Inpatient Enoxaparin, outpatient Aspirin following primary hip and knee arthroplasty

Abstract:

Our institution has employed a thromboprophylaxis regimen using inpatient enoxaparin and outpatient aspirin for patients at standard risk for venous thrombosis following hip and knee arthroplasty. We reviewed 500 cases. Inpatient treatment with enoxaparin averaged 2.75 days, followed by a 28 day course of aspirin. The overall thrombosis rate was 0.6 % (1 deep venous thrombosis and 2 pulmonary emboli). Bleeding requiring more than 3 units of transfusion was 1.8%. 15 (3%) infections were noted, 14 superficial and 1 deep. This compared favorably to a control group utilizing a 14 day course of enoxaparin. We believe that a brief course of inpatient enoxaparin and outpatient aspirin is a safe and effective form of thromboprophylaxis. (113 words)

Introduction:

Thromboembolic disease is a well recognized complication following hip and knee arthroplasty. There is near universal agreement regarding the need for perioperative thromboprophylaxis1. The optimal regimen would be safe, effective, and inexpensive 2. Such a regimen has been elusive. Modern hip and knee replacement protocols emphasize early mobilization and mechanical compression devices. These methods alone have proven safe and beneficial 3, 4. The major controversy remains chemoprophylaxis. Conflicting recommendations from the American College of Chest Physicians (ACCP) 5 and the American Academy of Orthopedic Surgeons (AAOS) 6 have added to this dilemma. Pay for performance and medical liability must also be factored in to the decision making for the practicing joint replacement surgeon7, 8, 9.

Enoxaparin is a parenteral low molecular weight heparin. It has demonstrated efficacy in preventing deep venous thrombosis in numerous clinical trials 9, 10, 11. It is recommended by both the AAOS and ACCP 5, 6 for chemical thromboprophylaxis following hip and knee arthroplasty. Safety concerns regarding bleeding and wound complications do exist 12, 13.  The exact duration of treatment is also controversial 10, 11. The increased cost especially with extended treatment regimens10 must be recognized.

Aspirin (acetylsalicylic acid) has been advocated by multiple authors and is included in the AAOS guidelines 6, 14, 15. Aspirin has shown benefit in preventing pulmonary emboli16 and is believed to be the safest and least expensive regimen1. It is not recommended by the ACCP secondary to concerns regarding efficacy in preventing deep venous thrombosis5. Historical data certainly raise concern regarding aspirin following hip and knee arthroplasty17, 18. More recent studies combining aspirin with modern techniques and multimodal thromboprophylaxis protocols have shown very low rates of thromboembolic disease19, 20.

At our institution, we have been using inpatient enoxaparin and outpatient aspirin following hip and knee arthroplasty for our patients at standard risk for venous thrombosis. This regimen incorporates recommendations from both the ACCP 5 and the AAOS 6. It allows the hospital to comply with Medicare and regulatory guidelines21, and is relatively easy to administer. The main point of contention with an inpatient only enoxaparin regimen is duration of treatment especially with decreasing lengths of stay22. Our hypothesis is that inpatient enoxaparin followed by a 28 day course of aspirin is a safe and effective means of chemical thromboprophylaxis.

Materials and Methods:

We performed a retrospective review of all primary hip and knee arthroplasties performed at our institution between January 2009 and February 2010. 500 primary hip and knee arthroplasties in 472 patients were selected. Exclusion criteria included prior history of thromboembolic disease, current treatment with warfarin, current diagnosis of malignancy, and history of bleeding disorder or major bleeding episodes defined as intracranial bleed, or gastrointestinal bleed requiring transfusion. All surgeries were performed by 2 experienced arthroplasty surgeons at a dedicated orthopedic hospital. Patient demographics are included in table 1. Average age was 62.9, body mass index (BMI) 29.0, American Society of Anesthesiologists (ASA) grade 2.418. There were 247 hip and 253 knee arthroplasties.

