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Tranexamic Acid Intravenous Overdose Administration in Primary Total Knee Arthroplasty: Case Report

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ABSTRACT

Background: Topical application of tranexamic acid (TXA) to bleeding wound surfaces reduces blood loss in patients undergoing some major surgeries, without systemic complications. TXA decreases blood loss and, therefore, may minimize pain.

Objective: To know the efficacy and safety of tranexamic acid intravenous overdose administration in primary total knee arthroplasty.

Case study: We reported a 53 years old Saudi female ambulatory with no assisting aid and was not known to have any medical illnesses, presented to the orthopedic clinic complaining of bilateral knee pain and difficulty to ambulate for long distances for the last 5 years. This complain gradually worsened since last 2 years with no history of trauma prior to presentation or even after the follow up. The pain was localized at the knee joints and it was sharp in nature. The pain used to improve with rest and paracetamol intake and aggravated while standing or walking for long period of time. She was treated surgically by total knee arthroplasty, however during the operation by mistake she was given 4000 mg of tranexamic acid through IV route instead of topical application.

Conclusion: Administration of 4000 mg of tranexamic acid through IV route is unusual but it seems to be safe without side effect on the patient in the early postoperative period.

Keywords: Intravenous overdose administration, Total knee arthroplasty, Tranexamic acid

INTRODUCTION

Tranexamic acid (TXA) is a synthetic lysine derivative that exerts its action by competitively occupying the lysine binding site of plasminogen, thereby blocking interaction with fibrin and subsequent clot breakdown. TXA has a molecular weight of 157.2 g/mol, and its injectable formulation is marketed under the name cyklokapron [(1)].

The pharmacokinetics of TXA in healthy individuals after administration of a 10 mg/kg dose demonstrate peak concentrations at 60 minutes post administration, with a half-life of approximately 2 hours for the terminal elimination phase, and 90% excretion at 24 hours. An antifibrinolytic dose remains in tissues for up to 17 hours and in serum for up to eight hours. It has also been shown to cross the placental barrier, is excreted in breast milk, and rapidly appears in synovial fluid. The overdose complications of TXA administration is mainly having seizure. The mechanisms of seizure are still poorly understood. Other side effects are nausea and vomiting, blurred or loss of vision [(2)].

Several meta-analyses have shown that interventions administration of the antifibrinolytic agent tranexamic acid reduced postoperative bleeding and the need for transfusion.

However, concerns about the safety of systemic administration of tranexamic acid and the risk of thromboembolic events such as deep vein thrombosis or pulmonary embolism in this high-risk patient population have hindered the wide adoption of this medication in the sitting of total knee arthroplasty [(3, 4)].

In view of these safety concerns, topical application of the tranexamic acid to the knee joint before closure of total knee arthroplasty remains a safer route of administration that reduces postoperative bleeding without increasing the hypercoagulable state associated with total knee arthroplasty. In fact, topical application of tranexamic acid in the surgical filed is a cost-effective and simple route of administration that has been shown to reduce bleeding associated with dental cardiac and spine procedures [(5)].

This case report aimed to know the efficacy and safety of tranexamic acid intravenous overdose administration in primary total knee arthroplasty.

CASE STUDY

We reported a 53 years old Saudi female, ambulatory with no assisting aid and was not known to have any medical illnesses, presented to the Orthopedic Clinic at King Faisal Hospital complaining of bilateral knee pain and difficulty to ambulate for long distances for the last 5 years. This complain started to worsen since last 2 years with no history of trauma prior to presentation or even after the follow up. The pain was localized at the knee joints and was sharp in nature. The pain used to improve with rest and paracetamol intake. There were no other complaints.

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No constitutional symptoms no history of fever, loss of weight, loss of appetite, no night pain or sweating.

Past medical and surgical histories were unremarkable.

No chronic medication except the paracetamol consumption for knee pain.

Not known to have allergy.

Personal history:

- She was housewife not working with average income.
- Not smoker or alcoholic.
- No history of animal contact.

Physical examination:

- Patient was conscious, alert and oriented, vitally stable and afebrile.
- No gait abnormality.

For lower extremities examination:

- Normal limb alignment no deformities, skin integrity intact, no scars, no signs of inflammation such as swelling, discoloration over the joints particularly the knees.
- Tenderness over the bilateral knee joint line with normal temperature, stable knee in both varus and valgus stress tests.
- Full range of motion of the joints specially the knees with no limitations.
- Distal pulses were palpable with average volume and normal character.
- All dermatomes and myotomes were intact with power 5 out of 5.
- Bilateral standing knee view and anteroposterior and lateral views X-rays were ordered and revealed bilateral osteoarthritis grade 2-3.
- Laboratory investigations were all within normal limits.

