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[Intervention Review]

Anticoagulation for the initial treatment of venous thromboembolism in people with cancer

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ABSTRACT

Background

Compared with people without cancer, people with cancer who receive anticoagulant treatment for venous thromboembolism (VTE) are more likely to develop recurrent VTE.

Objectives

To compare the efficacy and safety of three types of parenteral anticoagulants (i.e. fixed-dose low molecular weight heparin (LMWH), adjusted-dose unfractionated heparin (UFH), and fondaparinux) for the initial treatment of VTE in people with cancer.

Search methods

A comprehensive search included a major electronic search of the following databases: Cochrane Central Register of Controlled Trials (CENTRAL) (2018, Issue 1), MEDLINE (via Ovid) and Embase (via Ovid); handsearching of conference proceedings; checking of references of included studies; use of the 'related citation' feature in PubMed; and a search for ongoing studies. This update of the systematic review was based on the findings of a literature search conducted on 14 January 2018.

Selection criteria

Randomized controlled trials (RCTs) assessing the benefits and harms of LMWH, UFH, and fondaparinux in people with cancer and objectively confirmed VTE.

Data collection and analysis

Using a standardized form, we extracted data in duplicate on study design, participants, interventions outcomes of interest, and risk of bias. Outcomes of interested included all-cause mortality, symptomatic VTE, major bleeding, minor bleeding, postphlebitic syndrome, quality of life, and thrombocytopenia. We assessed the certainty of evidence for each outcome using the GRADE approach.

Main results

Of 15440 identified citations, 7387 unique citations, 15 RCTs fulfilled the eligibility criteria. These trials enrolled 1615 participants with cancer and VTE: 13 compared LMWH with UFH enrolling 1025 participants, one compared fondaparinux with UFH and LMWH enrolling 477 participants, and one compared dalteparin with tinzaparin enrolling 113 participants. The meta-analysis of mortality at three months included 418 participants from five studies and that of recurrent VTE included 422 participants from 3 studies. The findings showed that LMWH likely decreases mortality at three months compared to UFH (risk ratio (RR) 0.66, 95% confidence interval (CI) 0.40 to 1.10; risk difference (RD) 57 fewer per 1000, 95% CI 101 fewer to 17 more; moderate certainty evidence), but did not rule out a clinically significant increase or decrease in VTE recurrence (RR 0.69, 95% CI 0.27 to 1.76; RD 30 fewer per 1000, 95% CI 70 fewer to 73 more; moderate certainty evidence).

The study comparing fondaparinux with heparin (UFH or LMWH) did not exclude a beneficial or detrimental effect of fondaparinux on mortality at three months (RR 1.25, 95% CI 0.86 to 1.81; RD 43 more per 1000, 95% CI 24 fewer to 139 more; moderate certainty evidence), recurrent VTE (RR 0.93, 95% CI 0.56 to 1.54; RD 8 fewer per 1000, 95% CI 52 fewer to 63 more; moderate certainty evidence), major bleeding (RR 0.82, 95% CI 0.40 to 1.66; RD 12 fewer per 1000, 95% CI 40 fewer to 44 more; moderate certainty evidence), or minor bleeding (RR 1.53, 95% CI 0.88 to 2.66; RD 42 more per 1000, 95% CI 10 fewer to 132 more; moderate certainty evidence)

The study comparing dalteparin with tinzaparin did not exclude a beneficial or detrimental effect of dalteparin on mortality (RR 0.86, 95% CI 0.43 to 1.73; RD 33 fewer per 1000, 95% CI 135 fewer to 173 more; low certainty evidence), recurrent VTE (RR 0.44, 95% CI 0.09 to 2.16; RD 47 fewer per 1000, 95% CI 77 fewer to 98 more; low certainty evidence), major bleeding (RR 2.19, 95% CI 0.20 to 23.42; RD 20 more per 1000, 95% CI 14 fewer to 380 more; low certainty evidence), or minor bleeding (RR 0.82, 95% CI 0.30 to 2.21; RD 24 fewer per 1000, 95% CI 95 fewer to 164 more; low certainty evidence).

Authors' conclusions

LMWH is possibly superior to UFH in the initial treatment of VTE in people with cancer. Additional trials focusing on patient-important outcomes will further inform the questions addressed in this review. The decision for a person with cancer to start LMWH therapy should balance the benefits and harms and consider the person's values and preferences.

PLAIN LANGUAGE SUMMARY

Blood thinners for the initial treatment of blood clots in people with cancer

Background

People with cancer are at increased risk of blood clots. The blood thinner (anticoagulant) administered in the first few days after identifying a blood clot can consist of unfractionated heparin (infused through a vein),low molecular weight heparin (injected under the skin once or twice per day; dalteparin, and tinzaparin are two different types of low molecular weight heparin), or fondparinux (injected under the skin once daily). These blood thinners may have different effectiveness and safety profiles.

Study characteristics

We searched scientific databases for clinical trials comparing different blood thinners in people with cancer with a confirmed diagnosis of deep vein thrombosis (a blood clot in the limbs) or pulmonary thrombosis (a blood clot in the lungs). We included trials of adults and children with either solid tumors or blood cancer irrespective of the type of cancer treatment. The trials looked at death, recurrent blood clots, and bleeding. The evidence is current to January 2018. We included 15 trials.

Key results

In this systematic review, data from five studies with 422 participants suggested that the effect of low molecular weight heparin on death compared with unfractionated heparin was uncertain, but if anything of small size. There was not enough evidence to prove superiority in reducing recurrence of blood clots or risk of bleeding. We found no data to compare the safety profile of these two medications. Also, fondaparinux did not prove or exclude any important effect compared to heparins, on death, blood clots, or bleeding. Similarly,the available evidence did not show any difference between dalteparin and tinzaparin for all tested outcomes.

Certainty of the evidence

We judged the certainty of evidence for low molecular weight heparin versus unfractionated heparin to be moderate for all assessed outcomes.

We judged the certainty of evidence for fondaparinux versus heparin to be moderate for all tested outcomes.

We judged the certainty of evidence for tinzaparin versus dalteparin to be low for all tested outcomes.