All hip and knee replacements were performed under general anesthesia. Knee replacement patients were also given femoral and sciatic nerve blocks. Mechanical compression devices were utilized in all patients. Physical therapy was begun the day of surgery or on postoperative day one for afternoon operations. Enoxaparin was begun on postoperative day one and renally dosed. For a creatinine of less than 1.5, enoxaparin dosing was 30 mg twice daily for knee arthroplasty and 40 mg once daily for hip arthroplasty. For a creatinine of greater than 1.5, enoxaparin dosing was 30 mg daily for both hip and knee arthroplasty. Upon discharge from the hospital, patients were prescribed enteric coated aspirin 325 mg twice daily for 28 days. Routine follow up care was performed at 6 weeks, and 6 months. Investigations for deep venous thrombosis or pulmonary emboli were initiated only in symptomatic patients. Review of records for deep venous thrombosis, pulmonary emboli, acute blood loss, infection, and general complications was performed.

For comparison, a control group of 500 hip and knee arthroplasty cases was selected. This group received surgery by a different experienced surgeon at the same institution. The control group received enoxaparin for a total of 2 weeks postoperatively, and then aspirin 325 mg twice daily for an additional 2 weeks. Anesthesia, therapy, and general postoperative protocol were otherwise similar between the two groups. Demographic data are included in table 1.

Results:

For the study group, 500 cases in 472 patients were reviewed. There was one (0.2%) documented deep venous thrombosis and two (0.4%) pulmonary emboli. Seven additional patients were evaluated but had negative investigations for either DVT or PE but investigations were negative. 9 (0.18%) patients required 3 or more units of packed red blood cells (RBC), with 2 gastrointestinal bleeds, and 1 patient with newly diagnosed lymphoma who required 6 units of RBC and factors. There were 15 (3%) infections, 1 of which was deep requiring a 2 stage exchange. There were 14 superficial infections, one requiring a superficial irrigation and debridement. There were 5 other readmissions in the 3 month postoperative period (transient ischemic attacks, atypical chest pain, constipation / dehydration, Crohns exacerbation, and pancreatitis.) There were no deaths.

In the control group, 500 cases in 473 patients were reviewed. There were 4 (0.8%) deep venous thromboses and 2 (0.4%) pulmonary emboli. 14 (2.8%) patients required 3 or more units of RBC. There were 27 (5.4%) infections. Four were deep, 2 requiring an incision and drainage with polyethylene exchange, and 2 requiring a 2 stage exchange. 23 were superficial infections, one requiring a superficial incision and drainage. There were 7 readmissions in the 3 month postoperative period (bowel obstruction, nausea/dehydration, acute renal failure, congestive heart failure, transient ischemic attacks, and arrhythmia). There were no deaths.

For the study group, the average length of stay was 3.75 days (3.49 for hips and 4.00 for knees.) The average number of enoxaparin doses given was 4.26 (2.494 for hips, and 5.984 for knees.) Our institution’s unit price for enoxaparin was $28.91 per 40 mg dose, and $21.69 per 30 mg dose. The cost of 325 mg enteric coated aspirin was $ 0.226 per dose. Comparing our inpatient only enoxaparin group with a 2 week regimen, this corresponds to a total savings of $200,148.57 or $400.30/case. Savings for hip and knee arthroplasty were $327.59 and $ 471.28 per case respectively.

Discussion:

Thromboembolic disease is a well recognized phenomenon following hip and knee arthroplasty. The exact incidence of deep venous thrombosis and pulmonary emboli is controversial. Incidence rates of over 50% are reported without prophylaxis 1,5. With modern joint protocols utilizing early mobilization, mechanical compression devices, and improved anesthetic techniques, the incidence has dramatically decreased. . A recent review of 1179 cases by Dorr et al15 using a multimodal approach for thrombosis prevention reported a 0.25% rate of pulmonary emboli and 5.2% rate of deep venous thrombosis (only 0.4% which were clinically symptomatic.) Even protocols using no chemical prophylaxis have shown a thrombosis rate of less than 5%3,27.

Enoxaparin is a low molecular heparin (LMWH) which has rapid antithrombotic action, limited variability in its effects, and linear pharmacokinetics2. It is advocated by both the AAOS and ACCP for chemical thromboprophylaxis following hip and knee arthroplasty5,6. It is also approved by the SCIP and almost all oversight groups21. The efficacy of LMWH is well documented28,29,30,31. Concerns regarding safety do exist and attempts by some centers to adhere to the ACCP guidelines have met with increased bleeding and wound complications13,32,33,34. Also, the exact duration of treatment with enoxaparin is debatable. The AAOS recommends a 7-10 day course. The ACCP recommends a 28-35 day course. Extended dose treatment has been shown to significantly decrease the rate of venographically documented thomboembolism11,35. It is unclear whether this will result in any significant clinical improvements or cost savings36,37,38.

