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Reduction of Postoperative Haemorrhage with the Use of a Haemostatic Thrombin Matrix in Patients Who Underwent Decortication

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OBJECTIVE: To assess the efficacy of two measures for the control of postoperative haemorrhage in patients with fibrothoracic disease secondary to symptomatic extraparenchymal restrictive disease (e.g. empyema, haematoma) undergoing decortication. METHODS: This randomized, prospective study was performed in 50 adult patients with fibrothoracic disease secondary to symptomatic extraparenchymal restrictive disease who were scheduled to undergo decortication. Patients were randomized to receive either electrocautery plus hot compressor application or a thrombin-added haemostatic matrix (THM) for intraoperative haemostasis (*n* = 25 per group). Control of postoperative haemorrhage was compared between groups by evaluation of pre- and postoperative blood characteristics and mean postoperative drainage volume and blood transfusion requirements. RESULTS: Mean postoperative drainage and blood transfusion volumes were significantly lower in the THM group versus the electrocautery plus hot compress group. There was no difference in preoperative and postoperative blood tests in the THM group, whereas significant differences were observed in the electrocautery plus hot compress group. There were no infections, systemic allergies or sensitization, or reoperations in either group. CONCLUSIONS: Compared with electrocautery plus hot compress, the use of a THM significantly reduced postoperative haemorrhage and blood transfusion requirements in patients who underwent decortication.

KEY WORDS: THROMBIN HAEMOSTATIC MATRIX; ELECTROCAUTERY; EXTRAPARENCHYMAL RESTRICTIVE DISEASE; DECORTICATION; POSTOPERATIVE HAEMORRHAGE; BLOOD TRANSFUSION

Introduction

Secondary to symptomatic extra-parenchymal restrictive diseases such as clotted haemothorax, pleural tuberculosis, chronic empyema or mesothelioma, a membrane (shell) may develop and compress the lung parenchyma.[1] Fibrothorax can develop and abnormal fibrous tissue may also be found in the pleural cavity.[2] Consequently, this fibrosis may cause pulmonary compression and atelectasis, leading to perfusion and

ventilation changes.[3 – 5] In two large physiological animal studies, significant decreases in oxygen uptake and in lung ventilation and perfusion were observed in atelectatic lungs.[6,7] Thus, restrictive fibrotic membranous tissue should be removed using a process known as decortication – decortication literally means 'stripping off the bark of a tree' in French. Fowler[8] and Delorme[9] were the first physicians to describe and perform decortications; during this operation, fibrotic tissue from the diaphragm, mediastinum and thoracic pleura, in addition to the restrictive fibrous pleura covering the outer pulmonary surface, is removed.[4,10]

Postoperative haemorrhage is a serious problem associated with decortication and patients may require blood transfusions.[11 – 13] In decortication, the loss of surfactant – which provides lung surface elasticity – causes fibrinolysis, resulting in blood leakage on the surface of the lungs.[14] The numerous bleeding foci on the lung surface may increase the risk of haemorrhage in patients undergoing decortication compared with other types of thoracic surgery.[15] In addition, the fine dissection that is a necessary component of decortication, or haemorrhagic leaks which can be caused by the application of inadequate surgical haemostasis, may also lead to postoperative haemorrhage.[16] Haemorrhage as a consequence of decortication may necessitate reoperation, a situation that is problematic for surgeons and potentially life-threatening for patients. Taking measures to reduce the incidence of postoperative haemorrhage may help to prevent excessive mortality and morbidity.

Various methods have been used to reduce postoperative haemorrhage in patients undergoing decortication. Thrombin-added haemostatic matrix (THM) is one of these methods and comprises sterile absorbable bovine gelatin that aids haemostasis when applied to the bleeding surface.[3,17,18] Use of THM has increased gradually and it is now widely employed in many branches of surgery, including urology, neurosurgery, cardiovascular surgery and orthopaedic surgery.[19]

The present study investigated the effects of electrocautery plus hot compress compared with THM for controlling postoperative haemorrhage following decortication in adult patients with fibrothoracic disease secondary to symptomatic extra-parenchymal restrictive disease.

