Use of gelatin powder added to rifamycin versus bone wax in sternal wound hemostasis after cardiac surgery

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Abstract

Bone wax is the substance which has been used for hemostasis in different surgical fields for up to one hundred years and historically in our center to prevent sternal bleeding and subsequent complications. Recently, reabsorbable gelatin powder has come into use. Up to now there are no clinical studies that compare these two substances. Between 1st January and 31st December 2004, 1249 subsequent patients have been operated on for different cardiac surgical procedures in our center, of them 557 were enrolled in a randomized perspective monocentric study. They have been divided into two similar subgroups: one treated with swine gelatin plus rifamycin (group one) and the other with bone wax (group two). The two hemostatic products have been applied just after the sternotomy and before the chest closing. Each patient was evaluated for bleeding, sternal infections and was followed-up for two months for bone and wound healing. Postoperative bleeding at the tenth hour was 315 ml±269 (mean±S.D.) in the first group and 395 ml±265 in the second (P<0.001). In the 10th–20th hour interval time bleeding was 120 ml±74 and 205 ml±132, respectively (P<0.001). Total bleeding was 415 ml±87 in group one and 580 ml±150 in group two (P<0.001). Chest reopening for bleeding not due to surgical problems was carried out in 14 patients (4.7%) (group one) and 19 (7.3%) (group two) (n.s.). Superficial sternal wound infection occurred in two patients (0.7%) in group one and three patients (1.1%) in group two (n.s.). There were no deep sternal wound infections. Bleeding was significantly higher in patients treated with bone wax compared to those with absorbable gelatin plus rifamycin.

Keywords: Sternal bleeding; Sternal infection; Swine gelatin

1. Introduction

Excessive blood loss with heavy transfusion requirements seems to be a common risk factor for wound infections and subsequent sternal dehiscence [1,2].

The spectrum of complications in healing of sternotomy wounds ranges from simple seromas to dehiscence of all layers, with instability of the thorax, and to severe osteomyelitis, purulent pericarditis and mediastinitis [1–3]. Surgical site infection prevention is really important for postoperative morbidity and mortality reduction so that specific guidelines have been published by the Atlanta Center for Disease of Control and Prevention (CDC) [4].

In heart surgery the sternal wound is a vulnerable site especially in some procedures such as mono-bilateral internal thoracic artery harvesting in which the whole blood supply is sacrificed [5]. The bone seems to be a low vascularized tissue on its own, showing low sensibility to systemic antibiotic therapy [2,3]. Sternal wound healing may be impaired by osteoporosis, or risk factors such as chronic obstructive pulmonary disease, smoking, obesity, chronic renal failure, diabetes [2].

Bone wax has been used since the turn of the century as a physical barrier to aid hemostasis on the surface edge of surgically altered bone following various operative procedures [6]. In cardiothoracic surgery it is currently used on the sternotomy edges, plugging exposed osseous canals that are bleeding. Wax use, presently, represents a substance which is not absorbed by the spongiosa giving off some noxa that may give rise to bacterial implantation. Indeed the wax will never be absorbed, making a mechanical resistance to sternal ossification and producing a foreign body giant cell reaction [1,6–8].

Absorbable gelatin powder (Spongostan®) is a hemostatic product constituted by swine origin protein which has recently come into use in the heart surgery field. It adheres to the hemorrhage spot and, due to its uniform porosity, absorbs roughly 45 times its proper weight. When implanted in the tissues, it is absorbed in a period of two weeks [9].

Some authors reported that topical antibiotic application to the sternal edge in a vehicle of powdered gelatin reduces sternal infections [10]. As pointed out by Halasz, topical
antibiotics, especially in a dry or powdered form, achieve much higher local wound concentrations than do systemic ones, and this high antibiotic concentration persists for several hours after wound closure [11]. We choose rifamycin in combination with gelatin because, in our institution, sternal infections are usually due to Staphylococcus aureus which is sensitive to it.

2. Methods

Between 1st January and 31st December 2004, 1249 patients have been operated upon in our center, of them 557 were randomized and prospectively enrolled following the entry criteria: patients 2 ASA Classification, male and female. Exclusion criteria: patients on alendronates treatment, calcium-phosphate disorder, chronic renal insufficiency, re-do operations. Five hundred and fifty-seven patients so recruited were divided into two subgroups. The first (297 patients) was treated with gelatin (Spongostan\textsuperscript{®}), the second (260 patients) with bone wax (Johnson & Johnson). There was no control group because bone wax is extensively and historically used in our center to prevent sternal bleeding. Gelatin preparation technique: 1–2 g of the soluble powder is diluted in 2–3 ml of saline, then 1 cc of rifamycin is added to the semisolid compound that can be mixed and spread by a simple digital pressure on the sternal section surfaces, just after sternotomy and at the end of the operation, before chest close-up (Fig. 1).