The advantages of aspirin especially in the outpatient setting are numerous. It is inexpensive and well tolerated with a low side effect profile. It has demonstrated efficacy especially when combined with a multimodal approach14,15,39. Aspirin is not recommended by the ACCP as the older literature has shown a high rate of thromboembolic disease with isolated use5,17,18.

A short course of aggressive inpatient only anticoagulation is not a new concept. The prior literature using such regimens has noted an average length of stay of 7-10 days40,41. As the length of stay has decreased considerably, protocols must adapt. In our study, the average length of stay was 3.75 days. As enoxaparin was initiated on postoperative day 1, the average length of treatment with enoxaparin was 2.75 days . This was followed by a 28 day course of enteric coated aspirin 325 mg. When combined with early mobilization and mechanical compression devices, our inpatient enoxaparin, outpatient aspiring regimen proved to be an effective means of thromboprophylaxis. Symptomatic deep venous thrombosis was noted in one patient (0.2%) and pulmonary emboli in 2 patients (0.4%). Complications associated with this regimen were low with 9 bleeding complications (requiring 3 or more units of RBC) and 15 infections only one of which was deep. Compared with a control group which utilized a 2 week course of enoxaparin, there was actually a lower rate of symptomatic thrombosis, bleeding, and infection. Using inpatient only enoxaparin resulted in cost savings of $200,148.157 for the 500 cases, or $400.30 per case, compared with a 14 day enoxaparin regimen.

This was a pilot study to review our thromboprophlaxis protocol. This is a retrospective review so criticisms associated with such a study design are present. The control group was with a different surgeon and there were minor demographic differences with the study group. No routine monitoring was employed for venous thrombosis and only symptomatic patients were evaluated for thromboembolic disease42. Strengths of this study are that it was unfunded, and the endpoints of symptomatic thromboses, infection, and bleeding represent the major concerns of the practicing joint replacement surgeon.

In summary, our protocol of inpatient enoxaparin and outpatient aspirin proved safe and effective in standard risk patients following hip and knee arthroplasty. When combined with mechanical compression devices and early mobilization, a low rate of symptomatic thromboembolic disease was noted. There were significant cost savings with a low complication rate and no deaths.

