered for selected patients.[8] Chemotherapy or radiotherapy should be considered for an adjuvant treatment. Patients with pleomorphic rhabdomyosarcoma are recommended to have adjuvant radiotherapy over the primary site, even after complete removal of the tumor.[9] Despite an aggressive treatment, adult rhabdomyosarcoma is still becoming a highly malignant tumor with a significant incidence of metastasis.[10] The overall 5- and 10-year survival rates are approximately 31% and 27% respectively.[11]

Skeletal metastasis from soft-tissue sarcoma is uncommon, regardless of extremely rare cardiogenic sarcoma in origin. Yoshikawa H, et al. reviewed 277 patients with soft-tissue sarcoma and then reported that 28 patients (10.1%) had metastases at an average of within 18.6 months after time of admission. Eighteen patients (64.3%) of those with metastases had lesions at spines and pelvic bones.[12] The median survival of patients with bone metastases in soft-tissue sarcomas is 6 months after diagnosis of bone metastases.[13] A pooled analysis from United States and European Cooperative Groups obtained data from 788 metastatic rhabdomyosarcoma patients and performed univariate analysis. They revealed that 3-year disease free survival was significantly and adversely affected by alveolar histology, age, and unfavourable site of the primary tumor. By multivariate analysis, disease free survival was strongly associated with all previous mentioned factors except histology.[14]

Surgical resection is one of the most important modality for the treatment of metastatic spinal neoplasm. Although en bloc resection is the standard treatment for malignant primary neoplasms of the spine, the concept of metastatic treatment is slightly different. Goals of surgery include restoration of neurological function, oncological control, pain control, and deformity correction and stabilization. Risks and benefits must be discussed among healthcare professionals, patients, and the family so that everyone has an understanding of the treatment and expected outcomes.[15] Rao G., et al. had studied 110 surgeries from 80 patients with either primary or metastatic sarcomas of the spine, of which 98 surgeries were intralesional resections (89%) and 11% were en bloc resections. Overall, the patients had a median survival time at 20.6 months, while the median survival for primary spinal sarcoma and metastatic sarcoma patients were 40.2 months and 17.3 months, respectively. Tumors with high grades have been identified from multivariate analysis as an adverse predictor of overall survival.[16]

Radiotherapy for spinal metastasis from soft-tissue sarcoma should be considered either for adjuvant after surgery or definite palliative treatment. Although higher doses of radiotherapy (35 fractions of 1.8 Gy) tend to have benefits for eradication of microscopic diseases without concerning of spinal cord damage in lumbar lesions; however, lower doses of 10-fractions of 3 Gy could be used for palliative purposes.[17] On the other hand, chemotherapy is not widely administered because this tumor is considered relatively chemoresistant but might have a role in selective cases. Bisphosphonate treatment, including pamidronate or zoledronic acid, could delay the first skeletal related event and might have a positive effect on overall survival.[13]

There were few literature reports about metastatic cardiac sarcoma at vertebras.[18-21] As far as we know, this is the first case report of metastatic cardiac pleomorphic rhabdomyosarcoma at lumbar spine. Although it is an extremely rare condition, it should always be considered in the differential diagnosis in patients who have history of sarcoma and present with spine lesions.

Acknowledgement

This case report is dedicated to the memory of our beloved Associate Professor Vinai Parkpian who had been a great doctor and great teacher from the beginning until the end of his life.

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รายงานผู้ป่วยมะเร็งทุติยภูมิที่กระดูกสันหลังส่วนเอวแพร่กระจายมาจากมะเร็งในหัวใจชนิดแรบโดมัยโอซาร์โคมา

