Changes in Blood Coagulation and Fibrinolysis Markers Before and After Spinal Surgery in Adolescent and Older Patients

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Abstract

Aim: To investigate changes in blood coagulation and fibrinolysis markers before and after spinal surgery in adolescent and older patients and to explore possible reasons for the development of postoperative venous thromboembolism (VTE).

Methods: This retrospective two-center study enrolled 57 low-risk patients who underwent spinal surgery at either our children’s institution or our public hospital between October 2012 and April 2015. Altogether, 27 adolescent idiopathic scoliosis (AIS) patients (3 boys, 24 girls; mean age 15 years, range 11–19 years) underwent instrumentation for posterior fusion. Also, 30 lumbar spinal canal stenosis (LSCS) patients (16 men, 15 women; mean age 71 years, range 52–88 years) underwent laminectomy for posterior decompression. Plasma levels of soluble fibrin monomer complex (SFMC), D-dimer, and plasminogen activator inhibitor type 1 (PAI-1) were measured 1 day preoperatively and on postoperative days (PODs) 1, 3, and 7.

Results: No patients in this study developed symptomatic or asymptomatic VTE postoperatively. The SFMC level showed significant increases on PODs 1 and 3 in the AIS patients and on POD 1 in the LSCS patients. The D-dimer level showed significant increases on PODs 1, 3, and 7 in both groups. The PAI-1 levels showed significant increases on POD 7 in the AIS patients and on PODs 1, 3, and 7 in the LSCS patients.

Conclusion: The significantly higher postoperative PAI-1 levels in older patients could be associated with the development and progression of symptomatic VTE.

Keywords: Venous thromboembolism; Adolescent idiopathic scoliosis; Spinal surgery; Blood coagulation-fibrinolysis marker; D-dimer; Soluble fibrin monomer complex; Plasminogen activator inhibitor type 1

Introduction

Venous thromboembolism (VTE) is a common complication after spinal surgery in adults. It is important to identify postoperative VTE, particularly fatal pulmonary embolism (PE) and symptomatic PE, which can be life threatening. Antithrombotic drugs are administered to reduce the postoperative risk of VTE, but these medications cannot be administered during or after spinal surgery because of the risk of postoperative paralysis resulting from hematoma. The overall reported incidence of symptomatic deep vein thrombosis (DVT) associated with spinal surgery ranges from 0.3% to 31.0% [1], and that of symptomatic VTE associated with spinal fusion surgery is 0.4% [2]. In Japan, the reported incidence of symptomatic PE is 0.6% [3] and that of asymptomatic VTE is 19% (DVT 5%, PE 18%) [3].

The incidence of VTE after spinal surgery in adolescent patients [4,5], as in younger children [6,7], is rare compared with the incidence among older patients. It is not known how blood coagulation and fibrinolysis, which are related to VTE, change after spinal surgery in adolescent patients, whereas a few studies have investigated those changes in older patients. It is possible that VTE could be prevented if differences in the changes in blood coagulation and fibrinolysis markers after spinal surgery in adolescent and older patients without VTE could be clarified. The purpose

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of this study was to investigate the changes in blood coagulation and fibrinolysis markers before and after spinal surgery in adolescent and older patients and to attempt to determine the reasons for VTE development after spinal surgery.

**Materials and Methods**

The ethics review board of our university approved the study protocol. This retrospective two-center study enrolled patients who underwent spinal surgery at our children’s institution or public hospital between October 2012 and April 2015. Patients with a past history of symptomatic VTE, cerebral hemorrhage, cerebral infarction, cardiac infarction, or allergy to contrast medium were excluded, as were older patients with asymptomatic VTE diagnosed with preoperative antithrombotic therapy or hemodialysis were also excluded, as were congenital clotting factor deficiencies and those undergoing antithrombotic therapy initiated.

**Results**

No patients in either the AIS or LSCS group developed symptomatic VTE after spinal surgery. Also, MDCT showed that none of the patients in the LSCS group developed asymptomatic VTE, the study was discontinued and aggressive antithrombotic therapy initiated.

**Blood coagulation and fibrinolysis markers**

Blood samples were obtained to measure the plasma levels of soluble fibrin monomer complex (SFMC), D-dimer, and plasminogen activator inhibitor type 1 (PAI-1) 1 day preoperatively and on postoperative days (PODs) 1, 3, and 7. Citrated plasma samples were stored at −80°C until analysis. Plasma SFMC and D-dimer levels were measured with latex immunoagglutination assays (Mitsubishi Chemical Medience Corporation, Tokyo, Japan) using the monoclonal antibodies IF-43 and JIF-23, respectively [9,10]. Plasma PAI-1 levels were measured with a latex photometric immunoassay (Mitsubishi Chemical Medience Corporation) using the polyclonal antibody F(ab’)_2 fragment [11].

