Evidence Review

ALBERTA BONE & JOINT INSTITUTE HEALTH

Topic: Sequential Compression Devices plus LMWH for DVT prophylaxis

Background.

Deep vein thrombosis (DVT) is a potentially dangerous complication in patients who receive elective total hip (THA) or total knee arthroplasty (TKA). These patients are at a high risk for the development of DVT following surgery. In fact, up to 60% may develop this condition [1]. Thromboembolic complications, such as DVT, increase the likelihood of a potentially fatal pulmonary embolism (PE). Thus, DVT prophylaxis must be given to this group of surgical patients.

Clinicians are confronted with a multitude of DVT prophylactic therapy options. There are numerous pharmacological agents (e.g., warfarin, heparin. LMWH, aspirin) and mechanical systems (e.g., elastic compression stockings, pneumatic compression devices, foot pumps) that are prescribed for this purpose. Each specific method varies in dose and duration, and these options are routinely combined as a multimodal prophylactic package. Although DVT prophylaxis is administered to virtually all THA and TKA patients, the ideal prophylactic regimen has yet to be identified [2].

LMWHs (e.g., dalteparin, enoxaparin) have become the widely accepted alternatives to other pharmacological agents due to their safety and efficacy in the postoperative period [3]. Mechanical systems are often combined with LMWH therapy following THA or TKA, although there has been limited evidence for this multimodal approach.

The aim of this review is to summarize, using evidence-based principles and techniques, the thromboprophylactic efficacy of sequential compression devices (SCD), a form pneumatic compression therapy, used in combination with LMWH following elective THA or TKA.

Review Design.

- This review is structured on the basis of Cochrane systematic review formats
- Relevant Cochrane reviews will be initially identified
- Using search and inclusion criteria of identified Cochrane reviews, RCTs published subsequent to the reviews will be selected for review
- Selected RCTs must pass quality control (discussed below) for inclusion into this review

LMWH: low molecular-weight heparin (e.g., dalteparin, enoxaparin)

SCD: sequential compression device. This device typically features a leg sleeve that extends from just above the ankle to the upper thigh (some systems also cover the foot). SCDs have multiple chambers that are sequentially inflated from the ankle to the upper thigh with decreasing gradients of pressure, which serves to "milk" the veins in the leg from distal to proximal. This system differs from intermittent compression devices, which have one or more inflatable chambers that inflate and deflate simultaneously at regular intervals.

Search Strategy.

A search of the Cochrane Database of Systematic Reviews was conducted with the following search strategy:

> Search Term: (prophylaxis).mp AND (arthroplasty OR hip OR knee OR orthopaedic OR orthopedic).mp

No Cochrane systematic review was found on the DVT prophylaxis with LMWH *in combination* with SCDs

following elective THA or TKA.

Search for non-Cochrane reviews and RCTs.

Searches for systematic reviews, meta-analyses and RCTs were performed on MEDLINE, EMBASE and CINAHL databases. The search was limited to English language studies published in 1990 or later. The following selection criteria were used:

Specific search strategies:

> Search Term: (sequential OR SCD) AND (compression) AND English[la] AND (thrombotic OR prophy* OR DVT OR thrombosis OR thromboprophylaxis OR VTE OR embolism) AND (heparin OR LMWH OR pharmacological) AND (arthroplasty OR orthopaedic OR orthopedic OR hip OR knee) AND 1990:2006[pdat]

Articles selected:

- Valle et al. (2006). Venous thromboembolism is rare with a multimodal prophylaxis protocol after total hip arthroplasty. Clin. Orthop. Relat. Res. 444:146-53.
- Westrich et al. (2005). Thromboembolic disease prophylaxis in patients with hip fracture: a multimodal approach. J. Orthop. Trauma. 19(4):234-40.
- Geerts et al. (2004). Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest. 126(3 Suppl):338S-400S.
- Silbersack et al. (2004). Prevention of deep-vein thrombosis after total hip and knee replacement. Low-molecular-weight heparin in combination with intermittent pneumatic compression. J. Bone Joint Surg. Br. 86(6):809-12
- Handoll et al. (2003). Heparin, low molecular weight heparin and physical methods for preventing deep vein thrombosis and pulmonary embolism following surgery for hip fractures. Cochrane database of systematic reviews.
- Hull et al. (2001). Extended out-of-hospital low-molecular-weight heparin prophylaxis against deep venous thrombosis in patients after elective hip arthroplasty: a systematic review. Ann Intern Med. 135(10):858-69.
- Westrich et al. (2000). Meta-analysis of thromboembolic prophylaxis after total knee arthroplasty. J. Bone Joint Surg. Br. 82(6):795-800.