ชินดนัย หงสประภาส, พบ, วิชาญ ยิ่งศักดิ์มงคล, พบ, พงศ์ศักดิ์ ยุกตะนันทน์, พบ

รายงานผู้ป่วยและบทความปริทรรศน์ของผู้ป่วยชายอายุ 78 ปีที่มีอาการหอบเหนื่อยมากขึ้นมา 1 เดือน ได้รับการวินิจฉัยว่าเป็นโรคมะเร็งในหัวใจชนิดแรบโดมัยโอซาร์โคมาแพร่กระจายมาที่ปอดและหนังศีรษะ ผู้ป่วยได้รับการผ่าตัดเอาเนื้องอกออก หลังจากนั้น 1 เดือนผู้ป่วยมีอาการปวดหลังอย่างรุนแรง ภายหลังจากการตรวจเพิ่มเติมโดยละเอียด พบว่ามีการแพร่กระจายของมะเร็งมาที่กระดูกสันหลังส่วนเอวและเนื้อเยื่ออ่อนข้างเคียง ผู้ป่วยได้รับการผ่าตัดอีกครั้งโดยมีผลการผ่าตัดเบื้องต้นเป็นที่น่าพอใจ แต่ผู้ป่วยเสียชีวิตในเวลาประมาณ 6 สัปดาห์ต่อมาเนื่องจากภาวะน้ำท่วมปอดและระบบทางเดินหายใจล้มเหลว

รายงานผู้ป่วยนี้เป็นฉบับแรกที่มีการรายงานถึงผู้ป่วยมะเร็งทุติยภูมิที่กระดูกสันหลังส่วนเอวแพร่กระจายมาจากมะเร็งในหัวใจชนิดแรบโดมัยโอซาร์โคมาซึ่งถือเป็นโรคที่พบได้ยากและมีความรุนแรงมาก

คำสำคัญ : *มะเร็งทุติยภูมิ, มะเร็งในหัวใจ, มะเร็งแรบโดมัยโอซาร์โคมาชนิดพลีโอมอร์ฟิก, กระดูกสันหลังส่วนเอว, รายงานผู้ป่วย*

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Redundant or duplicate publication is a paper that overlaps substantially with one already published in print or electronic media. At the time of manuscript submission, authors must inform the editor about all submissions and previous publications that might be regarded as redundant or duplicate publication of the same or very similar work. Any such publication must be referred to and referenced in the new paper.Copies of such material should be included with the submitted paper as a supplemental file.

Authors must not:

- Willfully and knowingly submit false data
- Submit data from source not the authors' own
- Submit previously published material (with the exception of abstracts) without correct and proper citation
- Omit reference to the works of other investigators which established a priority
- Falsely certify that the submitted work is original
- Use material previously published elsewhere without prior written approval of the copyright holder

Title Page

The title page must be written in both Thai and English and should include:

- The name(s) of the author(s)
- A concise and informative title
- The affiliation(s) and address(es) of the author(s)
- The e-mail address, telephone and fax numbers of the corresponding author

Abstract

Please provide a structured abstract in both Thai and English of 250 words which should be divided into the following sections:

- Purpose (stating the main purposes and research question)
- Methods
- Results
- Conclusions

Keywords

Please provide 4 to 6 keywords which can be used for indexing purposes.

The manuscript: The manuscript must be written in English or Thai.

Text Formatting

The text should be organized in the following order: Introduction, Methods, Results, Discussion, Acknowledgements, References, Tables and Figures. Manuscripts should be submitted in Word.

- Use a normal, plain font (e.g., 10-point Times Roman) for text.
- Use italics for emphasis.
- Use the automatic page numbering function to number the pages.

- Do not use field functions. Use tab stops or other commands for indents, not the space bar.
- Use the table function, not spreadsheets, to make tables.
- Use the equation editor or MathType for equations.
- Note: If you use Word 2007, do not create the equations with the default equation editor but use the Microsoft equation editor or MathType instead.
- Save your file in doc format. Do not submit docx files.

Headings

Please use no more than three levels of displayed headings.

Abbreviations

Abbreviations should be defined at first mention and used consistently thereafter.

Footnotes

Footnotes on the title page are not given reference symbols. Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data).

Acknowledgements

Acknowledgements of people, grants, funds, etc. should be placed in a separate section before the reference list. The names of funding organizations should be written in full.

Tables

- All tables are to be numbered using Arabic numerals.
- Tables should always be cited in text in consecutive numerical order.
- For each table, please supply a table heading. The table title should explain clearly and concisely the components of the table.
- Identify any previously published material by giving the original source in the form of a reference at the end of the table heading.
- Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.