Patients and methods

STUDY POPULATION

Consecutive patients with fibrothoracic disease secondary to symptomatic extraparenchymal restrictive disease who underwent decortication at Antakya State Hospital or at the Thorax Surgery Clinics, Faculty of Medicine, Mustafa Kemal University, Antakya, Hatay, Turkey, between October 2008 and August 2010, were enrolled in this prospective randomized study. Prior to surgery, patients were assessed using preoperative radiographs and computed tomography scans and complete blood count. Mesothelioma patients with pleural thickening, empyema patients with empyema pouches and pleural thickening, and haematoma patients with pleural thickening were included in the study. Patients were not permitted to receive any antiaggregant or anticoagulant medication that could affect bleeding in the 7 days prior to decortication. Patients were randomized into two groups using a computer-generated randomization schedule: in the first group, patients received electrocautery plus hot compress for intraoperative haemostasis; and, in the second group, they received THM.

All patients provided written informed consent and the study protocol was approved by the Ethics Committee of Mustafa Kemal University (approval number 05-28).

ANAESTHESIA AND SURGICAL PROCEDURES

All patients underwent general anaesthesia using inhalation anaesthetics and muscle relaxants. Patients were intubated using a No. 36 double lumen endotracheal tube, which makes ventilation changes possible and facilitates decortication. Inhalation anaesthesia was achieved using sevoflurane 1 – 2% minimum alveolar concentration and the muscle relaxant cisatracurium besylate 0.15 mg/kg, followed by a maintenance dose of 2 mg, administered together with fentanyl 2 mg/kg. During single-lung ventilation to ensure patient comfort during decortication, the dependant lung was ventilated to keep the 1-min ventilation volume at a mean ± SD partial pressure of carbon dioxide ($PaCO_2$) of 35 ± 3 mmHg and the plateau airway pressure < 25 cmH_2O. The night before surgery, all patients received 5 mg of the H_2-receptor blocker diazepam and postoperatively they received anti-inflammatory drugs and opioids, as individually requested, to relieve pain. After surgery patients remained for one night in intensive care and were discharged from hospital 7 days later. Patients were, therefore, followed postoperatively for a total of 9 days. They were also monitored after discharge.

All operations were performed by the same two surgeons (T.D.Y., I.Y.). In the event of haemorrhage in either group, warm compresses, cautery and ligation were performed as necessary. In all decortication operations, standard posterolateral thoracotomy was performed. Dissection was started between the parietal pleura and endothoracic fascia and was carefully advanced from the chest wall to the diaphragm and mediastinum. The intrathoracic cavity was washed with physiological saline and dried after decortications in both groups. After the fixation of anterior and posterior chest drains placed in the intercostal spaces, patients underwent either electrocautery plus hot compress or THM in order to reduce postoperative bleeding.

In the electrocautery plus hot compress group, long compresses were dipped in boiled sterile saline and pressed on the bleeding site. Although specific vessels were not cauterized in this group, general areas at the bleeding site were cauterized. In the THM group a THM (Vascular Solutions, Minneapolis, MN, USA) was applied, according to the manufacturer's instructions, 30 s after product preparation to ensure optimum performance. Following application of the THM, maximum expansion volume was observed in about 10 min and excess THM was removed with a sponge. After cauterization in both groups, the thorax was closed and the operation completed.

STUDY ASSESSMENTS

Haemoglobin (Hb), haematocrit (Hct), platelet count, prothrombin time (PT) and activated partial thromboplastin time (APTT) were studied for 24 h preoperatively and 24 h postoperatively. Mean Hb was maintained at approximately 11 g/dl; no intervention was taken if Hb fell below 11 g/dl, but a blood transfusion was given if the level fell below 10 g/dl. Blood transfusion was also administered when Hct fell below 30%. Transfusions were performed using 300-ml units of whole blood and the mean volume of transfused blood was recorded. The mean volume of blood loss from the chest drains in the first 24 h postoperatively

was measured in both groups; up to 250 ml of blood in the drain in the first 24 h was considered normal.

