Is there adequate provision of venous thrombo-embolism prophylaxis following hip arthroplasty? An audit and international survey

BA Rogers¹, S Phillips², J Foote³, KJ Drabu⁴

¹Adult Lower Extremity Reconstruction, Mount Sinai Hospital, Toronto, Canada

²Department of Emergency Medicine, East Surrey Hospital, Redhill, UK

³Department of Trauma and Orthopaedics, St George's Hospital, London, UK

⁴Department of Orthopaedic Surgery, East Surrey Hospital, Redhill, UK

ABSTRACT

INTRODUCTION The peak incidence of venous thrombo-embolism (VTE) occurs 3 weeks following hip arthroplasty surgery and current guidelines proposing VTE prophylaxis continuing for 4 weeks after surgery. This study first compares the duration of treatment and satisfaction between patients prescribed low molecular weight heparin (LMWH) and rivaroxaban, a new oral Factor Xa inhibitor, following elective hip arthroplasty; and second, surveys the duration of LMWH use in other units.

SUBJECTS AND METHODS An international survey detailing the use of LMWH was performed. A prospective audit was performed of 100 hip replacements, with 50 prescribed 40 mg once daily of subcutaneous enoxaparin and subsequently 50 patients prescribed 10 mg once daily of oral rivaroxaban. The duration of treatment, patient satisfaction and complications for both cohorts was quantified and compared against published evidence-based guidelines.

RESULTS The survey demonstrated that four out of 39 (10.2%) units that routinely prescribe LMWH do so for at least 4 weeks following surgery. The audit demonstrated that rivaroxaban afforded a superior mean duration of postoperative VTE prophylaxis (35 days vs 5.4 days; $P < 0.05$) and superior patient satisfaction. There was no difference in the incidence of bleeding, wound infection or thrombotic complications.

CONCLUSIONS This study demonstrates that patients are exposed to an increased VTE risk following hip replacement surgery due to the inadequate prescription of LMWH. This is poor clinical practice, contrary to current evidence-based guidelines and has potential medicolegal implications. The prescription of rivaroxaban affords a superior patient compliance compared with subcutaneous LMWH, thus ensuring that patients receive VTE prophylaxis for the current recommend period of time.

KEYWORDS

Rivaroxaban – Low molecular weight heparin – Thromboprophylaxis

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CORRESPONDENCE TO

Benedict A Rogers, E: benedictrogers@hotmail.com

Venous thrombo-embolism (VTE) prophylaxis following orthopaedic surgery remains a controversial topic and the incidence of fatal pulmonary embolism is approximately 0.4% if no measures are taken, equating to over 5000 fatalities a year for the 1.5 million hip and knee replacements performed in Europe.^{1–3} The 2009 National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report has highlighted that prophylaxis against VTE was less than ideal, with nearly 50% of surgical patients not receiving VTE precautions.⁴ Furthermore, the current President of The Royal College of Surgeons of England has urged surgeons to make the ‘prevention of VTE a clinical priority’.⁵

Recent studies investigating the incidence of postoperative VTE demonstrate that the mean time to thrombo-embolism is greater than previously estimated. Two large meta-analyses advocate VTE prophylaxis be continued for up to 4 weeks following total hip arthroplasty surgery (THA).^{6,7} The Global Orthopaedic Registry recently published that the mean duration to peak incidence of venous thrombo-embolism following THA to be 21.5 days.⁸ Concern now exists that the length of treatment varies depending upon the prophylaxis used.

Few pharmaceutical options exist for VTE prophylaxis and rivaroxaban (Xarelto®, Bayer), a new once-daily oral

Factor Xa inhibitor, is licensed in the UK for VTE prophylaxis following elective lower limb arthroplasty surgery.⁹ Published evidence has demonstrated the efficacy of rivaroxaban to be equal to LMWH.^{10,11} In the UK, LMWH is commonly used following lower limb arthroplasty, supported by the recommendations of the National Institute for Health and Clinical Excellence (NICE) that have been recently been updated to incorporate oral VTE prophylaxis, such as rivaroxaban and dabigatran (Pradaxa®, Boehringer Ingelheim).^{12–14} These guidelines advocate an extended period of VTE prophylaxis of 28–35 days following hip arthroplasty surgery.¹⁴

The rationale of this two-part study was to assess, using a local audit and international survey, the duration of VTE prophylaxis currently achieved with LMWH and to examine whether this may be improved with the use of rivaroxaban, an oral Factor Xa inhibitor.