Patient was diagnosed with bilateral knee osteoarthritis. Before the symptoms increased patient was advised to reduce her weight and start to have physiotherapy sessions and pain medications. Then she came back seeking for surgery because the pain was not tolerable anymore. It was more in the left than the right knee. Patient had full explanation about the plan of management for the knee osteoarthritis. She fully understood that she would have total knee arthroplasty surgery and she agreed to undergo the procedure.

Course of Hospitalization:

- Patient was admitted through the outpatient clinic to the female surgical ward for preparation and medical optimization.
- Anesthesia consultation.
- Insertion of the urinary catheter before going to the operating room (OR) with ciprofloxacin 400 mg IV before indwelling the catheter then 200 mg every 12 hours till discontinued.
- Cefazolin 2 g IV antibiotic on call to OR
- Tranexamic acid 4000 mg, divided into 1000 mg IV 30 minutes before the tourniquet inflation and the remaining 3000 mg intra-articular 3 minutes before closure as recommended in the literature.
- Laboratory investigations were repeated and were all within normal limits with hemoglobin level 13.2 mg/dl.
- Chest X-ray was unremarkable.

Operation Theater:

Patient was received in holding area, sign in was done by anesthesiologist, the patient was shifted to operation room then transferred to the radiolucent table. Under general anesthesia tourniquet was applied, skin preparation and draping was done after positioning. Before the tourniquet inflation and incision made, the anesthesiologist gave the prophylactic antibiotic and tranexamic acid 4000 mg IV bolus to the patient. Skin incision was made through medial parapatellar approach for the left knee. After the total knee arthroplasty procedure had been done and before the closure, we asked for the 3000 mg of tranexamic acid for topical application intra-articular but it has been already given by the anesthesiologist by mistake through IV route. Wound closure was done then the patient was shifted to recovery and she was vitally stable and after that she was shifted to regular ward.

We consulted medical specialists and they advise to apply pneumatic compression device in addition to therapeutic enoxaparin dose of 80 mg subcutaneous daily for the first 2 days postoperatively plus close monitoring of the vital signs every 2 hours and encouraging mobilization out of bed as soon as the patient could.

Postoperative laboratory investigations were all within normal limits including the coagulation profile.

Chest X-ray was unremarkable and normal.

Postoperatively the patient was fully conscious and oriented, vitally stable with oxygen saturation maintained above 95% on room air, no GIT symptoms, no neurological symptoms, no respiratory symptoms and she was able to ambulate out of bed on a walker.

Patient was discharged home on medications and followed up in the clinic and she was happy and totally satisfied with no new complaint or active issue.

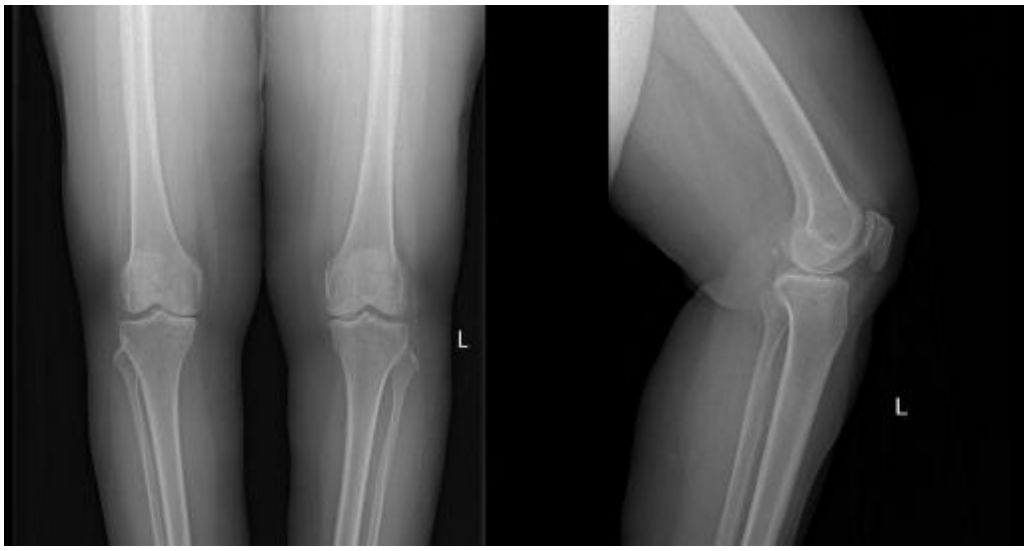

Figure (1): Preoperative left knee X-ray.

