A Pilot Study of the Effects of Vivostat Patient-derived Fibrin Sealant in Reducing Blood Loss in Primary Hip Arthroplasty

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Summary: A pilot study evaluated the effectiveness of Vivostat patient-derived fibrin sealant in reducing blood loss in patients who underwent primary hip arthroplasty. Eighty adult patients undergoing elective surgery were randomized to receive either Vivostat sealant or control (no additional hemostatic treatment). Patients allocated Vivostat sealant donated 120 mL of blood, which was then processed perioperatively to produce a fibrin sealant that was applied to the bleeding wound surfaces just before closure. Transfusion requirements, blood loss during surgery, drain volumes, and daily hematocrit and hemoglobin levels were measured. Hospitalization times, adverse events, and postoperative wound complications were also monitored. Blood loss during surgery and wound drainage volume was lower in the Vivostat group than in the control group, although the differences were not significantly different. Transfusion requirements (median, 270 mL of packed red blood cells) and hospitalization times (both median 7 days) were the same for both groups. No adverse events related to the use of Vivostat occurred. There were indications of a possible reduction in the incidence of postoperative wound oozing (15% vs 25%) and hematomas (6% vs 11%) with the use of Vivostat compared with the control group, although differences were not statistically significant. In conclusion, in this pilot study, use of Vivostat patient-derived fibrin in hip arthroplasty was not associated with a significant reduction in blood loss. Further studies, with larger numbers of patients, may be warranted to investigate a possible benefit of Vivostat in reducing postoperative wound complications.

Key Words: Fibrin sealant—Arthroplasty—Hip surgery—Surgical blood loss—Randomized clinical trial.

Hip arthroplasty is associated with significant blood loss. It is important that surgical blood loss is managed as effectively as possible, avoiding the risks from the blood loss itself and also from the infection and immunological risks of allogenic blood transfusion. Interventions that may be used to reduce blood loss include hypotensive anesthesia, autotransfusion, and pharmacological interventions such as aprotonin, aminocaproic acid, and synthetic vasopressin (desmopressin) (1). Fibrin sealants are effective hemostats and are used in many surgeries to reduce both intraoperative and postoperative blood loss (2) and have the potential for reducing blood loss in patients who undergo hip arthroplasty. Although clinical trials in patients who undergo knee arthroplasty have demonstrated the benefits of fibrin sealants (3,4), there are no previous published studies on the effects on the use of fibrin sealants in patients with hip arthroplasty.

The Vivostat system (Vivolution, Denmark, Birkeroed) is an automated medical device for the preparation and application of patient-derived fibrin sealants within 30 minutes from a donation of 120 mL of blood (5). Vivostat-derived sealant is delivered with a controllable, low-pressure, nonblocking spray pen, allowing precise application to bleeding sites (6). Vivostat has been demonstrated to be an effective primary hemostat in a range of surgical procedures (7–9); however, it has not previously been evaluated in patients with hip arthroplasty.

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This clinical pilot study evaluated the use of Vivostat-derived sealant in reducing blood loss and the need for transfusion in patients undergoing elective primary hip arthroplasty operations. The purpose was to gather information on the effect of Vivostat on a range of quantifiable performance parameters, so that endpoints and sample numbers could be chosen for a subsequent, appropriately statistically powered study.

METHODS

Patients

The study was a prospective, randomized, open-label study in patients (age 18 years) undergoing elective primary hip arthroplasty surgery in one Danish hospital. The study was conducted within the current laws of Denmark.

Eighty patients were recruited into the study. All patients gave informed consent and the local ethics committee approved the study. No patients were excluded due hemophilia or because the surgeon thought that a donation of 120 mL of blood was inappropriate (for whatever reason).

Study Procedures

Patients were randomized to either the Vivostat group or the control group (no topical hemostatic treatment) when the patients arrived in the operating suite and opened an envelope containing details of the allocated treatment group (a computer-generated random sequence was used).

Patients allocated to receive Vivostat had 120 mL of blood drawn just before surgery directly into the preparation unit of the Vivostat system. The Vivostat-derived fibrin sealant was then prepared and applied in accordance with the manufacturer's instructions for use.

