

Pre-operative Amicar (Epsilon-Aminocaproic Acid): Does it reduce total blood loss in lumbar pedicle screw spinal fusion?

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Citation

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Abstract

Objective and Importance: Chronic low back pain and radiculopathy due to spondylolisthesis and spinal instability are frequent indications for decompressive lumbar laminectomy and spinal fusion with pedicle screw fixation. This procedure frequently involves a great deal of intra-operative blood loss for the patient. The objective of this study was to determine if pre-operative administration of Amicar (Epsilon-Aminocaproic Acid) reduced blood loss among patients who underwent open decompressive lumbar laminectomy and spinal fusion surgery. **Study variables:** 19 randomly selected patients were consented to receive Amicar preoperatively. Their intraoperative estimated blood loss as well as the Jackson-Pratt drain output were analyzed and compared to a matched group of retrospectively selected patients from our records. **Technique:** Data obtained from our patients were analyzed for various factors. After obtaining informed consent, patients involved in the groups were given one adult dose (5 gr IV) prior to surgery. The two groups were then compared to determine if Amicar had an effect on the EBL and other variables that might be related to blood loss. **Conclusion:** Although the Amicar-treated patients had lower amounts of blood loss and blood given, the differences were not significant. The non-significant differences could be due to the large observed variability for EBL and blood given in both groups and the small sample sizes for the two groups.

INTRODUCTION

Symptomatic spinal stenosis and instability are frequent indications for decompressive lumbar laminectomy and spinal fusion with pedicle screw fixation. This surgery frequently involves significant intra-operative blood loss. To help minimize the use of allogenic blood products which risks include infectious diseases, immunosuppression, transfusion reactions, and graft-versus-host disease, many techniques are employed to limit intraoperative blood loss. These include: optimization of preoperative coagulation function, intraoperative anesthetic technique, proper patient positioning, maintenance of normothermia, acute normovolemic hemodilution, intraoperative and postoperative blood salvage, controlled hypotension, and finally pharmacologic manipulation of the coagulation cascade with TA, aprotinin, DDAVP, rFVIIa. In this study, we hypothesized that administration of Amicar (epsilon-aminocaproic acid) in the pre-operative setting, would reduce total blood loss and thus reduce potential complications due to excessive blood loss.

OBJECTIVE

Amicar (Epsilon-Aminocaproic Acid, EACA) was pre-operatively administered to patients undergoing lumbar laminectomy with postero-lateral pedicle screw fusion (PLF) in order to determine if it had any effect on intra-operative blood loss.

STUDY DESIGN

This project's design was similar to a matched-cohort analysis, including both retrospective as well as prospective patient group analysis. For the prospective arm of the study, we recruited 19 patients who were scheduled to undergo a single level fusion using the standard clinical criteria. We then counseled them and consented them to receive 5 grams of Amicar in the holding room immediately prior to surgery. Exclusion criteria included peripheral vascular disease, renal disease, heart disease, any prior cardio-vascular intervention, history of stroke, any hematologic condition, prior lumbar surgery, and documented allergic reaction to the medication. We retrieved and matched from our files a control group of

nineteen patients who had undergone the same one-level lumbar fusion with pedicle screw placement. All patients underwent surgery by the senior author (AN).

MATERIALS/ METHODS

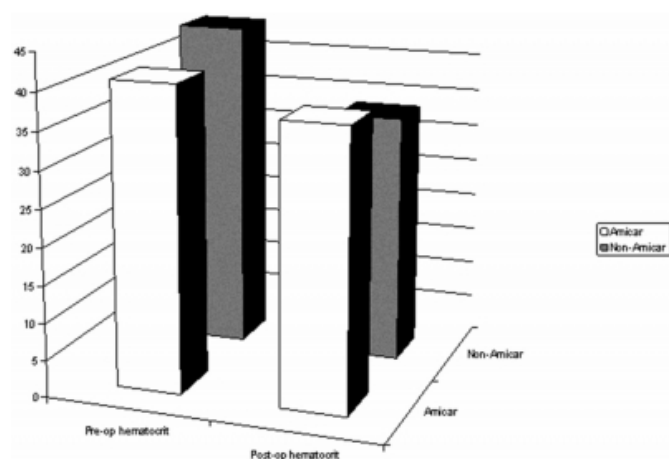
Patients between 21-80 years old were analyzed for the following factors: sex, age, length of surgery, EBL, fluids given, pre- and post-operative hemoglobin and hematocrit levels, blood transfusions, urine output, JP drain output, and days in the hospital. After obtaining informed consent, patients involved in the prospective study were given a single adult dose bolus (5 gr IV) in the immediate pre-operative period. No other dosages of the drug were given after this initial bolus. The two groups were then compared to determine if Amicar had an effect on the EBL and other variables that might be related to blood loss. Either the two-sample t-test (if variable was observed to be normally distributed in both groups) or the Wilcoxon rank sum test was used to compare the two groups on the quantitative variables. The chi-square test was used to compare them on sex distribution. A multiple regression analysis with a stepwise selection of variables was used to determine independent significant predictors of blood loss.

