Central venous catheter-related thrombosis and thromboprophylaxis in children: a systematic review and meta-analysis
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CRD summary
This review concluded that there was no evidence to suggest that any type of prophylaxis against thrombosis reduced the risk of deep vein thrombosis related to central venous catheters in children; inadequate statistical power and missing outcome data could have compromised the results. These conclusions reflect the evidence and seem reliable; the recommendations for further research are justified.

Authors' objectives
To evaluate the efficacy of treatment to prevent thrombosis in children with a central venous catheter.

Searching
MEDLINE, EMBASE, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched in December 2013, with no language and publication status restrictions. The search strategy was reported in an online supplement. The Conference Proceedings Citation Index was searched, as were the reference lists of retrieved studies and relevant reviews.

Study selection
Eligible for inclusion were randomised controlled trials (RCTs) evaluating the efficacy of prophylaxis against thrombosis in patients aged up to 18 years, with any type of central venous catheter. The outcome of interest was the incidence of deep venous thrombosis related to the central venous catheter (defined in the paper) during the study period.

In the included trials, the types of prophylaxis were heparin-bonded catheters, unfractionated heparin, low molecular weight heparin, warfarin, antithrombin concentrate, and nitroglycerin. Control groups received standard care or placebo. Just under half of the trials were multicentre.

Two reviewers independently selected trials for inclusion in the review; any discrepancies were resolved with a third reviewer.

Assessment of study quality
Trial quality was assessed for allocation concealment, blinding of investigators, blinding of outcome assessors, and completeness of outcome data (no further details reported).

It appears that more than one reviewer assessed quality.

Data extraction
The numbers of events were extracted by two independent reviewers; any discrepancies were resolved by discussion. Authors were contacted for missing data.

Methods of synthesis
Pooled risk ratios and 95% confidence intervals were calculated using random-effects meta-analysis. Statistical heterogeneity was assessed using $I^2$.

Results of the review
One crossover RCT and nine parallel RCTs were included in the review and meta-analysis (exact number of patients unclear). Most trials reported adequate allocation concealment (nine), blinding of investigators (seven), and blinding of outcome assessors (eight). The percentage of missing outcome data ranged from none to 22. Five trials were stopped early due to futility or poor recruitment, and four were not statistically powered to detect a reduction in deep vein thrombosis.
No statistically significant difference in the incidence of deep venous thrombosis related to catheters was found between controls and both heparin-bonded catheters (RR 0.34, 95% CI 0.01 to 7.68; two RCTs; $I^2=80\%$) and unfractionated heparin (RR 0.93, 95% CI 0.57 to 1.51; four RCTs; $I^2=0\%$). For all other types of prophylaxis only one trial was identified; no statistically significant differences were found between intervention and control (reported in the paper).

**Authors' conclusions**

There was no evidence to suggest that any type of prophylaxis against thrombosis reduced the risk of deep vein thrombosis related to central venous catheters in children. Inadequate statistical power and missing outcome data may have compromised the results.

**CRD commentary**

The review question and inclusion criteria were clearly defined. Relevant databases were searched and no restrictions were made on language and publication status, reducing the risk of trials being missed. Efforts were taken to minimise reviewer error and bias in study selection and data extraction, and they appear to have been taken for quality assessment. Trial details were limited, making it difficult to ascertain if the statistical synthesis was appropriate. The authors acknowledged that only a few RCTs, with small samples, could be included in the review and meta-analyses.

The authors' conclusions reflect the evidence and seem reliable; their recommendations for further research are justified.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that a multicentre RCT powered to detect a modest, clinically significant reduction in thrombosis was needed. They stated that adjustment for the type of central venous catheter might be required in this trial, and they recommended a pilot trial to investigate how recruitment might be maximised and missing outcome data minimised. Investigation into the efficacy of novel anticoagulants was also recommended.

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