COMPARISON OF MEAN FALL IN POST-OPERATIVE HEMOGLOBIN LEVEL AFTER INTRA-ARTICULAR TRANSAMINE VERSUS INTRAVENOUS TRANSAMINE IN TOTAL KNEE ARTHROPLASTY

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ABSTRACT

Objective: To compare the mean fall in post-operative hemoglobin level after intra-articular transamine versus intravenous transamine in total knee arthroplasty.

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Orthopedic Surgery, Combined Military Hospital (CMH) Rawalpindi, from Jan 2018 to Jul 2018.

Methodology: A total of 60 patients having osteoarthritis of knee undergoing total knee replacement were included in the study. In the group A, intra-articular transamine (2 grams) was given after end of operation while in group B intravenous transamine (2 grams) was given. All patients in both groups were followed by the researcher himself and fall in hemoglobin levels were measured after 24 hours post-operatively.

Results: The mean age of patients in group A was 58.27 ± 7.01 years and in group B was 58.13 ± 7.90 years. Out of these 60 patients, 35 (58.33%) were females and 25 (41.67%) were males. Mean fall in post-operative hemoglobin in group A (intra-articular transamine) was 0.42 ± 0.23 g/dl and in group B (intravenous transamine) was 1.11 ± 0.43 g/dl (p-value<0.001).

Conclusion: Mean fall in post-operative hemoglobin level after intra-articular transamine is less as compared to intravenous transamine in total knee arthroplasty. Therefore intra articular route should be preferred for this purpose and screening of blood indices should be performed routinely on those who have been given intravenous transamine.

Keywords: Fall in hemoglobin, Intra-articular transamine, Total knee arthroplasty.

INTRODUCTION

Osteoarthritis (OA) refers to a heterogeneous group of conditions that lead to joint symptoms and signs associated with loss of integrity of the articular cartilage, in combination with changes in underlying bone and joint margins[1]. OA affects more than 40 million individuals in the United States alone, and is the leading cause of disability nationwide[2]. It is the most common articular disease worldwide, although frequencies vary by country. The high prevalence of OA makes it one of the principal reasons for office visits in the primary care setting. OA causes with both direct and indirect economic costs to society. Clinician visits, medications, and surgical interventions comprise the direct costs, while comorbidities and time lost from work because of the effects of disability make up the indirect costs[3]. This situation is more evident among the elderly, who may lose their independence and may later need assistance with their daily living activities, thus adding to the economic burden[4].

Total knee arthroplasty (TKA) is the most commonly performed joint replacement surgery worldwide. With an estimated two million surgeries every year worldwide this number is set to increase */five fold by 2025[5]. The major beneficial effects are pain relief, increase range of movements and better quality of life. The most common indication is tri-compartmental arthritis of the knee either primary (idiopathic) or secondary (rheumatoid, posttraumatic, post-septic, etc)[6]. The possible complications include post-operative blood loss necessitating transfusion, infection and implant loosening. The cause of

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potential blood loss in the post-operative period is the extensive bone resection and soft tissue release during surgery[7].

Tranexamic acid (TXA) has come to light as an effective method to decrease blood loss and transfusion rates in total knee arthroplasty (TKA) without increasing the risk of thromboembolic events (TEE)[8]. Many initial studies utilized intravenous (IV) TXA and more recently intra-articular TXA has also been shown to be effective[9]. In these studies, various dosing regimens have been used for both IV and intra-articular TXA. Some have attempted to find the most beneficial regimen, demonstrating better results with two IV doses compared to a single IV dose[10]. The proposed benefits of IA administration of TXA as compared to IV TXA are direct targeting of bleeding at its source, lower plasma level concentrations, the potential for reduced prothrombotic systemic events (e.g. arterial vascular thrombosis, potentiation of a venous thromboembolic event), and less requirements to administer the drug in the postoperative phase. In a study, the fall in post-op Hb level was 0.72 ± 0.64 gm/dl for intra-articular transamine group and 1.36 ± 0.72 gm/dl for intravenous group.

There is always a debate for better route of transamine for reducing blood loss during total knee arthroplasty. We planned this study to compare the fall in post-operative hemoglobin level after intra-articular transamine versus intravenous transamine among the patients undergoing total knee arthroplasty at a tertiary case teaching hospital of Pakistan.

METHODOLOGY

This study was conducted at Combined Military Hospital Rawalpindi, from January 2018 to July 2018. The sample size calculated was 60 i.e. 30 in each group, by taking significance level (α) as 5%, power (1-β) as 80% and taking mean fall in post-op Hb level as 0.72 ± 0.64 gm/dl[11] for intra-articular transamine group and 1.36 ± 0.72 gm/dl for intravenous group. Non-probability, consecutive sampling was used to collect the sample. All the patients between the age of 40 and 70 years who had been suffering from osteo-arthritis knees and undergoing TKR and have given written informed consent were included in the study. Non consenting subjects and those with age less than 40 or more than 70 were excluded from the study. Patients with more than one blood transfusion during surgery or known hepatic (assessed on history and medical record i.e. s/bilirubin >1 mg/dl) were also not included. Patients with renal failure (assessed on history and medical record i.e. s/creatinine >1.1 mg/dl) or those with known allergy to tranexamic acid were also the part of exclusion criteria. History of clotting and bleeding disorders i.e. hemophilia or anemias (assessed on history and medical record) were also not included in this analysis.