All patients received 24-h prophylactic systemic antibiotic therapy (cefuroxim 2 g tid). Each patient was evaluated for bleeding at the 10th and 20th hour after the chest closure and the total amount of blood collected until the chest drainage removal was considered. The amount of blood (concentrated erythrocytes) transfused in the postoperative period until the discharge from the hospital was also evaluated. Follow-up data were recorded from clinical investigations at the 20th, 30th and 60th postoperative days and they were set on wound healing and superficial (anterior to the sternum plate with sternal stability) or deep sternal infections (posterior to sternal plane with or without bone stability).

The study wants to verify whether reabsorbable material like gelatin plus antibiotic can prevent sternal bleeding or infections compared to substances not reabsorbable, nor mixable, like wax.

2.1. Statistical analysis

To test whether the differences in the endpoint between the two groups were significant, the \(\chi^2\)-test for categorical variables and two-sample \(t\)-test for continuous variables were used. As the observed number of superficial sternal infections was very low, the statistical test was based on the Poisson distribution. To account for multiple testing, the Bonferroni adjustment was also applied. \(P<0.05\) was considered significant.

3. Results

A total of 557 patients were enrolled in the study. They were divided into two groups: one treated with swine gelatin plus rifamycin (297 patients) and the other treated with the traditional treatment by bees wax (260 patients).

The demographic characteristics of the two groups are similar as for the risk factors and the surgical procedures, and cardiopulmonary bypass interval time (Table 1). Urgent procedures were 11% in the first group and 16% in the second group.

Bleeding in the first 10 h after the sternal closure was 315 ml \(\pm\) 269 (mean \(\pm\) S.D.) in the first group (treated with gelatin) and 395 ml \(\pm\) 265 in the second group (treated in the traditional manner with bees wax) (Table 2). Bleeding from the 10th–20th hour was 120 ml \(\pm\) 74 and 205 ml \(\pm\) 132, respectively. Total blood collected until the drainage tube’s removal was 415 ml \(\pm\) 87 and 580 ml \(\pm\) 150 in the first and second group, respectively.

In summary, treatment with gelatin significantly reduced bleeding within the first or within the next 10 h (\(P<0.001\)). Total bleeding was also significantly reduced by gelatin (\(P<0.001\)).

Chest reopening for bleeding was carried out in 24 patients (8%) in the first group and 31 (12%) in the second group, but the difference was not statistically significant. A surgical leakage was detected in 10 patients (41.6%) and in 12 patients (28.7%), respectively. Diffuse bleeding without any surgical direct source was found in 14 patients.
Table 1
The demographic characteristics of the two groups are similar as for the risk factors and the surgical procedures

<table>
<thead>
<tr>
<th>Type of Group</th>
<th>G1 (Gelatin)</th>
<th>G2 (Wax)</th>
</tr>
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<tbody>
<tr>
<td>Age years (mean ± S.D.)</td>
<td>63 ± 3</td>
<td>62 ± 6</td>
</tr>
<tr>
<td>Urgent procedure</td>
<td>33 (11%)</td>
<td>42 (16%)</td>
</tr>
</tbody>
</table>

Risk factors:
- Systemic arterial hypertension: 37% vs. 38%
- Diabetes: 25% vs. 26%
- Hypercholesterolemia: 23% vs. 28%
- COPD: 12% vs. 14%
- Vasculopathy: 10% vs. 16%
- Renal insufficiency: 5% vs. 9%
- Hepatic insufficiency: 6% vs. 7%
- Antiaggregant therapy: 63% vs. 58%
- Type of surgery:
  - Aorta: 8% vs. 10%
  - Single valve aortic: 16% vs. 13%
  - Single valve mitral: 4% vs. 5%
  - CABG: 54% vs. 52%
  - CABG – valve: 12% vs. 13%
  - Others: 6% vs. 7%
- CABG surgery:
  - IMA single harvesting: 93% vs. 91%
  - IMA double harvesting: 5% vs. 6%
- Surgery on cardiopulmonary bypass: 96% vs. 94%
- Mean cardiopulmonary bypass time (min): 104 ± 53 vs. 115 ± 46

((58.4%) and 19 patients (61.3%), respectively (difference not significant).

There was a lower blood transfusion requirement in the first group compared to the second: 450 ml ± 45 vs. 690 ml ± 63 of concentrated erythrocytes (P < 0.001).

After a two-month follow-up, surgical superficial infections were detected in two patients (0.7%) in the first group and in three patients (1.1%) in the second group (difference not significant). No deep sternal infections occurred.

4. Discussion

The present study is to confirm that gelatin powder added to rifamycin can decrease sternal bleeding, infection rate, favoring sternal ossification, compared to the use of bees wax.

Recently many issues have been reported about the numerous complications that may arise: Jennings and colleagues report angiosarcoma growth related to foreign material long-time retention [7]. They, in a literature review, show that implanted foreign material like wax should produce a giant cell reaction which may lead to any form of sarcoma induction in humans. Sorrenti et al. report that the use of purified bees wax in the human tibia is correlated to giant cell formation which removes wax-forming ectopic bone, fibrous reaction that could prevent osteosynthesis [12]. The Authors conclude that it should be used sparingly. Harjula and Jarvinen say that avoidance of excessive application of bone wax is important to prevent sternotomy dehiscence [1]. Difficult calcification was also demonstrated by Shuller et al. on a mandibular reconstruction plate fixed with bone wax: radiographic and histology study showed bone resorption [13]. That the liberal use of wax really increases the risk of mediastinitis was also reported by Bhatti and Dunning [8].