Subjects and Methods

Local departmental approval had been granted for the prescription of rivaroxaban following hip arthroplasty surgery, in conjunction with the discussions with the anaesthetic and pharmacy departments. All surgical procedures were performed or directly supervised by the senior author (KJD).

Verbal and written consent was obtained for all patients and the inclusion criteria were all primary and revision hip arthroplasty surgery in patients with an American Society of Anesthesiologists (ASA) score of 1. The exclusion criteria for this study were; previous anticoagulation therapy, clotting or bleeding abnormalities, significant medical co-morbidities with an ASA score of 2 or more and patient withholding consent.

An initial retrospective survey of 56 consecutive patients who were prescribed 4 weeks of once daily dose of 40 mg of

enoxaparin (Clexane®, Sanofi-Aventis), a low molecular weight heparin (LMWH) administered subcutaneously. This was routine practice in our department for all patients following primary or revision hip arthroplasty surgery. For each patient, we documented the duration of prophylaxis received, the incidence of any notable complications and a simple patient satisfaction rating score from 1–5 (most dissatisfied, dissatisfied, ambivalent, satisfied, most satisfied).

Following assessment of the results from the initial survey, and in collaboration with the anaesthetic and pharmacy colleagues, a planned introduction of rivaroxaban was instigated, in accordance with the current evidence for extended VTE prophylaxis, to continue for 35 days following THA surgery.

The prospective portion of this audit commenced immediately following the analysis of the initial survey and there was no other change in patient management. An initial consecutive cohort of 54 patients were prescribed a once daily oral dose of 40 mg rivaroxaban, commenced within 24-h of surgery. Patients received a standard rivaroxaban information sheet prior to surgery and had the opportunity to ask questions when pre-operative consent was obtained.

A local and international survey of 50 English-speaking orthopaedic units regarding current VTE prophylaxis practice following THA surgery was performed by both post and telephone, with a proforma utilised for standardisation. Responses were obtained from 43 units, a response rate of 86%. The local survey included district general and teaching hospitals from all UK regions, with the international survey was limited to large university departments in Australia and Canada.

This was an unsponsored study and we confirm there was no conflict of interest and no financial support has been received in relation to this research. Statistical analysis was carried out using SPSS v11.0.

Results

There was no statistical difference in the demographics or the numbers of primary and revision hip arthroplasty surgery performed for each cohort, as shown in Table 1.

The initial retrospective survey of 56 patients prescribed LMWH, the mean duration of treatment of 5.4 days (range, 2–16 days). Further, only 39 out of these 56 patients (69%) received LMWH every day whilst an in-patient. The mean patient satisfaction rating for LMWH was 1.2 out of 5. The secondary survey of 54 patients prescribed rivaroxaban, the mean duration of treatment was 35 days (no variance), with all patients reported taking exactly 35 days. The mean patient satisfaction rating for this patient cohort was 3.5 out of 5, significantly superior ($P < 0.05$) to LMWH. The comparison of the mean duration of treatment and respective satisfaction ratings for both cohorts is shown in Figures 1

Table 1 Patient demographics and associated surgical procedure for low molecular weight heparin (LMWH) and rivaroxaban cohorts

	LMWH group	Rivaroxaban group	P-value
Total number	56	54 ^a	>> 0.05
Male	23	26 ^b	
Female	33	28 ^b	
Age (years)	72 (41–85)	67 (35–79) ^a	
Primary THA	45	47 ^a	
Revision THA	11	7 ^a	

Statistical tests: ^aStudent's *t*-test; ^bchi-squared test.

and 2. There was a statistically significant difference ($P = 0.003$) in the duration of treatment between the two cohorts.

However, there was no statistical difference in the documented associated complications for both cohorts are shown in Table 2. One patient in the LMWH cohort devel-

oped a pulmonary embolism 23 days following surgery and was re-admitted under the care of the physicians and was anti-coagulated with warfarin.

The results of the national and international postal and telephone survey regarding the use of LMWH in orthopaedic units for elective hip arthroplasty survey are shown in Table 3. Overall, of the 43 orthopaedic units surveyed, 39 routinely prescribe LMWH following surgery. However, only four units out of the 39 (10.2%), prescribe LMWH for at least 5 weeks.

Discussion

The risk of post-discharge symptomatic thrombosis following hip surgery can be reduced by two-thirds if VTE prophylaxis is continued for at least 28 days.^{15–18} The issue now exists as to how VTE prophylaxis can best be provided for 28–35 days following a surgical procedure that routinely requires a hospital stay of less than 7 days?