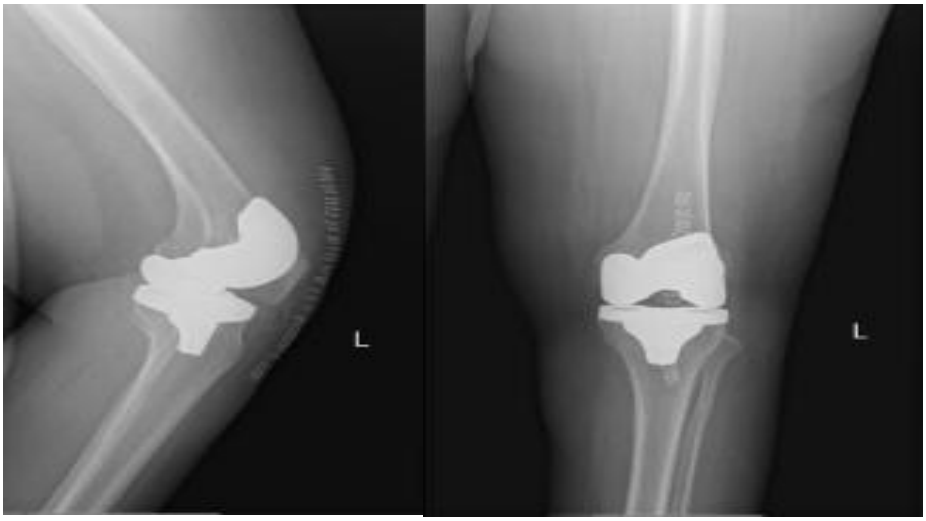

Figure (2): Postoperative left knee X-rays.

Declaration of patient consent:

An approval of the study was obtained from King Faisal Hospital, Mecca (Saudi Arabia) Academic and Ethical Committee. The patient and her relative were informed that the case would be published as case report and this was accepted. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

DISCUSSION

Administration of tranexamic acid (TXA) perioperatively is a well-recognized strategy used by orthopedic surgeons to reduce blood loss during total knee arthroplasty (TKA) [(6)]. Total knee arthroplasty (TKA) is an excellent surgical procedure for patients with painful arthritic knees. However, TKA has some potential unresolved problems, including blood loss, pain after operation and leg swelling. Resolution of these problems would increase patient satisfaction and serve to raise the overall quality of TKA [(7)].

Good *et al.* [(8)] reported that the administration of TXA intravenously decreased external blood loss but not hidden blood loss after TKA. The application of TXA in orthopedic surgery has been well established in the literature [(8-10)]. **Camarasa *et al.*** [(9)] reported that 10 mg/kg TXA used before the tourniquet was deflated and 3 hours later in unilateral TKA could lower the total blood loss from 1784 mL to 1099 mL and reduce the transfusion rate from 38.3% to 7.5%.

Good *et al.* [(8)]**, Camarasa *et al.*** [(9)] **and Yang *et al.*** [(10)] also reported that TXA could decrease drainage volume by about 50% to 385 mL. In our study, we used dose of tranexamic acid 4000 mg that should be divided into 1000 mg IV 30 minutes before the tourniquet inflation and the remaining 3000 mg intra-articular 3 minutes before closure but the anesthesiologist gave the whole 4000 mg wrongly through IV route of administration, which was not the plan and unusual but we observed that it seems to be safe and no serious effect on the patient in the early postoperative period as well as similar reduced total blood loss, transfusion rate, no drains used and postoperative laboratory were all within normal limits

including the coagulation profile. More studies have focused on the topical application of TXA in the TKA and the results are promising [11, 12]. Compared with the TXA in TKA, topical TXA was considered to be of less systemic absorption and better local effect.

Ishida *et al.* [13] found topical TXA could reduce not only blood loss but also knee joint swelling. After further analysis, they attributed the reduced knee joint swelling to the diminished hidden blood loss in the joint, this was in agreement with our case.

CONCLUSION

Administration of 4000 mg of tranexamic acid through IV route is unusual but it seems to be safe and without side effect on the patient in the early postoperative period.

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