RESULTS

The two groups differed significantly on age, pre-op hemoglobin and hematocrit, post-op hematocrit, changes in hemoglobin and hematocrit before and after surgery, JP drain output post-op day 1 and days in the hospital (Figure 1).

Figure 1

Figure 1: Graph showing Comparison of pre-op hematocrit and post-op hematocrit in Amicar and Non-Amicar treated Patients

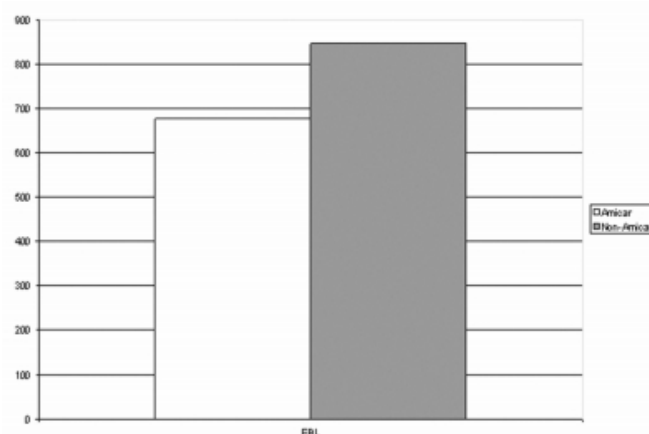


The controls were younger, had larger average changes in

hemoglobin and hematocrit levels (before and after surgery) and JP-day 1 values, and spent longer time in the hospital. Although the Amicar-treated patients had lower amounts of blood loss and blood given, the differences were not significant ($p=0.31$) (Figure 2).

Figure 2

Figure 2: Graph showing Estimated Blood Loss among Amicar and Non-Amicar Treated Patients



The independent significant predictors of blood loss (EBL) were shown to be the amount of fluid given and urine output. Additionally, the more fluid given and the greater the urine output, the greater the blood loss (EBL).

DISCUSSION

Intraoperative blood loss in posterior lumbar spine fusion results largely from injury to the internal venous plexus which covers the spinal floor (10). Evaluation of blood loss in this procedure is largely subjective and further complicated by significant blood loss occurring after wound closure which highlights the importance of measuring both intraoperative and postoperative blood loss to ascertain the effectiveness of various techniques used to limit hematologic complications (8). Mean loss of blood per vertebral level in this procedure has been reported to be as high as 503mL (6). Allogenic blood transfusion is less than ideal due to its associated risks of allergic reactions, graft vs. host disease, hemolytic reactions, increased infection rates, and disease transmission (13). In a study by Cha et al, the efficacy of using preoperatively procured autologous blood in patients undergoing posterior lumbar surgeries was investigated. This technique decreased the amount of allogenic blood used, but was inadequate without the use of other conservation techniques (3). Additional preoperative techniques such as hemodilution by the deliberate lowering of hematocrit with

crystalloid have also been shown to be efficacious in lowering the number of transfusions needed following spine surgery (5). Mandel et al. assessed the effectiveness of hypotensive anesthesia to lower mean arterial pressure in various spinal surgeries including spinal fusions and found that a decrease of blood pressure by approximately 20 mm Hg systolic could result in a decrease in intraoperative and postoperative blood loss by 50% (9). Because of the complications occurring with the use of hypotensive anesthesia such as impaired renal function and cerebral vascular accidents, a study by Kakuchi concluded that under normotensive conditions intraoperative blood loss could be reduced by using an epidural blockade in patients undergoing lumbar spinal fusion (7). Intraoperatively, blood salvation with the use of the Cell Saver has been associated with a decrease in the number of transfusions by as much as 47% (2,4).

Despite these measures, blood loss can sometimes exceed 5L and the use of antifibrinolytics has been evaluated for these instances (14). Two agents in particular have been studied for spinal fusions, Aprotinin and EACA. In numerous studies Aprotinin has been reported to reduce blood loss and transfusion rates in patients undergoing major orthopedic and cardiac surgery (12); however data for the efficacy of EACA is sparse (1). A Cochrane database review of both Aprotinin and Amicar in 2007 concluded: "There is no need for further placebo-controlled trials of aprotinin or lysine analogues in cardiac surgery. The principal need is for large comparative trials to assess the relative efficacy, safety and cost-effectiveness of anti-fibrinolytic drugs in different surgical procedures." However, in May of 2008, after a clear relationship was demonstrated between increased renal failure, stroke, and death in cardiac patient populations receiving aprotinin, it was pulled off the market.

