

THROMBOPROPHYLAXIS IN PATIENTS WITH EPIDURAL ANALGESIA AFTER HIP OR KNEE ARTHROPLASTY

Ahmed Zafar, Umair Abu Bakar Siddiq, Hafeez Ur Rehman, Abu Bakar Siddiq, GA Shah

Doctors Hospital & Medical Centre Lahore Pakistan

ABSTRACT

Objective: To propose a management plan for prevention of enoxaparin-induced epidural hematoma in patients with indwelling epidural catheters

Study Design: Cross sectional study.

Place and Duration of Study: Department of Orthopaedics and Spine, Doctors Hospital & Medical Centre, Lahore, Pakistan, from Jan to Dec 2016.

Material and Methods: Sixty-eight patients undergoing hip or knee arthroplasty met our inclusion criteria. All patients received postoperative epidural analgesia and concomitant thromboprophylaxis with enoxaparin. Epidural was placed/removed 24 hours after the last dose of enoxaparin. Subsequent dose of enoxaparin was given 8 hours after removal of catheter. Patients were monitored for development of neurologic deficit according to American Spinal Injury Association (ASIA) impairment scale (appendix) on daily basis until discharge. Thereafter, patients were examined at 2 weeks postoperatively.

Results: Of the Sixty-eight patients enrolled, 47 (69.1%) were females and 21 (30.8%) males. Hip arthroplasty was done in 25 (36.7%), unilateral knee arthroplasty in 32(47%) and bilateral knee arthroplasty in 11 (16.1%) patients. Maximum neurologic score was set at 102 which was satisfactorily achieved in all patients. No patient reported any new sensory or motor deficit after the index surgery.

Conclusion: Low-molecular-weight heparin (enoxaparin) is safe for use in conjunction with indwelling epidural catheter if appropriate interval is provided for catheter insertion and removal.

Keywords: Arthroplasty, Enoxaparin, Epidural hematoma, Neurologic deficit, Thromboprophylaxis.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Major orthopedic surgery such as elective hip or knee arthroplasty carries the highest risk of postoperative deep vein thrombosis (DVT) and can lead to fatal pulmonary embolism (PE)¹. The incidence of DVT without thromboprophylaxis in such surgeries has been reported to be as high as 40-60%²; The risk of fatal PE being 0.5-2.0%^{1,3}. In a study by Dismuke⁴, It was highlighted that fatal PE may be the first manifestation of DVT. Hospitalized patients often tend to have asymptomatic DVT and non-invasive tests, such as ultrasonography, have limited sensitivity in the detection of calf-vein thrombosis⁵. With these considerations in mind, the most effective strategy devised over time is to consider some form of thromboprophylaxis in all patients

undergoing major orthopedic surgery. Various mechanical and pharmacological modalities have been described in literature for prevention of DVT and subsequent PE⁶. Incidence of DVT and subsequent PE following hip or knee arthroplasty has dramatically decreased after implementation of the clinical practice guidelines recommended by American Academy of Orthopaedic Surgeons (AAOS) which stratifies at-risk patients and suggests single or combination of modalities for prevention of DVT⁷.

Fear of postoperative pain, complications after surgery and prolonged recovery are some of the reasons why total joint arthroplasty is still not in vogue despite surgeons having better experience and increased level of surgical skills⁸. Various trials have, however, made it possible to devise multiple pain control programs which have effectively been incorporated into the management protocols of every healthcare setup

Correspondence: Dr Ahmed Zafar, Doctors Hospital Johar Town Lahore Pakistan (Email: doc.abuyahya@gmail.com)

Received: 10 Jan 2018; revised received: 22 Jan 2018; accepted: 23 Jan 2018

across the globe. Multimodal analgesia which includes combination of opioids, nonsteroidal anti-inflammatory drugs (NSAIDs) and bupivacaine have proven to be a breakthrough in pain management⁹. Preemptive analgesia given preoperatively, intraoperative nerve blocks and postoperative epidural infusion of local anesthetic have revolutionized pain management⁸. Epidural analgesia remains the mainstay of pain management during the postoperative period. Patients receiving epidural analgesia report lower pain scores on visual analog scale at rest as well as after mobilization out of bed when compared to those who receive systemic analgesia¹⁰. Although proportional reduction in mortality is not clear but epidural has shown to reduce postoperative cardiopulmonary and other complications and is associated with less sedation as compared to systemic analgesia¹¹.

Spinal epidural hematoma leading to neurologic deficit is reported to be a dreaded complication of enoxaparin use in patients with indwelling epidural catheters¹² which precludes its use¹³. We have devised a protocol for postoperative use of enoxaparin with concomitant use of epidural analgesia that can safely be incorporated into the current management protocols.