After approval from ethics committee, total 60 patients admitted in the department of Orthopedics, CMH Rawalpindi fulfilling the inclusion criteria were selected for this study. Informed written consent was taken from each patient. After this, all patients were divided into two groups i.e. A & B by using random number tables. In all patients of both groups total knee replacement was done by the one consultant orthopedic surgeon (at least 5 years of post-fellowship experience). In the group A, intra-articular transamine (2 grams) was given after end of operation while in group B intravenous transamine (2 grams) was given. All surgeries were done under tourniquet control and the tourniquet was released after wound closure and sterile compression dressing. Suction drain was activated three hours after surgery by the ward staff. All patients in both groups were followed by the researcher himself and fall in hemoglobin levels were measured as per-operational defini-tion after 24 hours post-operatively. This all data was recorded on a predesigned Performa.

SPSS version 20 was used for data analysis. Age, pre-operative, post-operative and fall in hemoglobin were presented as mean and standard deviation. Gender, diabetes mellitus and hypertension were presented as frequency and percentage. Student' t-test was used to compare the mean fall in hemoglobin in both groups.

Stratification was done for age, gender, diabetes mellitus (yes/no) and hypertension (yes/no). Post-stratification student't' test was applied to see the effect of these on fall in hemoglobin and *p*-value ≤0.05 was taken as significant.

RESULTS

The total number of outcomes included age range from 40 to 70 years with mean age of 58.20 ± 7.41 years. The mean age of patients in group A was 58.27 ± 7.01 years and in group B was 58.13 ± 7.90 years. Out of these 60 patients, 35 (58.33%) were females and 25 (41.67%) were males. Mean pre-operative hemoglobin in group A (intra-articular transamine) was 11.27 ± 0.74 g/dl and in group B (intravenous transamine) was 11.10 ± 0.58 g/dl. Mean post-operative hemoglobin in group A (intra-articular transamine) was 10.85 ± 0.61 g/dl and in group B (intravenous transamine) was 9.99 ± 0.65 g/dl (*p*-value<0.001). Mean fall in post-operative hemoglobin in group A (intra-articular transamine) was 0.42 ± 0.23 g/dl and in group B (intravenous transamine) was 1.11 ± 0.43 g/dl (*p*-value<0.001) (table-I). Stratification of fall in hemoglobin with respect to age groups and gender was shown in table-II & III respectively. Stratification of fall in hemoglobin with respect to DM was shown in table-IV.

Table-I: Mean pre-operative, post-operative and fall in hemoglobin Hemoglobin levels (g/dl) (n=30).

	Group A Mean ± SD	Group B Mean ± SD	*p*-value
Pre-operative (g/dl)	11.27 ± 0.74	11.10 ± 0.58	0.3264
Post-operative (g/dl)	10.85 ± 0.61	9.99 ± 0.65	<0.001
Fall (g/dl)	0.42 ± 0.23	1.11 ± 0.43	<0.001

Table-II: Fall in hemoglobin with respect to age groups (n=30).

Age of Patients (years)	Group A (Fall in hemoglobin) Mean ± SD	Group B (Fall in hemoglobin) Mean ± SD	*p*-value
40-55	0.40 ± 0.23	1.36 ± 0.51	<0.001
56-70	0.44 ± 0.23	1.01 ± 0.36	<0.001

Table-III: Fall in hemoglobin with respect to gender (n=30).

Gender	Group A (Fall in hemoglobin) Mean ± SD	Group B (Fall in hemoglobin) Mean ± SD	*p*-value
Male	0.43 ± 0.23	1.18 ± 0.47	<0.001
Female	0.42 ± 0.23	1.07 ± 0.41	<0.001

Table-IV: Fall in hemoglobin with respect to diabetes mellitus (n=30).

Diabetes Mellitus	Group A (Fall in hemoglobin) Mean ± SD	Group B (Fall in hemoglobin) Mean ± SD	*p*-value
Yes	0.39 ± 0.24	1.08 ± 0.50	<0.001
No	0.36 ± 0.22	1.15 ± 0.35	<0.001

DISCUSSION

With the aging of the population, the number of patients with osteoarthritis of the knee has increased dramatically. In patients with severe osteoarthritis, total keen arthroplasty (TKA) is widely used as an effective method to relieve pain, correct deformity, and restore function. However, because of the large exposed surface of cancellous bone, intraoperative and postoperative bleeding is one of the major complications following TKA[11-15]. There is no doubt that a large amount of blood loss has a significant influence on morbidity and mortality, especially in old patients[16,17]. Thus, seeking an effective method to reduce the loss of blood is necessary.