**Statistical analysis**

Statistical analyses were performed with IBM SPSS for Windows, version 20.0 (SPSS, Chicago, IL, USA). If the SFMC, D-dimer, and PAI-1 levels did not fit a normal distribution, they were analyzed using the Shapiro–Wilks test. The SFMC, D-dimer, and PAI-1 levels 1 day preoperatively were compared with those on PODs 1, 3, and 7 using the Friedman test. If a significant difference was noted, the data were compared using the Wilcoxon signed rank test and corrected with Bonferroni’s inequality. Patients' sex in the AIS and LSCS groups was compared with Fisher’s exact test. Age, volume of intraoperative hemorrhage, and operation time were compared with an unpaired t-test. The level of statistical significance was set at P ≤ 0.05 for all tests.

**Results**

No patients in either the AIS or LSCS group developed symptomatic VTE after spinal surgery. Also, MDCT showed that none of the patients in the LSCS group developed asymptomatic VTE after spinal surgery.

**Changes in blood coagulation and fibrinolysis markers after AIS surgery**

The SFMC level was significantly higher on PODs 1 (median 10.0 μg/ml, P = 0.01) and 3 (median 10.0 μg/ml, P = 0.01) than preoperatively (median 3.0 μg/ml) (Figure 2). The D-dimer level was significantly higher on PODs 1 (median 1.8 μg/ml, P = 0.01), 3 (median 2.8 μg/ml, P = 0.01), and 7 (median 5.5 μg/ml, P = 0.01) than preoperatively (median 0.3 ng/ml) (Figure 2). The PAI-1 level was significantly higher on POD 7 (median 16.0 ng/ml, P = 0.01) than preoperatively (median 14.0 ng/ml) (Figure 2).

**Changes in blood coagulation and fibrinolysis markers after LSCS surgery**

The SFMC level was significantly higher on POD 1 (median 3.6 μg/ml, P = 0.01) than preoperatively (median 2.9 μg/ml) (Figure 3). The D-dimer level was significantly higher on PODs 1 (median 3.5 μg/ml, P = 0.01) and 7 (median 10.0 μg/ml, P = 0.01) than preoperatively (median 2.8 μg/ml) (Figure 3). The PAI-1 level was significantly higher on POD 7 (median 20.3 μg/ml, P = 0.01) than preoperatively (median 0.3 ng/ml) (Figure 3).

**Table 1: Patient Demographics.**

<table>
<thead>
<tr>
<th></th>
<th>AIS</th>
<th>LSCS</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Mean age (range)</td>
<td>15 yr (11-19)</td>
<td>71 yr (52-88)</td>
<td>0.01</td>
</tr>
<tr>
<td>Sex (Male: Female)</td>
<td>3:24</td>
<td>16:15</td>
<td>0.01</td>
</tr>
<tr>
<td>Mean intraoperative hemorrhage (range)</td>
<td>653ml (0-1285)</td>
<td>145ml (20-460)</td>
<td>0.01</td>
</tr>
<tr>
<td>Mean operation time (range)</td>
<td>430 min (238-799)</td>
<td>100 min (37-203)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

AIS: Adolescent Idiopathic Scoliosis; LSCS: Lumbar Spinal Canal Stenosis; "Unpaired t-test; "Fisher’s exact test.

**Figure 1: Flowchart of the 36 patients before surgery in the LSCS group.**

DVT: Deep Vein Thrombosis; LSCS: Lumbar Spinal Canal Stenosis; n: Number of Patients; PE: Pulmonary Embolism; VTE: Venous Thromboembolism.

**Figure 2:** Changes in blood coagulation and fibrinolysis markers before and after spinal surgery in adolescent patients (AIS) and older patients (LSCS) with lumbar spinal canal stenosis (LSCS) underwent laminectomy for posterior decompression under general anesthesia, in accordance with the Japanese Guideline for Prevention of Venous Thromboembolism [8]. No postoperative prophylactic antithrombotic therapy was administered in either group. If a patient developed symptomatic VTE, the study was discontinued and aggressive antithrombotic therapy initiated.
on PODs 1, 3, and 7 and the elevated SFMC on PODs 1 and 3 represent articles, we think it is possible that the elevation in the D-dimer levels statistically significant. And based on our results and those from past PODs 1, 3, and 7 would be elevated, although the elevation was not we speculated that SFMC levels on POD 1 and D-dimer levels on POD 7 in spinal surgery patients with VTE compared with those without VTE. Based on these data from the patients without VTE, D-dimer levels were significantly elevated on PODs 1, 3, and 10 in spinal surgery patients with VTE compared with those without VTE. Yoshioka et al. [13] reported that SFMC levels were significantly inhibited on PODs 3−7, as indicated by the significantly elevated inactivation of fibrinolysis due to PAI-1 may lead to VTE in older patients after spinal surgery.

A limitation of this study is that we did not investigate postoperative VTE using modalities such as MDCT or ultrasonography in the adolescent patients because the incidence of VTE after spinal surgery is rare in this age group [4,5]. Another limitation is that the sample size was relatively small.

Conclusions

We investigated changes in blood coagulation and fibrinolysis markers before and after spinal surgery in adolescent and older patients. The PAI-1 level was significantly elevated on PODs 1−3 after spinal surgery in patients treated for LSCS compared with that of patients treated for AIS. The significantly higher level of postoperative PAI-1 in older patients could be associated with the development and progression of symptomatic VTE.

References

8. Editorial Committee on Japanese Guideline for Prevention of Venous