PATIENTS AND METHODS

This cross-sectional study was conducted at Doctors Hospital & Medical Centre, Lahore. Ethical approval was sought from the institutional review board prior to starting the study. Duration of the study was from January 2016 to December 2016. Sample size of sixty eight patients calculated with 95% confidence interval and 10% margin of error, assuming 80% of patients with indwelling epidural catheters and concomitant enoxaparin will be prevented from an epidural hematoma. Patients were selected through a non-probability / consecutive sampling technique. After seeking informed written consent, patients undergoing primary total hip arthroplasty (THA) or total knee arthroplasty (TKA) indicated for advanced degenerative arthritis were included in the study whereas those

with acute fracture or posttraumatic arthritis were excluded. Patients admitted for revision arthroplasty and those for arthroplasty of joints other than hip or knee were also excluded from the study. Epidural catheter was inserted in all patients at the time of induction of anesthesia. Catheter placement, infusion of bupivacaine through the catheter, monitoring of normal catheter function and its removal were all managed by the team of anesthesiologists. Surgeons were involved in monitoring pain scores and complication of epidural infusion, if any. Enoxaparin was started 24 hours after the index surgery in prophylactic dosage of 40mg subcutaneous once a day. On 3rd postoperative day enoxaparin was skipped and epidural catheter was removed. This provided for a safe interval of 24 hours before catheter removal. Subsequent dose of enoxaparin was given 8 hours later in the same dosage as before and was continued for a total of 14 days post-operatively. Patients were evaluated clinically for development of neurologic deficit according to ASIA impairment scale for lower extremities. Sensory score was maintained as actually described in ASIA scale, with maximum of 4 points for each dermatome in each extremity. Motor power was however elicited only up to grade 3/5 since patients experienced acute exacerbation of pain on movement against resistance during the initial postoperative period. This provided for maximum sensory score of 36 points and maximum motor score of 15 points in each limb. Urinary catheter was removed on 3rd postoperative day to ensure retention does not occur. Although compression ultrasonography has been reported to have limited sensitivity, we still consider it in every patient before discharge since calf thrombi have also been implicated in causing pulmonary emboli in addition to pelvic thrombi. Patients were discharged on 4th postoperative day and were again examined for neurologic deficit 2 weeks after the index surgery. Data was analyzed using IBM SPSS Statistics 20. Frequency and percentages were calculated for type of surgical intervention and neurological

deficit at the end of treatment. Chi-square test was used to assess the statistical significance with $p < 0.05$ as statistically significant.

RESULTS

Sixty-eight patients fulfilling our inclusion criteria were enrolled in the study from January to December 2016. They included 47 (69.1%) females and 21 (30.8%) males. Age varied from 23 to 82 years with mean of 56.96 ± 12.58 years. Comorbidities were present in all patients but were optimized by respective specialties before patient admission and only after documented approval by the medical specialists, were patients admitted for surgery. Hip arthroplasty was done in 25 (36.7%), unilateral knee arthroplasty in 32 (47%) and bilateral knee arthroplasty in 11

and warfarin have been suggested for use as evidenced in the recommendations by *Johanson et al*¹⁸. Subcutaneous LMWH or enoxaparin has been the standard prophylactic in patients undergoing arthroplasty^{2,16}. It is modestly superior to unfractionated heparin in preventing recurrent DVT and has also proven to be cost-effective¹⁹. Sindali and colleagues in a study comparing enoxaparin with oral factor Xa inhibitor rivaroxaban demonstrated that rivaroxaban had more hemorrhagic wound complications than enoxaparin²⁰. Similarly one of the authors of Regulation of Coagulation in Orthopedic surgery to prevent Deep vein thrombosis and pulmonary embolism (RECORD4) trials did not recommend rivaroxaban to his patients on the

Table: Distribution of cases.

Distribution of cases Procedure	Gender		Total
	Males	Females	
Total Hip Replacement	14	11	25
Unilateral Total Knee Replacement	7	25	32
Bilateral Total Knee Replacement	1	10	11
Total	22	46	68
n=68; $X^2=10.712$; $p=0.005$			

(16.1%) patients (table). Key sensory and motor points on lower limbs (L1 to S4-5) as depicted in ASIA impairment scale were checked. Sensory score was documented to be 36 out of 36 in each limb, and motor power 15 out of 15 in each limb in all patients. None of the patients reported to have any new sensory or motor deficit after the index admission.

