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SCIENTIFIC ARTICLE

A randomized, double blind trial of prophylactic fibrinogen to reduce bleeding in cardiac surgery

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KEYWORDS
Blood transfusion;
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Abstract
Background and objectives: Postoperative bleeding has a great clinical importance and can contribute to increased mortality and morbidity in patients undergoing coronary artery bypass graft surgery. In this prospective, randomized, double-blind study, we evaluated the effect of prophylactic administration of fibrinogen concentrate on post-coronary artery bypass graft surgery bleeding.
Methods: A total of 60 patients undergoing coronary artery bypass surgery were randomly divided into two groups. Patients in the fibrinogen group received 1 g of fibrinogen concentrate 30 min prior to the operation, while patients in the control group received placebo. Postoperative bleeding volumes, prothrombin time, partial thromboplastin time, INR, hemoglobin and transfused blood products in both groups were recorded. A strict red blood cell transfusion protocol was used in all patients.
Results: There were no significant differences between intra-operative packed red blood cells infusion in the studied groups (1.0 ± 1.4 in fibrinogen group, and 1.3 ± 1.1 in control group). Less postoperative bleeding was observed in the fibrinogen group (477 ± 143 versus 703 ± 179, $p = 0.0001$). Fifteen patients in the fibrinogen group and 21 in the control group required post-op packed red blood cells infusion ($p = 0.094$). No thrombotic event was observed through 72 h after surgery.
Conclusion: Prophylactic fibrinogen reduces post-operative bleeding in patients undergoing coronary artery bypass graft.

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PALAVRAS-CHAVE
Transfusão de sangue;
Sangramento;
Cirurgia cardíaca;
Circulação extracorpórea;
Hemostasia

Estudo randômico e duplo-cego de profilaxia com fibrinogênio para reduzir o sangramento em cirurgia cardíaca

Resumo
Justificativa e objetivo: A hemorragia no período pós-operatório é de grande importância clínica e pode contribuir para o aumento da morbidade e mortalidade em pacientes submetidos à cirurgia de revascularização coronária. Nesse estudo prospectivo, randômico e duplo-cego, avaliamos o efeito da administração profilática de concentrado de fibrinogênio sobre o sangramento após cirurgia de revascularização coronária.
Métodos: No total, 60 pacientes submetidos à cirurgia de revascularização coronária foram randomicamente divididos em dois grupos. Os pacientes do grupo fibrinogênio receberam 1 g de concentrado de fibrinogênio 30 minutos antes da operação, enquanto os doentes do grupo controle receberam placebo. Os volumes de sangramento no pós-operatório, tempo de protrombina, tempo de tromboplastina parcial, INR, hemoglobina e hemoderivados transfundidos em ambos os grupos foram registrados. Um protocolo de conduta rigoroso para transfusão de hemácias foi usado em todos os pacientes.
Resultados: Não houve diferenças significantes entre as infusões de concentrados de hemácias nos grupos estudados ($1{,}0 \pm 1{,}4$ no grupo fibrinogênio e $1{,}3 \pm 1{,}1$ no grupo controle). O grupo fibrinogênio apresentou menos sangramento no pós-operatório (477 ± 143 versus 703 ± 179, $p = 0{,}0001$). Quinze pacientes do grupo fibrinogênio e 21 do grupo controle precisaram de infusão de concentrado de hemácias no pós-operatório ($p = 0{,}094$). Evento trombótico não foi observado durante 72 h após a cirurgia.
Conclusão: Profilaxia com fibrinogênio reduz o sangramento no período pós-operatório de pacientes submetidos à revascularização coronária.

Introduction

Optimal prevention and management of intra- and post-operative bleeding has a great clinical importance in various types of surgeries, including coronary artery bypass graft surgery (CABG). Such management can efficiently decrease the amount of blood products transfusion and as a result, may lead to less transfusion related complications.

Two to 6 percent of CABG surgery patients would be re-explored due to intraorpost-operative hemorrhage, which can lead to high morbidity and mortality rates. Furthermore, complications such as sternal wound infections are more frequent along with post-operative transfusion.[1–2] Consequently, the importance of any approach or intervention to decrease intra- or post-operative hemorrhage is obvious.[2] Coagulopathy is one possible reason of excessive bleeding during and following surgery. Multiple factors including platelet dysfunction, fibrinolysis and coagulation factor deficiencies may affect post-operative bleeding following cardiac surgery.[3]

During CABG surgery, low fibrinogen plasma concentration may directly be associated with blood loss.[4] This association is likely since fibrinogen is essential in the cross-linking of platelets during primary hemostasis and plays a central role in the coagulation cascade,[5] and it had been shown that following hemorrhage, fibrinogen concentration decreases more than other coagulationfactors.[6–9]

The purpose of present study was to investigate the effect of pre-operative infusion of fibrinogen concentrate on post-operative bleeding volume in CABG surgery patients. The percentage and amount of transfused blood products were considered as secondary outcome parameters.

Methods

Following the approval of the study protocol by the Institutional Ethics Committee, this trial was registered by the Iranian Registry of Clinical Trial. All participants provided a written form of consent after they were fully informed of nature and design of the study.

Sixty patients, scheduled for first time elective CABG, were enrolled in this double-blinded randomized placebo-controlled clinical trial. The patients with the following criteria were not considered eligible to take part in this study: previously diagnosed hematologic or liver diseases, uncontrolled or insulin dependent diabetes, pregnancy, unstable angina, serum creatinine more than 130 μmol/L, left ventricular ejection fraction less than 35%, serum fibrinogen levels more than 3.5 g/L. The patients also needed to be mentally capable of giving a written informed consent.

Using a computer generated randomization list, patients were assigned to fibrinogen and control groups. All the required study drugs were prepared by an anesthetist who was not involved in the surveillance of the patients. Furthermore, all the fluid plastic containers were covered by textile, so content of plastic containers was invisible.

Anticoagulant therapy with aspirin, warfarin and clopidogrel was discontinued 48 h prior to surgery. On arrival to the operating room, all the patients received oxygen via a facemask at a rate of 4 L/min, and an 18-gauge intravenous catheter was placed in a peripheral vein to allow for hydration of the patients using lactated ringer's solution (7 mL/kg) and administration of medications. Standard monitoring which consisted of invasive and non-invasive arterial blood pressure, heart rate, electrocardiogram, pulse oximetry,