The surgeries in both groups were conducted according to normal practices; however, although electrocoagulation or mechanical means could be used for hemostasis during the surgery, topical hemostatic drugs or materials (except for Vivostat) were not allowed. No other methods of preventing blood loss (e.g., tranexamic acid, aprotinin) were used in those patients allocated to receive Vivostat. Vivostat-derived sealant was applied to the bleeding surgical wound surfaces after an appropriate attempt to dry the surface before application of Vivostat before closure, in an attempt to stop or prevent bleeding. The surgeons were asked to dry the surface to which the Vivostat was to be sprayed as much as possible before application. Placement of surgical drains and postoperative care were performed according to normal procedures.

Assessments

Transfusion requirements (packed red blood cells) during and after the operation were recorded. Intraoperative blood loss was monitored by standard operative procedures. Drain volumes were recorded for the first 2 days postoperatively, after which time they were removed. Hematocrit and hemoglobin levels were determined from blood samples taken daily. The surgical wound was inspected daily during hospitalization and follow-up. Adverse reactions were recorded during or after surgery, and their possible association with the use of the Vivostat system or the derived sealant considered by the investigators.

Statistical Analysis

Patients were excluded from the analysis if they were allocated to the Vivostat group, but did not have Vivostat applied (for whatever reason). As we were unaware of any previous data on the use of fibrin sealants in preventing blood loss in patients with hip arthroplasty, no information was available on which to base calculations for predicting sample size. It was the intention to use information gathered in the study to assess sample numbers for an appropriate statistically powered extended study.

Descriptive statistics was used to summarize the data. Continuous numerical data were compared between groups by unpaired *t* tests if data distributions did not differ significantly from a normal distribution (before or after log transformation); otherwise the nonparametric unpaired Mann-Whitney *U* test was used. Categorical data were analyzed by using the Fisher's exact test. Adverse events and reasons for withdrawals were tabulated. Analysis was performed by using SPSS software version 12.0.1 (SPSS Inc., USA).

RESULTS

Eighty patients were recruited into the study. Of these, 44 were randomized to the Vivostat group and 36 to the control group. Eleven patients (all Vivostat group) were excluded from the analysis as no Vivostat was applied during the surgery as intended; reasons included machine malfunctions, operator errors, not producing the fibrin on time, and forgetting to apply the sealant. Patients in each group were evenly

matched with regard to demographics and operation types (Table 1).

Data on the measured variables (blood loss, drain volume, transfusion requirements, hematocrit and hemoglobin, and hospitalization) and details of statistical analyses are summarized in Table 2 and Fig. 1. Changes in hemoglobin and hematocrit over time are shown in Fig. 1. Eighteen patients (55%) in the Vivostat group and 22 patients (56%) in the control group received autotransfusion; the average volumes of blood saved by autotransfusion were similar and not significantly different.

The mean volume of fibrin produced from each donation of blood was 5.0 ± 0.7 SD mL (range, 3.4–6.1). No problems occurred during application that were not rectified satisfactorily and quickly by on-site personnel. Application of the Vivostat sealant to the surgical wound was without problems. The wound bleeding, categorized before, immediately after, and a minute after application of the Vivostat sealant are shown in Fig. 2. There were no adverse events associated with the use of Vivostat.

There were no differences in hospitalization times between groups; the median postoperative hospital stay was 7 days in both groups. Inspections of the wounds during hospitalization identified several patients in whom wounds continued to ooze or hematomas developed. At the time of discharge, hematomas and oozing occurred at a lower frequency in the Vivostat group compared with the control group; however, numbers were low in both groups and there were no statistically significantly differences.

TABLE 1. Patient Characteristics

	Vivostat	Control
Number of patients (male/female)	33 (12/21)	36 (15/21)
Mean age, years (SD)	67.1 (8.9)	63.1 (10.9)
Mean weight, kg (SD)	75.9 (13.3)	77.4 (13.8)
Mean height, m (SD)	1.70 (0.08)	1.70 (0.09)
Mean body mass index	26.3 (4.1)	26.6 (3.5)
Operation type, n (%)		
Uncemented	24	28
Hybrid	8	8
Cemented	1	0