Tranexamic acid (TXA), as an antifibrinolytic agent, was introduced with the aim of reducing perioperative and postoperative bleeding. It can block the lysine binding sites on plasminogen molecules, inhibit the formation of plasmin, and is believed to be able to help the body retain blood clots more effectively[18]. The intravenous application of TXA in orthopedic surgery has been well established in the literature. Many clinical studies and several meta-analyses have confirmed that this way could effectively reduce the rates of blood loss and transfusion in TKA without increasing the risk of complications[19-23]. In comparison with intravenous application, the intra-articular application of TXA has the advantages of being easy to administer, providing a

maximum concentration of TXA at the bleeding site, and being associated with lower systemic absorption[24]. In recent years, intra-articular application of TXA has been put under the spotlight. However, based on current evidence, it is not clear whether intra-articular application of TXA is as effective as intravenous application measures[25].

We have conducted this study to compare the mean fall in post-operative hemoglobin level after intra-articular transamine versus intravenous transamine in total knee arthroplasty. Age range in this study was from 40 to 70 years with mean age of 58.20 ± 7.41 years. The mean age of patients in group A was 58.27 ± 7.01 years and in group B was 58.13 ± 7.90 years. Majority of the patients 41 (61.33%) were between 56 to 70 years of age. Out of these 60 patients, 35 (58.33%) were female and 25 (41.67%) were males with female to male ratio of 1.4:1. Mean pre-operative hemoglobin in group A (intra-articular transamine) was 11.27 ± 0.74 g/dl and in group B (intravenous transamine) was 11.10 ± 0.58 g/dl. Mean post-operative hemoglobin in group A (intra-articular transamine) was 10.85 ± 0.61 g/dl and in group B (intravenous transamine) was 9.99 ± 0.65 g/dl (p-value<0.001). Mean fall in post-operative hemoglobin in group A (intra-articular transamine) was 0.42 ± 0.23 g/dl and in group B (intravenous transamine) was 1.11 ± 0.43 g/dl (p-value=0.0001). In a study, the fall in post-op Hb level was 0.72 ± 0.64 gm/dl for intra-articular transamine group and 1.36 ± 0.72 gm/dl for intravenous group[13]. Digas *et al*[25] conducted a RCT with 90 patients in three groups (placebo, intra-articular and intravenous tranexamic acid) and reported that the mean drained blood loss in control, IV and intra-articular groups was 415 ± 24, 192 ± 21 and 121 ± 17 ml.

In a meta-analysis, six studies were included and found no statistically significant difference between intra-articular and intravenous administration of tranexamic acid in terms of total blood loss (WMD, 6.01; 95% CI:–96.78 to 108.79; p=0.91), drain output (WMD=–20.26; 95% CI: –51.34 to 10.82; p=0.20), hemoglobin drop (WMD=0.33; 95% CI: –0.31 to 0.98; p=0.31), or the incidences of transfusion (RR = 0.98; 95% CI: 0.56–1.70; p=0.93) as well as deep vein thrombosis (RR=0.49; 95% CI: 0.09–2.73; p=0.42). 153 In another meta-analysis[5,16] randomized controlled trials with 1308 cases were included. Compared with IV TXA, IA TXA had similar blood volume of drainage, hidden blood loss, transfusion rate and complications (p>0.05). IA TXA had lower total blood loss than IV TXA, and there was significant difference (p<0.05). Subgroup analysis of total blood loss based on times of IV TXA administration showed that repeat dose of IV TXA had a higher total blood loss and postoperative hemoglobin drop (p<0.05) than IA TXA. However, single dose of IV TXA had a similar efficacy on total blood loss and postoperative hemoglobin drop (p>0.05) when compared with IA TXA[5].

Intra-articular application of TXA has been investigated by many authors in recent years. As the drugs are applied predominantly to the joint cavity, the site of bleeding could achieve a higher therapeutic concentration. This could effectively limit blood loss with little or no systemic absorption or subsequent systemic side effects. Additionally, TXA is easy to administer in this way. Giving intra-articular TXA during TKR has only started to gain popularity in recent years. It can be given as a topical wash or into the knee joint after wound closure via the drain. Compared to intravenous administration, advocates of intra-articular TXA believe the benefits include ease of administration, ability to achieve maximum concentration at the bleeding site and minimal systemic absorption. Furthermore, the use of tourniquet in TKR results in negligible intra-operative blood loss but notable postoperative blood loss, which is the ideal scenario for using intra-articular haemostatic agents intra-operatively.

CONCLUSION

Mean fall in post-operative hemoglobin level after intra-articular transamine is less as compared to intravenous transamine in total knee arthroplasty. Therefore intra articular route should be

preferred for this purpose and screening of blood indices should be performed routinely on those who have been given intravenous transamine.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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