Patients were monitored for infection in the first 24 h postoperatively. Wound control and monitoring of white blood cells was performed every other day for a total of 9 days postoperatively. The incidence of infections, and allergy or sensitization reactions to the THM, and the need for reoperation due to postoperative haemorrhage were recorded and monitored prior to and after discharge.

STATISTICAL ANALYSES

Statistical analyses were carried out using the SPSS® software package, version 13.0 (SPSS Inc., Chicago, IL, USA) for Windows®. The Wilcoxon rank-sum test was used to compare parameters across both study groups and preoperative and postoperative values within study groups. A *P*-value < 0.05 was considered statistically significant.

Results

In total, 50 patients with fibrothoracic disease secondary to symptomatic extraparenchymal restrictive disease who underwent decortication were enrolled in this prospective randomized study: 25 in the electrocautery plus hot compress group (13 females, 12 males); and 25 in the THM group (14 females, 11 males). The mean ± SD age of all patients was 46 ± 1 years (range 25 – 70 years). The numbers of patients in each group who required decortication due to empyema, haematoma or mesothelioma are shown in Table 1.

Preoperative and postoperative Hb, Hct, platelet count, PT and APTT were evaluated (Table 2). There were no significant differences in the preoperative and 24-h postoperative values for any of these parameters in the THM group. In the group that received electrocautery plus hot compress a significant decrease was seen in the postoperative versus preoperative Hb level ($P = 0.049$), and significant increases were observed in the postoperative versus preoperative PT and APTT ($P < 0.001$ for both).

The rate of postoperative blood loss in the first 24 h was significantly lower in the THM group (median 120 ml, range 50 – 175 ml) than in the electrocautery plus hot compress group (median 300 ml, range 250 – 350 ml) ($P < 0.001$). The mean number of post-operative blood transfusion units used was also significantly lower in the THM group compared with the electrocautery plus hot compress group ($P < 0.001$; Table 2).

No infections, systemic allergies or sensitization were observed in patients in either group in the early postoperative period (first 24 h), in the period up to discharge, or in the first month after discharge. None of the patients in either group needed reoperation to control postoperative haemorrhage.

TABLE 1:
Clinical disease characteristics of patients with fibrothoracic disease secondary to symptomatic extraparenchymal restrictive disease who underwent decortication using either electrocautery plus hot compression or thrombin-added haemostatic matrix (THM) for the control of postoperative bleeding

Disease characteristic	Electrocautery plus hot compress ($n = 25$)	THM ($n = 25$)
Empyema	18	15
Haematoma	4	7
Mesothelioma	3	3

Data presented as number of patients.

TABLE 2:
Preoperative and 24-h postoperative blood parameters for patients with fibrothoracic disease secondary to symptomatic extraparenchymal restrictive disease who underwent decortication using either electrocautery plus hot compression or thrombin-added haemostatic matrix (THM) for the control of postoperative bleeding

Blood parameter	Electrocautery plus hot compress (n = 25)	THM (n = 25)	Statistical significance[a]
Haemoglobin, g/dl			
Preoperative	12.8 ± 1.3	12.8 ± 1.08	
Postoperative	11.7 ± 1.2	12.4 ± 1.1	
Statistical significance[b]	P = 0.049	NS	
Haematocrit, %			
Preoperative	42.4 ± 4.1	41.6 ± 5.2	NS
Postoperative	41.1 ± 4.0	39.3 ± 9.1	NS
Statistical significance[b]	NS	NS	
Platelet count, $\times 10^9$ /l			
Preoperative	311.5 ± 41.3	316.4 ± 34.9	NS
Postoperative	307.3 ± 43.4	316.8 ± 34.9	NS
Statistical significance[b]	NS	NS	
Prothrombin time, s			
Preoperative	13.2 ± 0.5	13.3 ± 0.5	
Postoperative	34.2 ± 0.5	13.1 ± 0.6	
Statistical significance[b]	$P < 0.001$	NS	
Activated partial thromboplastin time, s			
Preoperative	33.6 ± 0.8	33.6 ± 0.8	
Postoperative	34.2 ± 0.6	33.2 ± 0.9	
Statistical significance[b]	$P < 0.001$	NS	
Blood transfusion units	2.1 ± 0.7	1.2 ± 0.4	$P < 0.001$
Tube drainage, ml	290.6 ± 35.7	119.5 ± 41.5	$P < 0.001$