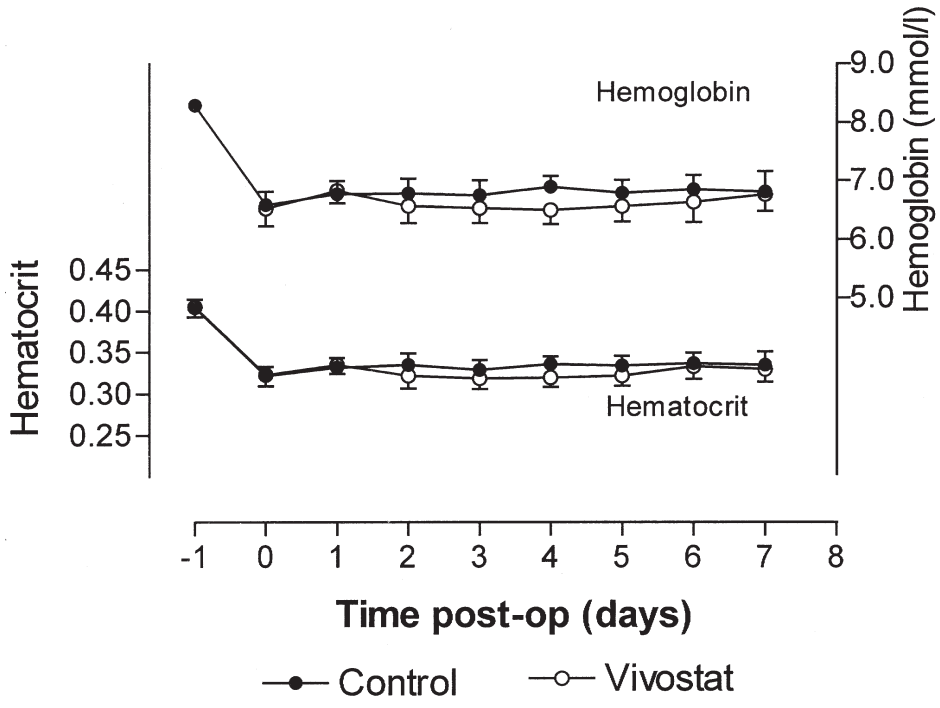

FIG. 1. Pre- and postoperative hematocrit and hemoglobin levels (mean ± 95% confidence intervals).

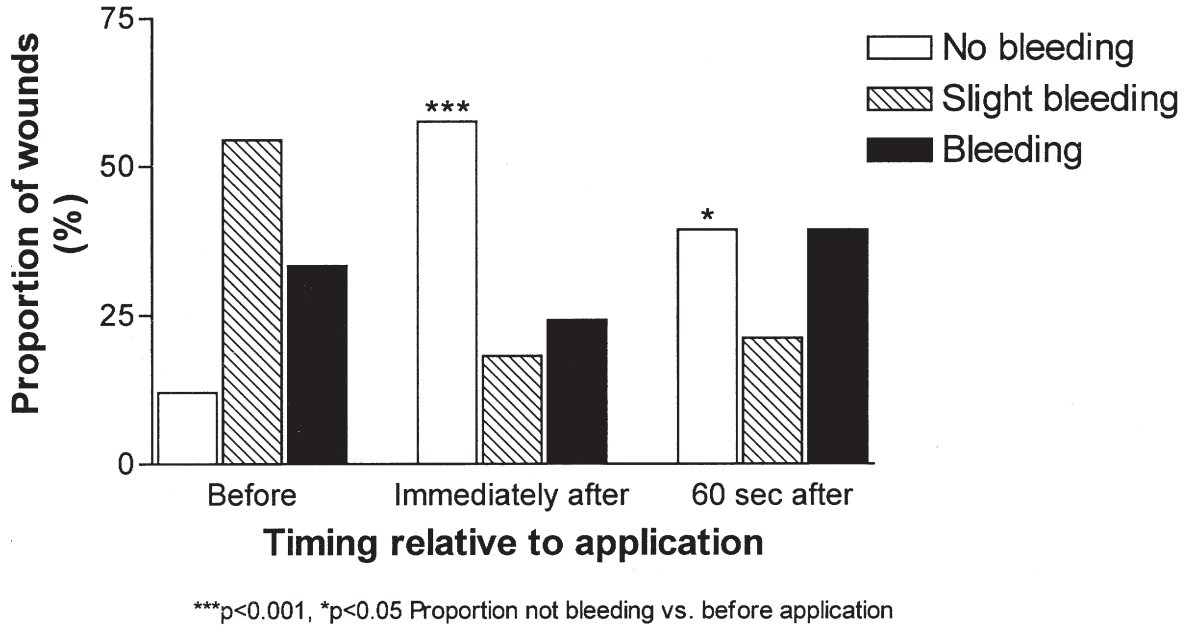

FIG. 2. The effect of Vivostat application on wound bleeding.