1. Markel DC, York S, Liston MJ, Flynn JC, Barnes CL, Davis CM, AAHKS Research Committee. Venous Thromboembolism. Management by American Association of Hip and Knee Surgeons. J Arthroplasty 2010;1:25.
2. Haas SB, Barrack RL, Westrich G, & Lachiewicz PF. Venous thromboembolic disease after total hip and knee arthroplasty. J Bone Joint Surg Am 2008:90A:2764.
3. Sugano N, Hidenobu M, et al. Clinical efficacy of mechanical thromboprophylaxis without anticoagulant drugs for elective hip surgery in an asian population. J Arthroplasty 2009;24(8):1254.
4. Lachiewicz PF, Kelley SS, Haden LR. Two mechanical devices for prophylaxis of thromboembolism after total knee arthroplasty. A prospective randomized study. J Bone Joint Surg Br 2004;86(8):1137.
5. Geerts WH, Bergqvist D, Pineo GF, et al. Prevention of thromboembolism: American College of Chest Physicians evidence-based clinical practice guidelines(8th edition). Chest 2008;133:381S.
6. Johanson NA, Lachiewicz PF, Lieberman JR, Lotke PA, Parvizi J, Pellegrini V, Stringer TA, Tornetta P, Haralson RH, Watters WC. Prevention of symptomatic pulmonary embolism in patients undergoing total hip or knee arthroplasty. JAAOS; 17:3.
7. Bhattacharyya T, Freibera AA, et al. Measuring the report card: The validity of pay-for-performance metrics in orthopedic surgery. Health Affairs 2009;28(2):526.
8. Upadhyay A, York S, et al. Medical malpractice in hip and knee arthroplasty. J Arthroplasty 2007:22(suppl 6):2.
9. Leclerc JR, Gent M, et al. The incidence of symptomatic venous thromboembolism during and after prophylaxis during and after prophylaxis with enoxaparin. Arch Intern Med 1998;158:873.
10. Skedgel C, Goeree R, et al. The cost-effectiveness of extended-duration antithrombotic prophylaxis after total hip arthroplasty. J Bone Joint Surg Am 2007;89A:819.
11. Comp PC, Spiro TE, et al. Prolonged enoxaparin therapy to prevent venous thromboembolism after primary hip or knee replacement. J Bone Joint Surg Am 2001:83A:336.
12. Stephen R, Burnett J, et al. Failure of the American College of Chest Physicians-1A protocol for lovenox in clinical outcomes for thromboembolic prophylaxis. J Arthroplasty 2007;22:317.
13. Sharrock NE, Della Valle AG, et al. Potent anticoagulants are associated with a higher all-cause mortality rate after hip and knee arthroplasty. Clin Orthop Relat Res 2008;466:714.
14. Bozic KJ, Vail TP, et al. Does aspirin have a role in venous thromboembolism prophylaxis in total knee arthroplasty patients? J Arthroplasty 2009;0:1.
15. Dorr, LD, Gendelman V, et al. Multimodal thromboprophylaxis for total hip and knee arthroplasty based on risk assessment. J Bone Joint Surg Am 2007;89:2648.
16. Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin. Pulmonary Embolism Prevention (PEP) trial. Lancet 2000;355:1295.
17. Harris WH, et al. Aspirin prophylaxis of venous thromboembolism after total hip replacement. N Eng J Med 1977;297:1246.
18. McKenna R, et al. Prevention of venous thromboembolism after total knee replacement by high dose aspirin or intermittent calf and thigh compression. Br Med J 1980;280:514.
19. Lotke PA, Lonner JH. The benefit of aspirin chemoprophylaxis for thromboembolism after total knee arthroplasty. Clin Orthop Relat Res 2006;452:175.
20. Lachiewicz PF, Solieau ES. Mechanical calf compression and aspirin prophylaxis for total knee arthroplasty. Clin Orthop Related Res 2007;464:61.
21. Bratzler DW. Development of national performance measures on the prevention and treatment of venous thromboembolism. J Thromb Thrombolysis 2010:29(2):148.
22. Yoon RS, Nellans KW, et al. Patient education before hip or knee arthroplasty lowers length of stay. J Arthroplasty 2010;25:547.
23. White RH, Romano PS, Zhou H, Rodrigo J, Bargar W. Incidence and time course of thromboembolic outcomes following total hip or knee arthroplasty. Arch Intern Med 1998;158:1525.
24. Gonzalez Della Valle G, Serota A et al. Venous thromboembolism is rare with a multimodal prophylaxis protocol after total hip arthroplasty. Clin Orthop Relat Res 2006;444:146.
25. Warwick D, Williams MH, Bannister GC. Death and thromboembolic disease after total hip replacement. A series of 1162 cases with no routine chemical prophylaxis. J Bone Joint Surg Am 1995;77:6.
26. Kim YH, Oh SH, Kim JS. Incidence and natural history of deep-vein thrombosis after total hip arthroplasty: A prospective and randomized clinical study. J Bone Joint Surg Br 2003;85:661.
27. Colwell CW, Froimson MI, Mont MA et al. Thrombosis prevention after total hip arthroplasty. A prospective, randomized trial comparing a mobile compression device with low molecular weight heparin. J Bone Joint Surg Am 2010;92:527.
28. Colwell CW, Spiro TE. Efficacy and safety of enoxaparin to prevent deep vein thrombosis after hip arthroplasty. Clin Orthop Relat Res 1995;319:219.
29. Fitzgerald RH, Spiro TE, Trowbridge AA, et al. Prevention of venous thromboembolic disease following primary total knee arthroplasty: A randomized multicenter, open label, parallel group comparison of enoxaparin and warfarin. J Bone Joint Surg Am. 2001;83:900.
30. Eikelboom JW, Karthikeyan G, Fagel N, Hirsh J. American Association of Orthopedic Surgeons and American College of Chest Physicians Guidelines for venous thromboembolism prevention in hip and knee arthroplasty differ. What are the implications for clinicians and patients?. Chest 2009;135:513.
31. Kwong LM, Happe LE, Horblyuk R, Farrelly E. Decreased venous thromboembolism with injectable vs oral anticoagulation after discharge for major orthopedic surgery. J Arthroplasty 2008;23:25.
32. Novicoff WM, Brown TE et al. Mandated venous thromboembolism prophylaxis. Possible Adverse Outcomes. J Arthroplasty 2008;23:15.
33. Neviaser AS, Chang C, et al. High incidence of complications from enoxaparin treatment after arthroplasty. Clin Orthop Relat Res 2010;468:115.
34. Patel VP, Walsh M, et al. Factors associated with prolonged wound drainage after primary total hip and knee arthroplasty. J Bone Joint Surg Am 2007;89:33.
35. Eikelboom JW, Quinlan DJ, Douketis JD. Extended-duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of the randomized trials. Lancet 2001;358:9.
36. McAndrew CM, Fitzgerald SJ, Kray MJ, Goldberg VM. Incidence of postthrombotic syndrome in patients undergoing primary total knee arthroplasty for osteoarthritis. Clin Orthop Relat Res 2010;268:178.
37. Jameson SS, Bottle A, et al. The impact of national guidelines for the prophylaxis of venous thromboembolism on the complications of arthroplasty of the lower limb. J Bone Joint Surg Br 2010;92:123.
38. Callaghan JJ, Warth LC, et al. Evaluation of deep venous thrombosis prophylaxis in low risk patients undergoing total knee arthroplasty. J Arthroplasty 2008;23:20.
39. Brown GA. Venous thromboembolism prophylaxis after major orthopaedic surgery. A pooled analysis of randomized controlled trials. J Arthroplasty 2009;24(suppl 6):77.
40. Larsen K, Hansen TB, et al. Cost-effectiveness of accelerated perioperative care and rehabilitation after total hip and knee arthroplasty. J Bone Joint Surg Am 2009;91:761.
41. Sarasin FP, Bounameaux H. Out of hospital antithrombotic prophylaxis after total hip replacement: low-molecular-weight heparin, warfarin, aspirin, or nothing. A cost effectiveness analysis. Thomb Haemost 2002;87:586.
42. Dhupar S, Iorio R, Healy WL, Dhimitri K. A comparison of discharge and two week duplex ultrasound screening protocols for deep venous thrombosis detection following total joint arthroplasty. J Bone Joint Surg Am 2006:88(11):2380.