Quality control.

The quality of the selected reviews and clinical studies were assessed by an independent reviewer. RCT study quality was measured using a validated scale [4] that considers the study design, randomization, blinding, data collection and statistical analysis procedures that minimize biases. Studies deemed to have good methodological quality were included in this review.

Results.

Current prophylactic schedules recommend pharmacological methods such as LMWH, mechanical techniques such as pneumatic compression devices, or a combination of these [5]. Unfortunately, few studies have evaluated the efficacy of combined prophylactic modalities in THA or TKA patients. Consequently, no Cochrane reviews are available on this topic.

A complicating factor in the identification of relevant studies for this review was the failure of many studies to distinguish the specific form of pneumatic compression used (i.e., sequential and/or intermittent compression). Although sequential devices feature multiple compartments that inflate to different pressures to form a "milking" pressure gradient on the limb, the same cannot be assured for intermittent (i.e., start and stop at regular intervals) compressive devices. Treatments with the general label of intermittent pneumatic compression may or may not provide sequential compression on the limb. Studies that used multiple prophylaxis regimens that included unspecified intermittent compression devices [6,7] were included in this review for completeness.

Studies which have assessed the efficacy of LMWH and compression devices either separately or in combination may provide insight into the effectiveness of multimodal prophylaxis protocols in general for THA or TKA patients. With that consideration in mind, this review is based on studies that provide information to towards this end.

Westrich et al (2000) [7] performed a meta-analysis of 23 studies with 6,001 patients that assessed the effectiveness of common DVT prophylactic measures following TKA. This review included RCTs, reviews and prospective studies that passed the authors' quality control criteria for inclusion. In a comparison of the four common prophylactic regimes following TKA (aspirin, warfarin, LMWH and pneumatic compression), the authors concluded that the incidence of total DVT was lowest among those who were given LMWH (29%) and pneumatic compression devices (17%). Furthermore, the rate of symptomatic PE was 0.5% (2/416) in the LMWH group, and 0% (0/177) in the pneumatic compression group. Based on their findings, the authors suggest that a combination approach to DVT prophylaxis would likely incorporate the advantages of various regimens to provide an additive or synergistic effect with combined therapy.

One study [8] has specifically looked at the prophylaxis use of LMWH in combination with SCD in THA and TKA patients. In this randomized, prospective study 131 patients were divided into two groups before surgery; one group received LMWH and SCD and the other received LMWH and graduated compression stockings. LMWH was administered until the 30th postoperative day, while SCD was continued until the 10th postoperative day, after which these patients switched to compression stockings. All patients wore the stockings to a maximum of 3 months after surgery. DVT formation was diagnosed with compression ultrasonography at 6-12 days and 6-12 weeks postoperatively. This study found a 100% relative risk reduction of DVT in THA and TKA patients who received LMWH + SCD compared to those who received LMWH + stockings. DVT was not observed in any of the 70 patients that received SCD, despite the fact that 26% of patients (18/70) in this group prematurely stopped using the device. The reasons stated for discontinuation are increased patient mobility limited the daytime usage of the device, and nighttime operation was uncomfortable. These results are promising in that they suggest LMWH plus SCD used in combination may provide highly effective DVT prevention in THA and TKA patients. However, criticism could be levelled at the low sample size, and thus low power of the study.

Another study [5] with 200 hip fracture patients examined the efficacy of multimodal DVT prophylaxis following surgery. In general, patients who have surgery to repair hip fractures experience postoperative DVT rates comparable to THA and TKA patients [5]. Westrich et al assessed the effectiveness of multimodal DVT prophylaxis in this group. Specifically, in their prospective study all patients received SCD plus either aspirin (67 patients) or warfarin (133 patients) immediately after surgery. The anticoagulant was continued for 6 weeks postoperatively for all patients. DVT formation was diagnosed with duplex ultrasound imaging at a mean postoperative time of 4.5 days and 3 months. The authors found only 7 cases (3.5%) of confirmed DVT (no evidence of symptomatic DVT was reported at 3 months postoperatively). Five of these cases were from the warfarin + SCD group, the other two from the aspirin + SCD group. The demonstrated rate of 3.5% DVT formation is noted as being considerably lower than previously reported rates using various prophylactic regimes. Westrich et al [5] conclude that their results show increased effectiveness in using multimodal prophylaxis for the prevention of DVT following major orthopaedic surgery.