Figures

Electronic Figure Submission

- Supply all figures electronically.
- Indicate what graphics program was used to create the artwork.
- For vector graphics, the preferred format is EPS; for halftones, please use TIFF format. MS Office files are also acceptable.
- Vector graphics containing fonts must have the fonts embedded in the files.
- Name your figure files with "Fig" and the figure number, e.g., Fig1.eps.

References: List the references in consecutive, numerical order, as they are cited in the text. Use the Vancouver style. If the list of authors exceeds 6, the first 6 authors followed by et al should be listed for those references. Abbreviate journal titles according to the style used in the Index Medicus. See also http://www.medscape.com/home/search/indexMedicus/ Index Medicus-A.html

Example of references:

Journal articles.

1. You CH, Lee KY, Chey RY, Menguy R. Electrogastrographic study of patient with unexplained nausea, bloating and vomiting. Gastroenterol 1980;79:311-4.
2. Gulgolgarn V, Ketsararat V, Niyomthai R, et al. Somatic growth and clinical manifestation in formula fed infants born to HIV-infected mothers during the first year of life. J Med Assoc Thai 1999;82:1094-9.

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1. Bengtsson S, Solheim BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Peimme TE, Reinhoff O, editors. MEDINFO 92. Proceeding fo the 7th World Congress on Medical informatics; 1992 Sep 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. p.1561-5.

Abstract in scientific presentation

1. Wettstein A, Dore G, Murphy C, Hing M, Edward P. HIV-related cholangiopathy in Australia. IX Annual Conference of the Australasian Society of HIV Medicine. Adelaide, November 1997 [abstract P45].
2. Clement J, De Bock R. Hematological complications of hantavirus nephropathy [abstract]. Kidney Int 1992;42:1285.

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1. Getzen TE. Health economics: Fundamentals of funds. New York: John Wiley & Sons; 1997.
2. Porter RJ, Meldrum BS. Antiepileptic drugs. In: Katzung BG, editor. Basic and clinical pharmacology. 6th ed. Norwalk: Appleton & Lange; 1995. p.361-80.

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1. Morse SS. Factors in the emergence of infectious disease. Emerg Infect Dis [serial online] 1995 Jan-Mar;1(1):[24 screens]. Available from: URL:http://www/cdc/gov/ncidoc/EID/eid.htm. Accessed December 25,1999.
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คำแนะนำสำหรับผู้ส่งบทความเพื่อลงตีพิมพ์

จุดมุ่งหมายและขอบเขต

วารสาร The Thai Journal of Orthopaedic Surgery เป็นวารสารทางวิชาการของราชวิทยาลัยแพทย์ออร์โธปิดิกส์แห่งประเทศไทยที่พิมพ์เผยแพร่อย่างสม่ำเสมอทุก 3 เดือน (4 ฉบับ/ปี) ทั้งแบบเป็นเอกสารรูปเล่ม และแบบออนไลน์ โดยเป็นวารสารที่ได้รับการประเมินบทความโดยผู้ทรงคุณวุฒิ (peer–reviewed journal) เพื่อเปิดโอกาสให้นักวิชาการที่สนใจเสนอบทความที่เกี่ยวข้องกับการรักษาผู้ป่วยและผลงานวิจัยทางศัลยศาสตร์ออร์โธปิดิกส์

เพื่อรักษามาตรฐานของวารสาร บทความที่จะลงตีพิมพ์ในวารสารจำเป็นต้องเขียนเป็นภาษาอังกฤษ ซึ่งประกอบด้วย Original Articles, Case Report, Review Articles, Letter to the Editor และ Miscellany

บทความประเภท Original articles เป็นรายงานผลการวิจัยทางด้านศัลยศาสตร์ออร์โธปิดิกส์ และสาขาอื่นที่เกี่ยวข้อง