EACA is a synthetic lysine analog which works by inhibiting fibrinolysis by the displacement of plasminogen and plasmin from fibrin during clot formation. Adverse reactions from its use include muscle weakness, pulmonary embolus, thrombosis, and elevated creatine phosphokinase. EACA has been found to decrease intraoperative blood loss in children and adults undergoing cardiac surgery (15). Several studies for its use for patients undergoing spinal surgery have been performed with varying results. In one study by Florentino-Pineda et al. the effectiveness of EACA vs. control in 59 children undergoing posterior spinal fusion for idiopathic scoliosis was evaluated. These researchers

found no significance in the preoperative or postoperative Hgb, but were able to note a decreased need in the amount of autologous transfusion in the group receiving EACA (6). One limitation to this study was their use of a historical control group rather than a double-blind placebo-controlled group. Ray et al. in 2005 performed a randomized double blind placebo controlled study of the efficacy of EACA and Aprotinin in reducing blood loss in patients undergoing total hip arthroplasty which concluded that both Aprotinin and EACA were able to decrease intraoperative bleeding, but the differences for EACA were not significant. Similar findings were made by Urban et al. who performed a similar study on 55 patients undergoing complex posterior spinal fusions. They concluded once again that Aprotinin, but not EACA was able to significantly decrease the amount of blood loss. (11)

In our study, although the Amicar-treated patients had lower amounts of blood loss and blood given than the control group, the differences were not statistically significant. The non-significant differences could be due to the large observed variability for EBL and blood given in both groups and the small sample sizes for the two groups. In an effort to minimize the number of variables, all patients were operated on by the same surgeon using the same anesthesiologist, and Cell Saver technician. Blood loss was determined by a comparison of hemoglobin and hematocrit drawn by ABG immediately following the administration of anesthesia and again immediately after the operation was concluded.

Figure 3

Table 1. Comparison between Patients Treated and Not Treated with Amicar Mean±SD or Number (%)

Variable	Amicar (N=19)	Non-Amicar (N=21)	p-value
Age	54.58±9.82	47.24±11.04	0.03*
Pre-op hemoglobin	13.77±1.75	14.94±1.46	0.03*
Post-op hemoglobin	12.33±1.81	11.48±1.72	0.14
Pre-op hematocrit	40.82±4.75	44.26±4.30	0.02*
Post-op hematocrit	37.31±6.33	33.46±4.85	0.04*
Hemoglobin change	1.44±1.16	3.46±1.23	<0.01**
Hematocrit change	3.51±4.68	10.8±3.53	<0.01**
EBL	676.32±195.34	846.43±722.34	0.31
Urine output	400.56±214.63	360.0±181.42	0.63
Fluids given	3,005.26±923.59	3,376.2±1292.05	0.34
Blood given	326.32±237.68	478.57±301.9	0.08
Surgery time	265.26±78.1	290.95±96.4	0.56
JP day1	205.94±104.91	271.38±95.48	0.049*
JP day2	190.83±99.12	160.67±64.17	0.26
Post-op fluid input	339.47±180.92	794.62±797.4	0.15
Post-op fluid output	233.16±175.14	330.24±286.76	0.41
Diff (input-output)	106.31±200.14	464.38±670.97	0.21
Days	4.05±0.97	5.19±1.40	0.006**
Male	10 (52.63)	17 (80.95)	0.06

*Significant at 5% level (0.01<p<0.05)

** Significant at 1% level (p<0.01)

Table 1 shows the comparison among the two groups of

patients on observed variables. They differed significantly on age, pre-op hemoglobin and hematocrit, post-op hematocrit, changes in hemoglobin and hematocrit before and after surgery, JP day 1 and days in the hospital. The controls were younger, had larger average changes in hemoglobin and hematocrit levels (before and after surgery) and JP-day 1 values, and spent longer time in the hospital.

Figure 4

Table 2. Independent Significant Predictors for Blood Loss (EBL)

Predictor	Est. regression coefficient	p-value
Fluids given	0.027	0.0003**
Urine output	0.77	0.048*

As shown in Table 2, the independent significant predictors of blood loss (EBL) are amount of fluid given and urine output. The more fluid given and the greater the urine output, the greater the blood loss (EBL).

One possible reason for the lack of significant reduction in blood loss with EACA usage in our study may be due to the fact that after the initiation of EACA treatment, a maximal steady state inhibition of fibrinolytic activity is not achieved for 2 days. The authors determined the hemoglobin and hematocrit from the administration of EACA immediately after the conclusion of the operation, possibly not allowing the EACA to reach its steady state maximum for its antifibrinolytic activity. Another possibility for the lack of efficacy is that for most 2-4 level spinal fusions the blood loss can be reduced to less than 20% of the patient's blood volume with conservative measures therefore it is difficult to ascertain the efficacy of the EACA in an adult patient undergoing posterior lumbar fusion with pedicle screw placement. It is difficult to distinguish between the efficacy of conservative measures vs. the use of EACA. In addition, the amount of blood loss during these procedures may be due to the amount of resident involvement, which has been associated with an increase in the amount of blood loss.

CONCLUSIONS

In this study, the authors looked at efficacy of antifibrinolytic EACA as a means to reduce the amount of perioperative blood loss in patients undergoing decompressive lumbar laminectomy and lumbar fusion with pedicle screw fixation. Although the Amicar-treated patients had lower amounts of blood loss and blood given, the differences were not significant. The non-significant differences could be due to the large observed variability for

EBL and blood given in both groups and the small sample sizes for the two groups. Further prospective, randomized double-blinded studies are needed to determine if Amicar is a cost-effective method of reducing perioperative blood loss and at which dosage.

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