Randomised Controlled Trial to Evaluate the Efficacy of TachoComb H Patches in Controlling PTFE Suture–hole Bleeding

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Objective. Suture–hole bleeding is a considerable problem in vascular procedures using polytetrafluoroethylene (PTFE) grafts. This study aimed to study the efficacy of TachoComb® H patches in controlling suture–hole bleeding.

Design. Prospective randomised controlled trial.

Materials and methods. Patients undergoing femoral anastomosis and femoral or carotid patch angioplasty with PTFE grafts were prospectively randomised to TachoComb® H patches or standard compression with surgical swabs.

Results. Twenty four patients were randomised (12 patients in each treatment group). The median time to haemostasis was 300 (range 180–600) s in patients treated with TachoComb® H and 660 (range 180–1200) s in the control group. The log rank test of equality over treatments based on the 22 patients with assessment of time to haemostasis showed statistical significance (\( p = 0.0134 \)). There were no serious complications associated with use of TachoComb® H patches.

Conclusion. TachoComb® H patches were found to be safe and effective for the control of suture–hole bleeding in patients undergoing vascular reconstruction with PTFE grafts.

Key Words: Suture–hole bleeding; TachoComb® H; Polytetrafluoroethylene (PTFE); Efficacy; Haemostasis.

Introduction

Suture hole bleeding is a considerable problem in vascular reconstructive procedures using polytetrafluoroethylene (PTFE) grafts. Traditionally this is managed by compression with surgical swabs and reversal of heparin. Other methods such as application of oxidised cellulose, gelatine sponge, different forms of collagen and glues have also been tried with variable success.

The TachoComb® H patch consists of an equine collagen sponge coated with the haemostatic factors fibrinogen and thrombin. It is a ready-to-use and absorbable haemostatic dressing.

The aim of the study was to compare the efficacy and safety of TachoComb® H patches against standard surgical compression to control the suture hole bleeding from PTFE grafts.

Materials and Methods

A total sample size of 60 patients (30 in each treatment group) was originally planned after a power calculation but as the effectiveness of TachoComb® H was also demonstrated in a similar study, conducted simultaneously, the present study was stopped prematurely and only 24 patients were randomised. Three centres participated in the study contributing 17, 5 and 3 patients, respectively. One patient was excluded prior to randomisation and two more had to be withdrawn because of deviation from study protocol and insufficient data collection, giving a total of 22 patients. Femoral anastomoses and femoral or carotid patch angioplasties were evaluated. The anastomoses and patches were performed using 5–0 or 6–0 prolene sutures.

The study was approved by the local ethics committee, and informed consent was obtained before inclusion. Patients were excluded if the patch length exceeded 8 cm, if fibrin glues or any local haemosthetics were used during the operation or if the patient was allergic to any of the components of TachoComb® H. Patients who did not require additional haemostatic measures on releasing the clamps were also excluded from the study. Patients were randomised by the sealed code envelope method to either treatment with TachoComb® H patches or to standard compression with surgical swabs. The randomization code...
envelopes were opened just before the application of haemostatic measures. The nature of the treatments precluded blinding of the study. Therefore, an independent nurse recorded all the variables assessed.

Patients in the TachoComb® H arm of the study were treated by applying TachoComb® H patches, after moistening with physiological saline. Dosage (the number of patches) used depended on the size of the wound area to be covered. One patch of TachoComb® H is 9.5×4.8×0.5 cm³ in size. It contains collagen from equine tendons, human fibrinogen, human thrombin, bovine aprotinin and riboflavin (to mark the active side). TachoComb® H is produced by Nycomed (Linz, Austria), and it is a further development of the original TachoComb®, where bovine thrombin has been replaced by human thrombin due to concerns of antibody formation against bovine thrombin and transmission of bovine spongiform encephalitis (BSE). The moistened patch of TachoComb® H was applied with the yellow active side onto the wound surface after blood and other fluids were cleansed from the wound area. The patch had to extend at least 1 cm beyond the wound edge and pressure was applied for 3 min. Haemostasis was assessed at the end of this period. If haemostasis was not achieved by this time, pressure was reapplied for another 2 min. If haemostasis was still insufficient, the first patch was replaced with a new one and compression applied for a maximum of 5 min before considering other methods. If a patch became displaced by bleeding during the first 5 min, it was replaced with a new piece. Patients in the control arm received compression with 10×10 cm² surgical swabs. If haemostasis was suboptimal at the end of 10 min then other methods were adopted as necessary.

