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Review

Use of aprotinin to reduce blood loss and transfusion in major orthopedic surgery: a meta-analysis

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ABSTRACT

Backgroud: Conflicting reports have been published regarding the effectiveness and safety of aprotinin in reducing blood loss and transfusion in patients undergoing orthopedic surgery. We performed a meta-analysis to evaluate the effectiveness and safety of aprotinin in reducing blood loss and transfusion in major orthopedic surgery.

Materials and methods: MEDLINE, PubMed, EMBASE and Cochrane databases were searched for relevant studies. Only randomized controlled trials were eligible for this study. The weighted mean difference in blood loss, and number of transfusions per patient and the summary risk ratio of transfusion requirements, and deep-vein thrombosis (DVT) were calculated in the aprotinin-treated group and the control group.

Results: Eighteen randomized controlled trials involving 1276 patients were included. The use of aprotinin reduced total blood loss by a mean of 498.88 ml (95% confidence interval [CI]; –735.03 to –262.72), intra-operative blood loss by a mean of 246.11 ml (95% CI; –352.11 to –140.11), post-operative blood loss by a mean of 169.11 ml (95% CI; –234.06 to –105.55), the number of blood transfusions per patient by 0.93 units (95% CI; –1.36 to –0.51). Aprotinin led to a signficant reduction in transfusion requirements (RR 0.59; 95% CI; 0.51 to 0.69) and no increase in the risk of DVT (RR 0.58; 95% CI; 0.38 to 1.08).

Conclusion: The meta-analysis shows that aprotinin could significantly reduce blood loss and blood transfusion requirements in patients undergoing orthopedic surgery, and it did not appear to increase the risk of DVT.

Contents

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Major orthopedic procedures may be associated with significant blood loss requiring transfusion of several units of blood [1]. However, blood transfusion carries the risk of immunological and non-immunological adverse effects, such as a higher rate of post-operative infections, intravascular haemolysis, transfusion induced coagulopathy, renal impairment or failure, and even increased mortality [2]. Numerous strategies, including autologous blood donation, autologous drain transfusion, regional anesthesia and acute normovolaemic haemodilution, have been used to reduce allogenic blood transfusion rates. However, their application is limited by their clinical and financial efficacy [3].

Antifibrinolytic therapy constitutes an effective method to control or reduce bleeding and to limit or avoid blood transfusion in current medical practice [4,5]. Aprotinin, a naturally occurring single-chain 58 amino acid polypeptide with a molecular weight of 6512 Da, is a proteinase inhibitor with antifibrinolytic properties that has found widespread application during cardiac surgical procedures due to its ability to decrease blood loss and transfusion requirements [6,7]. Numerous studies have investigated its efficacy in reducing blood loss and transfusion requirements in patients undergoing orthopedic surgery with various results. Thus, we conducted a meta-analysis of randomized controlled trials to assess the effectiveness and safety of aprotinin in reducing blood loss and transfusion in major orthopedic surgery.

1. Methods

1.1. Study design

This review was based on Cochrane methodology for conducting meta-analysis. All data were reported according to the Quality of Reporting for Meta-analyses provided by the Handbook for Systematic Reviews of Interventions Version 5.0.0 [8].

1.2. Search methodology

We sought published randomized controlled trials that evaluated aprotinin in patients undergoing orthopedic surgery. The published literature was searched by a literature search from 1966 to April 2013 using the electronic databases including the MEDLINE, PubMed, EMBASE and Cochrane Database of Systematic Reviews. The search terms included “antifibrinolytics”, “cyklokapron”, “aprotinin”, “orthopedic surgery”, “hip surgery”, “knee surgery”, “spine surgery” and “randomized controlled trials”. Manufacturers were contacted for additional unpublished trials. Reference lists of included studies and relevant reviews were checked for additional trials.

1.3. Inclusion and exclusion criteria

Studies were included if they met the following criteria: (i) participants undergoing orthopedic surgery; (ii) randomly assigned patients to the treatment group who received aprotinin and the control group who received a placebo or no treatment; (iii) neither the aprotinin-treated group nor the control group used anticoagulant drugs; (iv) both groups reported one of the following outcomes: the amount of blood loss, the number of patients receiving allogeneic transfusion, the number of blood transfusion units per patient and the number of patients with deep-vein thrombosis.

Studies were excluded if they were non-English language, or if there were nonrandomized controlled trials or randomized controlled trials that did not contain any of the above outcomes.

1.4. Study selection

The initial electronic databases searches to identify potential studies for inclusion based on title and abstract information were performed by two independent authors (H.F, Z.Q.C). When there was a dispute, the full article was retrieved for further scrutiny. Completely study reports were assessed for inclusion independently by both authors, and authors were contacted for more information and clarification of data as necessary. Any disagreement was resolved by consensus or consultation with the senior authors (M.G.W). References and data for each included study were carefully cross-checked to ensure no overlapping data was presented.

1.5. Data abstraction

Data extracted from the included studies were entered by two independent authors (H.F, Z.Q.C). Any disagreement was resolved by consensus or consultation with the senior authors (M.G.W). Data extracted included: sample size, study design, subject age, type of surgery, dose and