Swine gelatin powder is different from wax because it is reabsorbable, mixable and increases ossification. Also gelatin scaffold works as a cell delivery system when hyaluronic acid is added. This compound helps chondrocytes cultures to proliferate with matrix production and bone ossification. As assessed, gelatin is characterized by the possiblity to be mixed with antibiotic. Vander Salm et al. underline low sternal infection rate (0.45%), when added to vancomycin compared to 3.6% of the control untreated group [10]. This is due to the high antibiotic concentration kept by the gelatin sponge. Goldmann et al., comparing the prophylactic use of systemic antibiotic, show significant difference between high wound infection rate in patients with no detectable serum antibiotic level after the operation, and low infection rate in patients with a detectable serum antibiotic level [14]. This observation raises the question as to whether the use of topical antibiotic would increase local concentration and be more beneficial. In our series, infections are very low and differences not significant. What we can assess is that local antibiotic concentration decreases infection rate, although we don’t know how much systemic therapy may help, since all our patients are treated with 24-h prophylactic antibiotic therapy. The only infections that spread were superficial and due to possible contamination (Staph. epidermidis).

The most relevant result shown in this study is the significant cumulative, postoperative bleeding difference between patients treated with gelatin sponge (415 ml ± 87) vs. patients treated with bees wax (580 ml ± 150) at the same time interval. These differences may be explained by the two compounds’ different behavior: gelatin powder acts by increasing its volume once it has entered the bone pores. In so doing it completely fills the spongiosa close to the sternal cat edges resulting in a perfect cast [18]. Bone wax fills the spongiosa only with the given digital pressure which is different and not constant. Because of this all the pores may result in not being completely occluded because of air-trapped bubble counterpressure. Among patients who did not undergo chest reopening because they didn’t meet the reopening criteria [15], we don’t actually know what the amount of blood loss is due only to the sternum, or to mediastinal vascular bed mild leakage. On the other hand, we know that huge blood losses come from the sternum when, sometimes, it is left open for postoperative heart enlargement due to insufficienty. For this reason we can say that when the chest is closed, the main source of

<table>
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<tbody>
<tr>
<td>Bleeding 0–10th h</td>
<td>315 ml ± 269</td>
<td>395 ml ± 265*</td>
</tr>
<tr>
<td>Bleeding 10–20th h</td>
<td>120 ml ± 74</td>
<td>205 ml ± 132*</td>
</tr>
<tr>
<td>Total bleeding</td>
<td>415 ml ± 87</td>
<td>580 ml ± 150*</td>
</tr>
<tr>
<td>Chest reopening</td>
<td>24 patients (8%)</td>
<td>31 patients (12%)</td>
</tr>
<tr>
<td>– surgical bleeding</td>
<td>10/24 (41.6%)</td>
<td>12/31 (38.7%)</td>
</tr>
<tr>
<td>– diffuse bleeding</td>
<td>14/24 (58.4%)</td>
<td>19/31 (61.3%)</td>
</tr>
<tr>
<td>Superficial sternal wound infection</td>
<td>2 patients (0.7%)</td>
<td>3 patients (1.1%)</td>
</tr>
<tr>
<td>Deep sternal wound infection</td>
<td>0 patients</td>
<td>0 patients</td>
</tr>
</tbody>
</table>

*P < 0.001.
postoperative bleeding comes from the sternum. All the other variables that could interfere with the study results have been checked and corrected; among the enrolled patients there were no patients with hemophilia or congenital disorders. As for acquired blood clotting problems due to drugs or prolonged bypass time, multiorgan failure or infection, patients were surgically treated whenever clotting tests were correct. Also, patients treated with anticoagulants or fibrinolytic agents are postponed. Coagulation interference due to bypass was almost the same in the two groups because the surgical technique and average bypass time were very similar in the two groups (Table 1). Even risk factors that may interfere with coagulation, such as renal or hepatic failure, were almost equal in both groups (Table 1). Operative ACT control was checked and kept at the usual level with standard heparin administration. Complete neutralization of postoperative heparin rebound effect was reached with a continuous 25 mg/h protamine i.v. infusion during the first six operative hours.

To summarize, the present study shows two comparable groups in which all the preoperative discoagulopathies were similar, postoperative alterations of coagulation parameters (ACT, PT, aPTT, platelets count) were corrected, while bleeding amount during the first 20 postoperative hours is significantly in favor of the first group. For this reason we can assess that gelatin powder played an important role in limiting postoperative sternal bleeding and in reducing blood transfusion requirement.

5. Conclusions

Blood saving is very important nowadays, when blood transfusion requirement is highly cost effective in the hospital budgets. For this reason bone wax usage has been completely cancelled from our protocols, while gelatin powder plus antibiotic is specifically recommended in selected patients with decalcified sternum, double mammary harvesting, diabetes, multiorgan failure, in whom the risk of bleeding could interfere with good patient outcome.

References