บทความ Review articles เป็นบทความที่รวบรวมเอาผลงานในเรื่องใดเรื่องหนึ่งโดยเฉพาะ ซึ่งเคยลงตีพิมพ์มาแล้ว นำมาวิเคราะห์ วิจารณ์ เพื่อให้เกิดความกระจ่างในเรื่องนั้นยิ่งขึ้น

รายงานผู้ป่วย (Case report) เป็นรายงานผู้ป่วย วิจารณ์อาการทางคลินิกและผลตรวจทางห้องปฏิบัติการที่น่าสนใจ

เรื่องที่ส่งมาต้องไม่เคยพิมพ์เผยแพร่มาก่อน กองบรรณาธิการขอสงวนสิทธิ์ในการตรวจทาน แก้ไขต้นฉบับ และพิจารณาตีพิมพ์ข้อคิดเห็นในบทความเป็นความเห็นและเป็นความรับผิดชอบของเจ้าของบทความโดยตรง

การส่งบทความ

ทางราชวิทยาลัยฯ ขอแจ้งให้ทราบว่า เพื่อความสะดวกรวดเร็วและมีประสิทธิภาพในการส่งบทความ ราชวิทยาลัยฯ ผู้เขียนสามารถเสนอบทความเพื่อพิจารณาได้ทางจดหมายอิเล็กโทรนิกส์ secretariat@rcost.or.th

ประเภทของบทความ

- นิพนธ์ต้นฉบับ (original articles) ให้มีความยาวไม่เกิน 5,000 คำ, เอกสารอ้างอิงไม่เกิน 40 ข้อ, รูปภาพและตารางรวมกันไม่เกิน 6 รูป
- บทความปริทรรศน์ (review articles) ให้มีความยาวไม่เกิน 10,000 คำ, เอกสารอ้างอิงไม่เกิน 100 ข้อ, รูปภาพและตารางรวมกันไม่เกิน 10 รูป
- รายงานผู้ป่วย (case report) ให้มีความยาวได้ 1,500 คำ, รูปภาพและตาราง 1–2 รูป/ตาราง, เอกสารอ้างอิงไม่เกิน 20 ข้อ
- จดหมายให้มีความยาวได้ 500 คำ
- บทบรรณาธิการ

การเตรียมต้นฉบับ

- **เกณฑ์การเขียนบทความ**
  1. อธิบายเนื้อหาของบทความหรือวิเคราะห์ข้อมูลที่ได้มาให้ชัดเจน
  2. หากต้นฉบับมีข้อผิดพลาดของรูปแบบหรือมีความไม่สมบูรณ์ขององค์ประกอบในบทความ บทความนั้นจะถูกส่งกลับไปยังผู้เขียนเพื่อทำการแก้ไขต่อไป

3. แก้ไขปรับปรุงเนื้อหาของต้นฉบับตามคำแนะนำของผู้ประเมินบทความ

หากมีการเขียนบทความโดยกลุ่ม กรุณาระบุชื่อผู้เขียนทุกคน และระบุชื่อผู้วิจัยหลักให้ชัดเจน

ควรแสดงความขอบคุณแก่บุคคลที่ไม่ได้มีส่วนร่วมในการเขียนบทความ แต่มีส่วนช่วยเหลือโดยตรงในการวิจัย เช่น ผู้ช่วยทางเทคนิค, ที่ปรึกษาด้านการเขียนบทความ, ผู้สนับสนุนทุนและวัสดุในการทำงานวิจัย เป็นต้น ไว้ในกิตติกรรมประกาศ (acknowledgements)

- **บทความที่ส่งมาจะต้องเป็นเรื่องที่ไม่เคยตีพิมพ์ที่ใดมาก่อน และผู้เขียนจะต้องไม่ส่งบทความเพื่อไปตีพิมพ์ในวารสารฉบับอื่นในเวลาเดียวกัน**