In light of the evidential support for a 35-day extended period of VTE prophylaxis following hip arthroplasty surgery, the survey results presented in this study, in addition to those of large multicentre arthroplasty registries, highlight that few patients receive LMWH for an adequate duration.^{19,20} The results of a large postal survey of orthopaedic surgeons showed only 42% prescribe an extended duration of VTE prophylaxis beyond discharge, nearly all of which use aspirin.²¹ However, the use of aspirin for extended VTE prophylaxis is now questioned since the Pulmonary Embolism Prevention (PEP) study of over 4000 total hip and knee replacements concluded that aspirin provides no benefit over placebo, whilst the 160 mg dosage has an associated significant risk of gastrointestinal bleeding.²²

Table 2 Documented adverse affects with no significant differences between the low molecular weight heparin (LMWH) and rivaroxaban cohorts

	LMWH group	Rivaroxaban group	P-value
Significant bleeding	3	1	>> 0.05
Wound dehiscence	0	0	
Wound infection	3	1	
DVT	0	0	
Pulmonary embolism	1	0	

Table 3 National and international survey of use and duration of use of low molecular weight heparin (LMWH)

	Use LMWH	Patients prescribed 4 weeks of LMWH
Canada/Australia	10/12	2/10
UK district general hospital	23/25	2/23
UK teaching hospital	6/6	0/6

Extensive evidence exists supporting the efficacy of LMWH in VTE prophylaxis following lower limb joint arthroplasty; however, logistical and medical concerns exist regarding its use for an extended period of 28–35 days.^{25–25} Furthermore, heparin-induced thrombocytopenia (HIT) is a known complication of LMWH use and guidelines recommend that all patients should be monitored for this potentially fatal condition.^{26,27} However, recent evidence shows few patients are monitored for HIT and indeed very few orthopaedic surgeons are aware of the relevant guidelines.^{28,29} The practicalities of daily subcutaneous injections for up to 35 days can cause difficulties, often necessitating a nurse to administer LMWH to the patient, at considerable financial cost. Therefore, LMWH does provide adequate VTE prophylaxis provided it is correctly administered, for the correct duration and suitable monitoring for HIT is carried out.

Rivaroxaban is a new oral Factor Xa inhibitor that is licensed in the UK for VTE prophylaxis following lower limb arthroplasty.²⁷ Several multicentre studies compare LMWH with rivaroxaban to support its introduction into clinician practice.^{10,30–32} In summary, rivaroxaban has been demonstrated to be at least as effective as LMWH for VTE prophylaxis. The results of this study demonstrate that it is simple to introduce, and it affords a superior duration of prophylaxis in comparison to LMWH. All the patients in the rivaroxaban cohort received 35 days of treatment. Undoubtedly, the convenience of the oral preparation is the principal factor explaining this, highlighted by the associated superior patient satisfaction. The lack of the requirement for HIT monitoring is a further benefit.

Whilst the documented complications in Table 2 show a higher number of adverse effects in the LMWH cohort, including bleeding, wound infection and one case of pulmonary embolism, the low numbers in this study preclude any statistical judgement from being made.

In addition to rivaroxaban, a direct Factor Xa inhibitor, dabigatran (Pradaxa®, Boehringer Ingelheim) a direct thrombin inhibitor has also been similarly licensed for VTE prophylaxis. Recent studies provide evidence for the efficacy of dabigatran in comparison to LMWH; however, to date, no study has directly compared rivaroxaban with dabigatran.^{33–35} One area of debate is the bleeding risk profile of these therapeutic agents; however, since the only data available use surrogate comparisons with LMWH, no statistical difference has yet been shown.¹⁴ Long-term studies will hopefully provide clarification in the future.

The financial cost of the wide-spread introduction of a new drug must be considered. Using current pricing schedules from the British National Formulary,²⁷ the cost of 4 weeks' treatment with rivaroxaban (Xarelto® 10 mg once daily oral, Bayer) is £157, compared with £117 for a similar course of enoxaparin (Clexane® 40 mg once daily subcuta-

neous, Sanofi-Aventis). However, if one factors in the costs involved with actually administering enoxaparin, possibly including a district nurse, and correctly monitoring for HIT with regular platelet counts, the difference in cost is likely to be minimal. Furthermore, a UK cost analysis has been incorporated into the technology appraisal guidance by NICE,³⁶ concluding that both rivaroxaban and dabigatran were 'an appropriate use of NHS resources'.

Conclusions

This study highlights that the duration of VTE prophylaxis following hip arthroplasty surgery currently achieved with LMWH is inadequate in light of the evidence-based guidelines for extended prophylaxis of 35 days. Further, we demonstrate that this inadequate treatment may be improved with the use of rivaroxaban, a new oral Factor Xa inhibitor.

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