DISCUSSION

Epidural analgesia remains the mainstay of postoperative care after total hip or knee arthroplasty. It carries the benefit of effective pain management leading to early patient mobilization and better rehabilitation¹⁴. Another added benefit of epidural analgesia has been reduction in blood loss during surgery¹⁵. Pharmacological thromboprophylaxis is equally important in these patients^{16,17} and various agents including Aspirin, low-molecular-weight heparin (LMWH), synthetic pentasaccharides

basis of increased bleeding events²¹. Based on this evidence we have inferred that rivaroxaban may be more likely to cause epidural hematoma than enoxaparin. We have therefore, not opted for the new oral drug and still reside with our rationale for administering enoxaparin through subcutaneous route. Apixaban, recently marketed oral Factor Xa inhibitor, has although shown superior results as compared to enoxaparin²², but we have no experience with this drug. American College of Chest Physicians (ACCP) in their 7th conference on antithrombotic and thrombolytic therapy recommended enoxaparin to be given after hip or knee arthroplasty for at least 10 days^{17,23}.

Epidural hematoma leading to disastrous neurologic deficit¹³ has been implicated to be a major risk factor associated with all these preparations of chemical thromboprophylaxis²⁴, when used concomitantly with epidural analgesia. Rosero and Joshi in their nationwide study on

complications of epidural analgesia showed an incidence of epidural hematoma to be 18.5 per 100,000 cases²⁴. Protocol for prevention of epidural hematoma as suggested in the guidelines set forth by The New York School of Regional Anesthesia (NYSORA)²⁵ recommends that catheter placement or removal should be performed at least 12 hours after the last prophylactic dose of enoxaparin and subsequent dose be administered at least 2 hours after the catheter is removed. American Society of Regional Anesthesia and Pain Medicine (ASRA) practice advisory published by *Horlocker et al*, recommends the first dose of enoxaparin to be administered not earlier than 24 hours postoperatively, and subsequent dose after epidural removal to be administered at least 2 hours later²⁶. Another important point of note made by the authors is that twice-daily dosing is associated with an increased risk of spinal hematoma and once-daily dosing has shown to be safe, provided no other hemostasis-altering medication is administered²⁶. Complications have still been documented which may be largely due to noncompliance with the recommended protocols. McEvoy reported 52% noncompliance rate by healthcare providers in the administration of enoxaparin as compared with the published protocols²⁷.

We follow the guidelines recommended by ASRA²⁶ rather than those published by NYSORA²⁵ since it provides additional caution of catheter placement/removal 24 hours after the last dose of enoxaparin and subsequent dose is given after 8 hours instead of 2 hours. Thereafter, it is continued once daily for a total of 14 days postoperatively.

There are few shortcomings in our study. The technique of catheterization is not elaborated upon and we have not discussed individual efficacy of the two modalities of patient care, rather we have only documented their compatibility. The results however depict that when both used according to recommendations^{17,25,26}, complications generally do not arise. We suggest long term trials with a bigger

sample size to verify the safety of our proposed strategy. Even more studies are required to devise management of hematoma if one occurs. Moreover, incidence of epidural hematoma in patients taking oral rivaroxaban needs to be determined. Future concerns would raise question on efficacy of apixaban which has a long list of already documented drug interactions and major drawback being increased risk of thrombotic events following abrupt discontinuation.

CONCLUSION

Low-molecular-weight heparin (enoxaparin) is safe for use in conjunction with indwelling epidural catheter if appropriate interval is provided for catheter insertion and removal.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by author.

REFERENCES

- O'donnell M, Weitz JI. Thromboprophylaxis in surgical patients. *Can J Surg* 2003; 46(2): 129.
- Sasaki H, Ishida K, Shibanuma N, Tei K, Tateishi H, Toda A, et al. Retrospective comparison of three thromboprophylaxis agents, edoxaban, fondaparinux, and enoxaparin, for preventing venous thromboembolism in total knee arthroplasty. *Inter-national orthopaedics* 2014; 38(3): 525-9.
- Bergqvist D, Benoni G, Björgell O, Fredin H, Hedlundh U, Nicolas S, et al. Low-molecular-weight heparin (enoxaparin) as prophylaxis against venous thromboembolism after total hip replacement. *N Engl J Med* 1996; 335(10): 696-700.
- Dismuke SE, Wagner EH. Pulmonary embolism as a cause of death: the changing mortality in hospitalized patients. *JAMA* 1986; 255(15): 2039-42.
- Tovey C, Wyatt S. Diagnosis, investigation, and management of deep vein thrombosis. *BMJ* 2003; 326(7400): 1180.
- Falck-Ytter Y, Francis CW, Johanson NA, Curley C, Dahl OE, Schulman S, et al. Prevention of VTE in orthopedic surgery patients: Antithrombotic therapy and prevention of thrombosis: American College of Chest Physicians evidence-based clinical practice guidelines. *CHEST J* 2012; 141(Suppl-2): e278S-325S.
- Mont MA, Jacobs JJ. AAOS clinical practice guideline: preventing venous thromboembolic disease in patients undergoing elective hip and knee arthroplasty. *J Am Acad Orthop Surg* 2011; 19(12): 777-8.
- Ranawat AS, Ranawat CS. Pain management and accelerated rehabilitation for total hip and total knee arthroplasty. *J Arthroplasty* 2007; 22(7): 12-5.
- Skinner HB. Multimodal acute pain management. *Am J Orthop (Belle Mead NJ)* 2004; 33(Suppl-5): 5-9.
- Choi P, Bhandari M, Scott J, Douketis JD. Epidural analgesia for pain relief following hip or knee replacement. *Cochrane Data-base Syst Rev* 2003; 3: CD003071.
- Rodgers A, Walker N, Schug S, McKee A, Kehlet H, Van Zundert A, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. *BMJ* 2000; 321(7275): 1493.