หลักเกณฑ์สำหรับผู้เขียนบทความ

- ผู้เขียนบทความต้องไม่มีเจตนาส่งข้อมูลเท็จ
- บทความที่ส่งมาต้องเป็นผลงานของท่านเอง
- ผู้เขียนบทความจะต้องไม่ส่งบทความที่เคยลงตีพิมพ์ในวารสารอื่น โดยไม่ระบุว่าท่านได้เสนอผลงานนั้นในวารสารใดบ้างอย่างถูกต้องและสมเหตุสมผล
- ต้องระบุรายชื่อผู้เขียนทุกคนตามความเป็นจริง
- ผู้เขียนบทความต้องส่งต้นฉบับที่ได้รับการรับรองที่แท้จริง
- ผู้เขียนบทความต้องไม่ใช้วิธีการศึกษาที่มีผู้เผยแพร่มาก่อน โดยไม่ได้รับการอนุมัติจากเจ้าของลิขสิทธิ์

- **หน้าแรก (Title page)** เขียนเป็นภาษาไทยและภาษาอังกฤษ ประกอบด้วย
  (1) ชื่อ สกุลของผู้เขียน
  (2) ชื่อเรื่องอย่างย่อ ที่สื่อความหมายและชี้ให้เห็นสาระสำคัญของเนื้อหาในตัวบทความ
  (3) สถานที่ทำงาน
  (4) เบอร์โทรศัพท์, เบอร์แฟกซ์ และe-mail address ของผู้เขียน
- **บทคัดย่อ (Abstract)** ต้องมีทั้งภาษาไทยและภาษาอังกฤษมีความยาวไม่เกิน 250 คำ โดยเรียงลำดับเนื้อหา ดังนี้
  (1) วัตถุประสงค์ (Purpose)
  (2) วิธีการศึกษา (Methods)
  (3) ผลการศึกษา (Results)
  (4) สรุป (Conclusions**)**
- **คำสำคัญ (Keyword)** ระบุไว้ใต้บทคัดย่อ มีความยาว 4 – 6 คำ
- **ต้นฉบับ (Manuscript)** เป็นภาษาอังกฤษ
- **เนื้อเรื่อง (Text Formatting)** ให้ลำดับความสำคัญของเนื้อหาดังนี้คือ บทนำ (introduction), วิธีการศึกษา (methods), ผลการศึกษา (results), วิจารณ์ (discussion), บทขอบคุณ (acknowledgements), เอกสารอ้างอิง (references), ตารางและรูปภาพประกอบ (tables and figures) โดยต้นฉบับจะต้องใช้รูปแบบ ดังนี้
  (1) ใช้ตัวพิมพ์มาตรฐาน เช่นภาษาอังกฤษ ใช้ตัวอักษร “Times Roman” ขนาด 10 point ภาษาไทยใช้ ตัวอักษร “Angsana New” ขนาด 12 point
  (2) พิมพ์ข้อความสำคัญด้วยตัวเอน
  (3) ตั้งค่าเลขหน้าโดยอัตโนมัติ

(4) ไม่ใช้ “field functions”

(5) ใช้ปุ่ม “Tab” เมื่อขึ้นย่อหน้าต่อไป

(6) เลือกคำสั่งตาราง (Table) เมื่อต้องการพิมพ์ตาราง

(7) หากใช้โปรแกรม “Microsoft Word 2007” ให้ใช้โปรแกรม “Microsoft equation editor” หรือโปรแกรม “Math Type”

(8) ส่งต้นฉบับในรูปของแฟ้มข้อมูล โดยบันทึกข้อมูลเป็นไฟล์ “.doc” และห้ามบันทึกเป็นไฟล์ “.docx”

