Abstract:

Background: The prevalence of children diagnosed with thrombotic events has been increasing in the last decades. The most common thrombosis risk factor in neonates, infants and children is the placement of a central venous catheter (CVC). It is unknown if anticoagulation prophylaxis with low molecular weight heparin (LMWH) decreases CVC-related thrombosis in children. This is an update of the Cochrane Review published in 2014.

Objectives: To determine the effect of LMWH prophylaxis on the incidence of CVC-related thrombosis and major and minor bleeding complications in children. Further objectives were to determine the effect of LMWH on occlusion of CVCs, number of days of CVC patency, episodes of catheter-related bloodstream infection (CRBSI), other side effects of LMWH (allergic reactions, abnormal coagulation profile, heparin-induced thrombocytopenia and osteoporosis) and mortality during therapy.

Search methods: The Cochrane Vascular Information Specialist searched the Cochrane Vascular Specialised Register, CENTRAL, MEDLINE, Embase and CINAHL databases and World Health Organization International Clinical Trials Registry Platform and ClinicalTrials.gov trials registers to 7 May 2019. We undertook reference checking of identified trials to identify additional studies.

Selection criteria: We included randomised controlled trials (RCTs) and quasi-randomised trials comparing LMWH to no prophylaxis (placebo or no treatment), or low-dose unfractionated heparin (UFH) either as continuous infusion or flushes (low-dose UFH aims to ensure the patency of the central line but has no systemic anticoagulation activity), given to prevent CVC-related thrombotic events in children. We selected studies conducted in children aged 0 to 18 years.

Data collection and analysis: Two review authors independently identified eligible studies, which were assessed for study methodology including bias, and extracted unadjusted data where available. In the data analysis step, all outcomes were analysed as binary or dichotomous outcomes. The effects of interventions were summarised with risk ratios (RR) and their respective 95% confidence intervals (CI). We assessed the certainty of evidence for each outcome using the GRADE approach.

Main results: One additional study was included for this update bringing the total to two included studies (with 1135 participants). Both studies were open-label RCTs comparing LMWH with low-dose UFH to prevent CVC-related thrombosis in children. We identified no studies comparing LMWH with placebo or no treatment. Meta-analysis found insufficient
evidence of an effect of LMWH prophylaxis in reducing the incidence of CVC-related thrombosis in children with CVC, compared to low-dose UFH (RR 0.68, 95% CI 0.27 to 1.75; 2 studies; 787 participants; low-certainty evidence). One study (158 participants) reported symptomatic and asymptomatic CVC-related thrombosis separately and detected no evidence of a difference between LMWH and low-dose UFH (RR 1.03, 95% CI 0.21 to 4.93; low-certainty evidence; RR 1.17, 95% CI 0.45 to 3.08; low-certainty evidence; for symptomatic and asymptomatic participants respectively). There was insufficient evidence to determine whether LMWH impacts the risk of major bleeding (RR 0.27, 95% CI 0.05 to 1.67; 2 studies; 813 participants; low-certainty evidence); or minor bleeding. One study reported minor bleeding in 53.3% of participants in the LMWH arm and in 44.7% of participants in the low-dose UFH arm (RR 1.20, 95% CI 0.91 to 1.58; 1 study; 158 participants; very low-certainty evidence), and the other study reported no minor bleeding in either group (RR: not estimable). Mortality during the study period was reported in one study, where two deaths occurred during the study period. Both were unrelated to thrombotic events and occurred in the low-dose UFH arm. The second study did not report mortality during therapy per arm but showed similar 5-year overall survival (low-certainty evidence). No additional adverse effects were reported. Other pre-specified outcomes (including CVC occlusion, patency and CRBSI) were not reported.

Authors’ conclusions: Pooling data from two RCTs did not provide evidence to support the use of prophylactic LWMH for preventing CVC-related thrombosis in children (low-certainty evidence). Evidence was also insufficient to confirm or exclude a difference in the incidence of major and minor bleeding complications in the LMWH prophylaxis group compared to low-dose UFH (low and very low certainty respectively). No evidence of a clear difference in overall mortality was seen. Studies did not report on the outcomes catheter occlusion, days of catheter patency, episodes of CRBSI and other side effects of LMWH (allergic reactions, abnormal coagulation profile, heparin-induced thrombocytopenia and osteoporosis). The certainty of the evidence was downgraded due to risk of bias of the included studies, imprecision and inconsistency, preventing conclusions in regards to the efficacy of LMWH prophylaxis to prevent CVC-related thrombosis in children.

Reference:


Full Text