DISCUSSION

This pilot study evaluated the feasibility of using Vivostat patient-derived sealant to reduce blood loss in patients who undergo hip arthroplasty. Results showed that application of Vivostat was straightforward and was not causally associated with any adverse events. However, compared with controls, the use of Vivostat did not reduce blood loss by a significant amount, as determined by drainage volumes, transfusion requirements, or changes in hematocrit or hemoglobin levels. The reduction of total blood loss obtained with Vivostat (loss during surgery and in drains) was of a similar magnitude to the volume donated by the patient for preparation of the fibrin sealant.

Vivostat has been shown previously to be an effective hemostat in other surgeries and to reduce the time to hemostasis compared to oxidized-cellulose (Surgicel, Johnson and Johnson, New Brunswick, NJ) (7) in multiple surgical procedures, or in untreated controls in sternal marrow bleeding during coronary artery bypass graft surgery (9); however, in these studies the size of the wounds was generally smaller and the bleeding was probably less profuse than in the present study. In the present study, Vivostat was highly effective in reducing the bleeding immediately on application if the bleeding was categorized as slight, but was less effective in more profuse bleeding (Fig. 2). The effect on some of these wounds appeared to be short-lived. Nevertheless, Vivostat significantly increased the proportion of wounds that were not bleeding, both immediately and 60 seconds after application, compared with the proportion before application. It is possible that by modifying the mode of application, to allow greater volumes of Vivostat to be applied more quickly, more effective hemostasis could be achieved. The drawback of this, however, is that the area of coverage would be reduced.

Reduction of hospitalization time is an important aim of any new treatment, especially when justifying the use of expensive treatments such as fibrin sealants. The present study found no significant benefit of Vivostat over control in this regard, although there was an indication of a

TABLE 2. Performance Variables

	Vivostat (n=33)	Control (n=36)	p Value
Blood loss during surgery, mL (95% CI)	541 (446–625)	609 (524–694)	0.30*
Mean drain volume, mL			
Day 0 (day of operation)	257	330	
Day 1	240	264	
Day 2	219	203	
Days 0–2 (95% CI)	716 (693–889)	791 (617–814)	0.29*
Patients without transfusions, n (%)	17	15	1.0†
Median volume packed red blood cells transfused, mL (25–75% quartile)	271 (0–580)	272 (0–597)	0.71§
Median hospitalization time: days (25–75% quartile)	7 (6–7)	7 (6–8)	0.43‡
Patients with:			
Oozing, n (%)	5 (15%)	9 (25%)	0.38†
Hematoma, n (%)	2 (6%)	4 (11%)	0.68†

CI = confidence interval.

*Two-tailed *t* test.

†Fisher's exact test.

‡Two-tailed Mann-Whitney *U* test.

§p value less than 0.05 was considered statistically significant.

possible benefit of Vivostat in reducing wound complications. Patients treated with Vivostat had a lower incidence of wound hematomas or oozing on examination than controls, which was still present at the time of discharge. Although the long-term effects of this were not evaluated in this study, oozing and hematoma formation may be the source of retrograde infection of the surgical site, leading to increasing morbidity of the patients. Hematoma has been shown to be a significant predictor of superficial surgical site infection (odds ratio 11.8), and by implication an increased risk of deep wound infection, in patients after total hip and knee arthroplasty (10). Further trials of Vivostat may be warranted, with larger number of patients, for evaluating its influence on postoperative wound complications such as oozing and hematoma formation.

In summary, this pilot study in patients who undergo hip arthroplasty was unable to demonstrate clinical benefit for Vivostat with regard to blood loss or the need for transfusion compared with patients who did not receive Vivostat. Nevertheless, there were indications of a possible effect in reducing the incidence of wound oozing and hematomas. The results of this study will assist in the design of larger and appropriately statistically powered clinical studies to evaluate the performance of Vivostat in patients with hip arthroplasty.

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