- **หัวข้อ (headings)** ไม่ควรมีขนาดต่างๆมากกว่า 3 ระดับ
- **คำย่อ (abbreviations)** จะต้องมีคำเต็มเมื่อปรากฏเป็นครั้งแรกในบทความ หลังจากนั้นสามารถใช้คำย่อเหล่านั้นได้ตามปกติ
- **เชิงอรรถ (footnotes)** คือ การอ้างอิงข้อความที่ผู้เขียนนำมากล่าวแยกจากเนื้อหาอยู่ตอนล่างของหน้า โดยใส่หมายเลขกำกับไว้ท้ายข้อความที่คัดลอกหรือเก็บแนวคิดมา และจะไม่เขียนเชิงอรรถเอาไว้ที่หน้าแรกของบทความ ถ้าต้องการแสดงที่มาของตารางหรือภาพประกอบให้ใช้เครื่องหมายแทนตัวเลข โดยเขียนไว้ที่ส่วนล่าง ของหน้า หรือใช้เครื่องหมายดอกจัน (*) เพื่อแสดงความหมายของค่าหรือข้อมูลทางสถิติ
- **กิตติกรรมประกาศ (acknowledgements)** เป็นการแสดงความขอบคุณแก่ผู้ที่ช่วยเหลือในการทำวิจัย หรือผู้สนับสนุนทุนการวิจัย เป็นต้น โดยจะเขียนไว้ก่อนเอกสารอ้างอิงและควรเขียนชื่อสถาบันที่ให้การสนับสนุนทุนการวิจัยโดยใช้ชื่อเต็ม
- **ตาราง (tables)**

(1) ให้เขียนหมายเลขตารางเป็นเลขอารบิก

(2) ให้เรียงตามลำดับที่ของตารางอย่างต่อเนื่องกันจาก 1, 2, 3, ….

(3) การอธิบายผลในตารางต้องไม่ซ้ำซ้อนกันและมีใจความกระชับรัดกุม และมีคำอธิบายกำกับไว้เหนือตาราง

(4) เขียนคำอธิบายเพิ่มเติมเกี่ยวกับแหล่งที่มาของเอกสารอ้างอิงไว้ที่ใต้ตาราง

(5) เชิงอรรถ (footnotes) ของตารางจะเขียนไว้ใต้ตารางหรือใช้เครื่องหมายดอกจัน (*) เพื่อแสดงความหมายของค่าหรือข้อมูลทางสถิติ

- **รูปภาพ (figures)**

(2) ให้ใช้โปรแกรมกราฟฟิกคอมพิวเตอร์ในการวาดรูป

(3) รูปภาพที่เป็นลายเส้นควรใช้รูปแบบ EPS ในการวาดเส้นรูปภาพและรูปภาพที่เป็นโทนสีควรใช้รูปแบบ TIFF ในการไล่เฉดสี

(4) รูปภาพทุกรูปจะต้องมีหมายเลขและคำบรรยายภาพกำกับไว้ใต้ภาพ โดยใช้ชื่อรูปภาพเป็น “Fig” ตามด้วยลำดับที่ของรูปภาพ เช่น “Fig1” เป็นต้น

- **เอกสารอ้างอิง (references)** เรียงลำดับเลขการอ้างอิงตามเอกสารอ้างอิงท้ายบทความ และใช้ตาม Vancouver style การอ้างอิงถึงชื่อบุคคล ถ้ามีผู้เขียนมากกว่า 6 คน ให้ใส่ชื่อ 6 คนแรก แล้วตามด้วย et al. ส่วนการเขียนเอกสารอ้างอิงท้ายบทความ การย่อชื่อวารสารให้ใช้ตาม Index Medicus โดยศึกษาได้ในเว็บไซต์ http://www.medscape.com/home/search/indexMedicus/IndexMedicus-A.html

กรุณาลงนามในแบบฟอร์มการส่งบทความเพื่อขอตีพิมพ์ เพื่อแสดงว่าผู้เขียนได้อ่านเกณฑ์การเขียนบทความทั้งหมด

- **ตัวอย่างการเขียนเอกสารอ้างอิง (references) กรุณาดูในหัวข้อ “ Instruction to authors ”**

The Thai Journal of Orthopaedic Surgery

Acknowledgements to Reviewers 2016

Pongsak Yuktanandana
Editor in Chief

We are fortunate to have an outstanding group of reviewers who kindly volunteer their time and effort to review manuscripts for *The Thai Journal of Orthopaedic Surgery*. They are critical team players in the continued success of the journal, ensuring a peer review process of the high integrity and quality. The editor would like to thank the following reviewers who provided their expertise in evaluating manuscripts for *The Thai Journal of Orthopaedic Surgery* during 2016. A special thanks goes to Jutamas Chearanaya for being our managing editor.

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