The main variable measured was the time to haemostasis. Haemostasis was defined as the time when the wound was completely dry or sufficiently dry to complete the operation without additional haemostasis. Survivor functions of time to haemostasis for the two treatment groups were tested by a log rank test using SAS® software. Life time estimates were made based on recordings in one minute intervals from time 3 to 10 min. Recordings of time to haemostasis beyond 10 min were censored. Due to the small number of patients no other statistical analyses were performed. Blood loss during the operation, duration of operation, drain volume, requirement for blood transfusion, surgeons rating of efficacy (very good, good, satisfactory or unsatisfactory), and coagulation parameters were also recorded. Blood loss after release of cross-clamping was measured by weighing the swabs used in the relevant wound, from the time TachoComb® H or compresses were applied until achieving haemostasis. Graft type and size were recorded. Duration of the operation was measured from the time of incision to the completion of skin suture.

Results

Twenty four patients were randomised to give 12 patients in each treatment group of the study. One patient was withdrawn immediately after randomisation (surgical compression group), and one patient had no assessment of time to haemostasis (TachoComb® H group). The mean age of patients was 70.6 (range 55–86) years in the TachoComb® H group and 66.3 (range 51–71) years in the surgical control group. There were no significant differences in any patient or procedural characteristics including the use of antiplatelet agents.

In the TachoComb® H group half a patch was used in two patients, one patch in five patients and two patches in five patients. Postoperative clotting parameters were not altered by application of the patches. There were no instances of intravascular thrombosis or embolism subsequent to the application of TachoComb® H.

The median time to haemostasis was 300 (range 180–600) s in TachoComb® H group and 660 (range 180–1200) s in the surgical compression group (Fig. 1). The log rank test of equality over treatments based on the 22 patients with assessment of time to haemostasis showed statistical significance (p = 0.0134). The survivor
functions of time to haemostasis are illustrated using life table estimates based on the 22 patients with assessment of time to haemostasis (Fig. 2).

Complete haemostasis was achieved within 3 min in 3/12 patients (25%) in the TachoComb® H group and 2/11 patients (18%) in the surgical compression group. In the TachoComb® H group another 3/12 patients (25%) achieved haemostasis after application for another 2 min making a total of 50% haemostasis within 5 min. In the surgical compression group 2/11 more patients (18%) achieved complete haemostasis after additional 7 min, making a total of 36% in 10 min.

No statistical analyses were performed for the secondary endpoints. However, the mean blood loss after cross-clamping as well as the mean drain volume appeared to be substantially reduced in the TachoComb® H group despite no difference in the mean duration of surgery (Table 1).

A total of 16 adverse events occurred in nine patients in the TachoComb® H group and 12 events were recorded for 8 patients in the standard compression group. The most frequent adverse events were peripheral oedema, fever, post-operative haemorrhage, and post-operative wound infection. The adverse events were equally distributed between the two treatment groups except fever, which developed in 4 TachoComb® H patients and in only one patient in the standard compression group. Adverse events classified as serious developed in two patients in the TachoComb® H group and in two patients in the standard compression group. One TachoComb® H treated patient died of acute renal failure. None of the serious adverse events were considered related to test treatment, and only one non-serious adverse event (pyrexia) was considered to be possibly related to the test treatment.

Discussion

Collagen patches may be effective for delivering drugs locally. In this study collagen was used to provide fibrinogen and thrombin locally at the site of bleeding. Upon contact with fluid the clotting factors of TachoComb® H dissolve and form a fibrin network, which glues the collagen sponge to the wound surface. Combining the clotting factors in a collagen patch provides a high concentration of clotting factors at the site where it is specifically needed. The haemostatic effectiveness of using TachoComb® H has previously been proven in clinical studies.4,5 Liquid fibrin glue preparations are likewise found to be effective in achieving haemostasis.6–8 However, combining fibrin glue components in a collagen patch facilitates ease of application.

Despite the small number of patients enrolled, the present study showed that TachoComb® H significantly reduces the time to haemostasis. Haemostasis was achieved within 5 min in 50% of the patients in the TachoComb H group compared to only 36% within 10 min in the control group. In addition both intra- and postoperative bleeding appeared to be substantially reduced in the TachoComb® H arm.

TachoComb® H was well tolerated and none of the serious adverse events observed in TachoComb® H treated patients were considered related to test treatment. The higher incidence of fever in TachoComb® H treated patients may be coincidental as fever
has not occurred more frequently than in control patients, according to Nycomed safety reports.

In conclusion, TachoComb\textsuperscript{®} H was found to be safe and effective for control of suture hole bleeding in patients undergoing vascular reconstruction with PTFE grafts.

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**References**


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