Recently, Valle et al (2006) [6] reported on the prospective DVT outcomes of 1947 consecutive patients (2032 THAs) who were given a multimodal prophylaxis regimen. The objective of their combined therapies was to target the multiple factors associated with DVT formation while also minimizing the risks related to anticoagulant use (e.g., bleeding). Patients in this study were administered the following prophylaxis protocol:

- Preoperative discontinuation of procoagulant mediation and autologous blood donation
- Hypotensive epidural anesthesia
- Intraoperative IV heparin (15 U/kg) given before femoral preparation when the clotting mechanism is maximally activated
- Aspiration of femoral intramedullary contents
- Expedient surgery to minimize femoral vein occlusion and blood loss
- Immediate post-operative intermittent pneumatic compression (for 10 days)
- Knee-high elastic stockings and early mobilization
- Postoperative aspirin (83% of patients) or warfarin (17% - only for patients with predisposing factors or were on such medication before surgery); both for 4 – 6 weeks

It should be noted that details on the mechanism and duration of the compressive device used in this study are not provided. Based on comparisons to historical published values, the authors conclude that their multimodal prophylaxis regimen provides low DVT rates (2.5% DVT, 0.6% PE), and that following such regimens could obviate the need to use anticoagulants that increase the risk of bleeding (e.g., LMWH).

Conclusions.

The studies presented above indicate the additive effectiveness of chemoprophylaxis in conjunction with mechanical (SCD) prophylaxis in reducing DVT rates following THA, TKA and hip fracture surgery. This is not surprising as the guidelines established from the Seventh American College of Chest Physicians conference on antithrombotic and thrombolytic therapy state that the use of elastic stockings or intermittent pneumatic compression as adjuvant prophylaxis may provide additional protection for THA patients, and intermittent pneumatic compression is recommended as an alternative

method of thromboprophylaxis in TKA patients [1]. There is ample evidence in the literature towards the prophylactic effectiveness of either LMWH alone [9] or SCD alone [10] following major orthopaedic surgery. However, studies that have assessed the combined effectiveness of both LMWH and SCD in THA or TKA patients are surprisingly limited. Silbersack et al did examine that specific multimodal prophylaxis combination in THA and TKA patients and found that it completely ameliorated DVT formation compared to the group that received LMWH and elastic stockings, although only 131 patients participated in that study. Future studies with greater sample sizes should specifically focus on the effect of various chemoprophylaxes (e.g., aspirin, warfarin, LMWH) combined with SCDs on DVT rates in THA and TKA patients.

Conflict of interest.

Non known.

Reference List

1 Geerts,W.H. *et al.* (2004) Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 126, 338S-400S

2 Lieberman,J.R. and Hsu,W.K. (2005) Prevention of venous thromboembolic disease after total hip and knee arthroplasty. *J. Bone Joint Surg. Am.* 87, 2097-2112

3 Krotenberg,R. (2004) Current recommendations for extended out-of-hospital thromboprophylaxis following total hip arthroplasty. *Am. J. Orthop.* 33, 180-184

4 van,T.M. *et al.* (2003) Updated method guidelines for systematic reviews in the cochrane collaboration back review group. *Spine* 28, 1290-1299

5 Westrich,G.H. *et al.* (2005) Thromboembolic disease prophylaxis in patients with hip fracture: a multimodal approach. *J. Orthop. Trauma* 19, 234-240

6 Valle A.G.D. *et al.* (2006) Venous thromboembolism is rare with a multimodal prophylaxis protocol after total hip arthroplasty. *Clin. Orthop. Relat Res.* 444, 146-153

7 Westrich,G.H. *et al.* (2000) Meta-analysis of thromboembolic prophylaxis after total knee arthroplasty. *J. Bone Joint Surg. Br.* 82, 795-800

8 Silbersack,Y. *et al.* (2004) Prevention of deep-vein thrombosis after total hip and knee replacement. Low-molecular-weight heparin in combination with intermittent pneumatic compression. *J. Bone Joint Surg. Br.* 86, 809-812

9 Hull,R.D. *et al.* (2000) Low-molecular-weight heparin prophylaxis using dalteparin in close proximity to surgery vs warfarin in hip arthroplasty patients: a double-blind, randomized comparison. The North American Fragmin Trial Investigators. *Arch. Intern. Med.* 160, 2199-2207

10 Handoll,H.H. *et al.* (2000) Heparin, low molecular weight heparin and physical methods for preventing deep vein thrombosis and pulmonary embolism following surgery for hip fractures. *Cochrane. Database. Syst. Rev.*, CD000305

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