TITLE: Low Molecular Weight Heparins versus New Oral Anticoagulants for Long-Term Thrombosis Prophylaxis and Long-Term Treatment of DVT and PE: A Review of the Clinical and Cost-Effectiveness

DATE: 06 May 2013

CONTEXT AND POLICY ISSUES

Venous thromboembolism (VTE), the formation of a blood clot in one of the veins of the body, is a common complication in patients undergoing surgical procedures. VTE, which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), can be life-threatening and result in long-term morbidity, highlighting the importance of thrombosis prophylaxis. In the absence of prophylaxis, the overall risk of DVT is estimated to be 10-40% in general surgery patients and 40-60% in major orthopedic surgery patients. Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are two of the most commonly performed operations in orthopedic surgery.

In addition to surgical procedures, there are other risk factors for developing VTE including malignancies, limited mobility, obesity, pregnancy, myocardial infarction, ischemic stroke, varicose veins, and chronic kidney disease.

Low molecular weight heparins (LMWHs) are routinely used as an anticoagulant for thrombosis prophylaxis in both medical and surgical patients. LMWHs are administered subcutaneously and four of these drugs have been approved in Canada: enoxaparin, dalteparin, nadroparin, and tinzaparin. In the last decade, several new oral anticoagulants (NOACs) have been developed for thrombosis prophylaxis, offering a more targeted mechanism of anticoagulation. NOACs include the direct thrombin inhibitor dabigatran, and the direct factor Xa inhibitors rivaroxaban and apixaban.

The minimum recommended duration for anticoagulation is 10 to 14 days, but extended prophylaxis up to 35 days in the outpatient period after major orthopedic surgery is suggested. Several phase III randomized controlled trials (RCTs) have compared the efficacy and safety of NOACs to LMWHs for thrombosis prophylaxis in patients that have undergone THA and TKA, using a treatment period up to 35 days. Studies examining the effect of LMWHs and NOACs for thrombosis prophylaxis in acutely ill medical patients generally have treatment periods between 6 to 14 days, and up to 30 days.
The purpose of this review is to examine the comparative clinical and cost-effectiveness of LMWHs used as a single agent versus NOACs for long-term thrombosis prophylaxis and for long-term treatment of DVT and PE.

RESEARCH QUESTIONS

1. What is the comparative clinical effectiveness of low molecular weight heparins (LMWHs) used as a single agent versus new oral anticoagulants (NOACs) for long-term thrombosis prophylaxis?

2. What is the cost-effectiveness of LMWHs used as a single agent compared with NOACs for long-term thrombosis prophylaxis?

3. What is the comparative clinical effectiveness of LMWHs use as a single agent versus NOACs for long-term treatment of deep vein thrombosis and/or pulmonary embolism?

4. What is the cost-effectiveness of LMWHs use as a single agent versus NOACs for long-term treatment of deep vein thrombosis and/or pulmonary embolism?

KEY FINDINGS

No relevant literature was identified regarding the comparative clinical and cost-effectiveness of LMWHs used as a single agent versus NOACs for long-term thrombosis prophylaxis and for long-term treatment of DVT and PE.

METHODS

A limited literature search was conducted of key resources including Pubmed, The Cochrane Library (2013, Issue 3), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No methodological filters were applied. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2003 and April 8, 2013.

Literature Search Strategy

One reviewer screened the titles and abstracts of the retrieved publications and evaluated the full-text publications for the final article selection, according to selection criteria presented in Table 1.

Selection Criteria and Methods

Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Patients on long-term (&gt;38 days) prophylaxis for thrombosis associated with cancer, atrial fibrillation, post-operatively, or other medical conditions. Patients on long-term (&gt;38 days) treatment for DVT and/or PE</th>
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<tr>
<td>Intervention</td>
<td>Low molecular weight heparins (dalteparin, enoxaparin, nadroparin, tinzaparin) as a single agent</td>
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Comparator | New oral anticoagulants (dabigatran, rivaroxaban, apixaban)
---|---
Outcomes | Clinical effectiveness, adverse events, cost effectiveness
Study Designs | Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials (RCTs), non-randomized studies, and economic evaluations

Exclusion Criteria

Studies were excluded if they did not meet the selection criteria, were duplicate publications or included in a selected systematic review, or were published prior to 2003.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search yielded 271 citations. Upon screening titles and abstracts, 229 citations were excluded and 42 potentially relevant articles were retrieved for full-text review. No additional potentially relevant reports were identified through grey literature searching. Of the 42 potentially relevant reports, none met inclusion criteria. The study selection process is outlined in a PRISMA flowchart (Appendix 1). The majority of studies were excluded because the treatment period did not exceed 38 days.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

No relevant literature was identified; therefore, no conclusions can be presented regarding the comparative clinical and cost-effectiveness of LMWHs used as a single agent versus NOACs for long-term thrombosis prophylaxis and for long-term treatment of DVT and PE.

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REFERENCES


APPENDIX 1: Selection of Included Studies

271 citations identified from electronic literature search and screened

229 citations excluded

42 potentially relevant articles retrieved for scrutiny (full text, if available)

0 potentially relevant reports retrieved from other sources (grey literature, hand search)

42 potentially relevant reports

42 reports excluded:
- irrelevant population (2)
- irrelevant intervention and comparator - not long-term treatment (36)
- other (review articles, editorials) (4)

0 reports included in review