Data presented as mean ± SD.
Wilcoxon rank-sum test for: [a]the THM group versus the electrocautery plus hot compress group; [b]preoperative versus postoperative values.
NS, not statistically significant ($P > 0.05$).

Discussion

Thrombin-added haemostatic matrix is composed of absorbable bovine gelatin, which helps haemostasis when applied to bleeding surfaces.[19] The combination of gelatin and thrombin accelerates clot formation when it comes into contact with blood. Studies have revealed that THM has minimal antigenic properties and does not appear to be associated with a heightened risk of immune sensitization.[3,4] Collagen stimulates platelet aggregation, with platelets taking on an adhesive form in the presence of collagen, with the resulting plaque directly causing haemostasis and reducing haemorrhage at the application site. This relationship between platelets and collagen shortens the period of the intrinsic clotting by 60%.[4,20,21] Collagen attracts platelets to the surface of a wound to which it has been directly applied, causing them to precipitate and leading to clot formation.[22] THM not only causes platelet aggregation but also takes part in creating a wide and stable haemostatic plaque structure.[21]

The THM provides haemostasis during and after surgical operations[11,23–26] and has been shown as clinically effective in

controlling haemorrhage after endoscopic sinus surgery in 96.7% of patients, leading to haemostasis within 10 min.[12] Furthermore, no complications or notable side-effects have been observed following THM use.[12] THM has also been used safely in the following procedures: cardiac surgery and in controlling diffuse haemorrhage;[3,5,27,28] in nerve surgery[29] in which haemostasis is difficult to achieve; in multiple skin graft studies;[13] and in patients with liver haemorrhage due to various aetiologies where quite successful haemostasis was achieved and minimal foreign tissue reaction was observed.[30] Successful use of THM has also been reported in orthopaedic surgery,[31] and it can be used effectively in emergency cases.

The present study compared the effectiveness of THM with that of electrocautery plus hot compress in controlling postoperative haemorrhage. THM was more effective in achieving haemostasis than electrocautery plus hot compress in the first 24 h postoperatively. A significant decrease in postoperative drainage and blood transfusion requirements was observed in the THM group compared with the electrocautery plus hot compress group. None of the patients in either group required reoperation to control postoperative haemorrhage.

The risk of postoperative infections at the application site is higher with other local haemostatic agents, e.g. oxidized cellulose, gelatin sponge and bone wax, than with THM.[24,32] No infection was observed in patients in either group in the present study. With the exception of a few cases where there have been slight immune response and tissue reaction,[4,22] no significant side effects have been reported in patients receiving THM, and THM is completely absorbed in approximately 3 weeks to 3 months following application.[21,22,30] Reabsorption of THM takes place through the intra- or extracellular digestion of collagen by inflammatory cells.[21,23] The mechanisms of reabsorption of THM indicate that allergy/sensitization may be a potential problem and this has been reported previously;[33] although no such side-effects were observed in the present study in the first month after discharge.

In conclusion, the present study demonstrated that THM was effective and well tolerated in patients with fibrothoracic disease secondary to symptomatic extraparenchymal restrictive disease who underwent decortication. Compared with electrocautery plus hot compress, THM significantly reduced postoperative blood loss and the need for blood transfusions following decortication.

Conflicts of interest

The authors had no conflicts of interest to declare in relation to this article.

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