12. Meikle J, Bird S, Nightingale JJ, White N. Detection and management of epidural haematomas related to anaesthesia in the UK: A national survey of current practice. *Br J Anaesth* 2008; 101(3): 400-4.
 13. Han IS, Chung EY, Hahn YJ. Spinal epidural hematoma after epidural anesthesia in a patient receiving enoxaparin-A case report. *Korean J Anesthesiol* 2010; 59(2): 119-22.
 14. Tetsunaga T, Sato T, Shiota N, Tetsunaga T, Yoshida M, Okazaki Y, et al. Comparison of continuous epidural analgesia, patient-controlled analgesia with morphine, and continuous three-in-one femoral nerve block on postoperative outcomes after total hip arthroplasty. *Clin Orthop Surg* 2015 ; 7(2): 164-70.
 15. Moraca RJ, Sheldon DG, Thirlby RC. The role of epidural anesthesia and analgesia in surgical practice. *Ann Surg* 2003; 238(5): 663.
 16. Zanasi S. Innovations in total knee replacement: new trends in operative treatment and changes in peri-operative management. *Eur J Orthop Surg Traumatol* 2011; 2(1-2): 21-31.
 17. Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwell CW, et al. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *CHEST J* 2004; 126(Suppl-3): 338S-400S.
 18. Johanson NA, Lachiewicz PF, Lieberman JR, Lotke PA, Parvizi J, Pellegrini V, et al. Prevention of symptomatic pulmonary embolism in patients undergoing total hip or knee arthroplasty. *J Am Acad Orthop Surg* 2009; 17(3): 183-96.
 19. Segal JB, Streiff MB, Hofmann LV, Thornton K, Bass EB. Management of venous thromboembolism: A systematic review for a practice guideline. *Ann Intern Med* 2007; 146(3): 211-22.
 20. Sindali K, Rose B, Soueid H, Jeer P, Saran D, Shrivastava R. Elective hip and knee arthroplasty and the effect of rivaroxaban and enoxaparin thromboprophylaxis on wound healing. *Eur J Orthop Surg Traumatol* 2013; 23(4): 481-6.
 21. Turpie AG, Lassen MR, Davidson BL, Bauer KA, Gent M, Kwong LM, et al. Rivaroxaban versus enoxaparin for thrombo-prophylaxis after total knee arthroplasty (RECORD4): A randomised trial. *Lancet* 2009; 373(9676): 1673-80.
 22. Lassen MR, Gallus A, Raskob GE, Pineo G, Chen D, Ramirez LM. Apixaban versus enoxaparin for thromboprophylaxis after hip replacement. *N Eng J Med* 2010; 363(26): 2487-98.
 23. Yen SH, Lin PC, Kuo FC, Wang JW. Thromboprophylaxis after minimally invasive total knee arthroplasty: A comparison of rivaroxaban and enoxaparin. *Biomedical J* 2014; 37(4): 199.
 24. Rosero EB, Joshi GP. Nationwide incidence of serious complications of epidural analgesia in the United States. *Acta Anaesthesiol Scand* 2016; 60(6): 810-20.
 25. Tripković B. Anesthesia for hip replacement surgery. *Med Glas* 2012; 9(1): 143-51.
 26. Horlocker TT, Wedel DJ, Rowlingson JC, Enneking FK, Kopp SL, Benzon HT, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines. *Reg Anesth Pain Med* 2010; 35(1): 64-101.
 27. McEvoy MD, Bailey M, Taylor D, Del Schutte H. Noncompliance in the inpatient administration of enoxaparin in conjunction with epidural or spinal anesthesia. *J arthroplasty* 2000; 15(5): 604-7.
-