Table 1. Patient Demographics

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| --- | --- | --- | --- |
|  | Study (enoxaparin/ aspirin) | Control (enoxaparin) | P value |
| Age | 62.9±11.9 | 59.8±13.4 | <0.001 |
| Gender | 323 F, 177 M | 312 F, 188 M | 0.47 |
| BMI | 29.00/29.03±5.25 | 29.78/29.77±5.47 | 0.03 |
| ASA | 2.42±0.60 | 2.49±0.61 | 0.05 |
| Hips | 247 | 280/278 | 0.05 |
| Knees | 253 | 220/222 | 0.05 |
| Length of Stay - days | 3.75±0.90 | 3.79±1.35 | 0.54 |
| Transfusion RBC | 0.39±0.83 | 0.57±0.96 | 0.001 |

Table 2. Results

|  |  |  |  |
| --- | --- | --- | --- |
|  | Study (enoxaparin / aspirin) | Control (enoxaparin) | P value |
|  |  |  |  |
| DVT | 1 (0.2%) | 7 (1.4%) | 0.03(Chisq)/0.07(Fisher Exact) |
| Pulmonary Embolus | 2 (0.4%) | 2 (0.4%) | 1.00 |
| Bleeding | 9 (1.8%) | 14 (2.8%) | 0.29(Chisq)/0.40(Fisher) |
| Deep infection | 1 (0.2%) | 4 (0.8%) | 0.18(Chisq)/0.37(Fisher) |
| Superficial Infection | 14 (2.8%) | 23 (4.6%) | 0.13(Chisq)/0.18(Fisher) |
| Other readmission | 5 (1.0%) | 7 (1.4%) | 0.56(Chisq)/0.77(Fisher) |
| Death | 0 | 0 | 1.00 |