Surgical/tourniquet pain accelerates blood coagulability but not fibrinolysis

S. KOHRO, M. YAMAKAGE, J. ARAKAWA, M. KOTAKI, T. OMOTE AND A. NAMIKI

Summary
Tissue damage during surgery induces coagulation factors and activates platelets. Surgical pain may provoke release of catecholamines, leading to hypercoagulability. We have investigated the effect of surgical pain on blood coagulability and fibrinolysis in orthopaedic operations using tourniquets in 22 patients undergoing total knee replacement. Patients were allocated to one of two groups to receive extradural anaesthesia (EA; \( n = 11 \)) or general anaesthesia (GA; \( n = 11 \)). The EA group received lumbar extradural block with lidocaine. The GA group received only general anaesthesia, maintained with 1.5–2.5% sevoflurane and 66% nitrous oxide in oxygen. Using a thrombelastogram technique, blood coagulability and fibrinolysis were measured. Mean maximum amplitude (MA), which reflects coagulability, increased after tourniquet inflation (11%) in group GA whereas MA in group EA did not change. After tourniquet deflation, MA values in both GA and EA groups increased significantly (10% and 20%, respectively) (\( P < 0.05 \)), and there was also a significant difference in MA between groups (\( P < 0.05 \)). The fibrinolytic rate did not change in either group during tourniquet inflation, but increased significantly (160%) after tourniquet deflation. There was no significant difference in fibrinolytic rate between the groups. We conclude that the hypercoagulability seen in group GA could have been caused by surgical or tourniquet pain, or both, and that extradural anaesthesia is a useful technique to prevent hypercoagulability. (Br. J. Anaesth. 1998; 80: 460–463)

Keywords: blood, coagulation; blood, fibrinolysis; measurement techniques, thrombelastography; pain, surgical; pain, tourniquet

It is known that blood coagulability is exacerbated in the perioperative period.\(^1\)–\(^3\) Tissue damage during surgery induces coagulation factors and activates platelets at the surgical site.\(^4\) Surgical stress/pain also provokes catecholamine release intravenously,\(^5\) leading to increased blood coagulability. However, the degree to which these factors affect perioperative coagulability is unclear.

A tourniquet is often used to diminish bleeding during surgery on the lower or upper limbs. Systemic changes in coagulability and fibrinolysis may be affected by surgical pain and also by tourniquet pain because the latter apparently appears 45–60 min after tourniquet inflation under general anaesthesia.\(^6\)

We have investigated the effect of surgical or tourniquet pain, or both, on blood coagulability and fibrinolysis using the thrombelastogram (TEG) and tourniquet techniques, which allow assessment of the coagulability and fibrinolytic process in whole blood samples.\(^7\)–\(^9\)

Patients and methods
After obtaining approval from the Ethics Committee on Human Research, Sapporo Medical University, and informed consent, we studied 22 patients undergoing total knee replacement using a tourniquet. Patients were excluded if they had abnormalities of blood coagulability or had received medications such as non-steroidal anti-inflammatory drugs. With the exception of small amounts of midazolam (0.05 mg kg\(^{-1}\)), no other premedications were used.

Patients were allocated randomly to one of two groups to receive extradural anaesthesia (EA; \( n = 11 \)) or general anaesthesia (GA; \( n = 11 \)). In group EA, an extradural catheter was inserted via the L2–3 or L3–4 interspace. Lidocaine (1.5%) 8–12 ml with epinephrine 1:200 000 were administered through the extradural catheter; smaller doses were then administered, if necessary, to achieve anaesthesia to a level of T5–6. More local anaesthetic was administered as needed to maintain this level of anaesthesia, and patients were sedated with intermittent administration of midazolam 1 mg during surgery. Group GA received only general anaesthesia. Anaesthesia was induced with propofol 3–4 mg kg\(^{-1}\), and a laryngeal mask was inserted. Anaesthesia was maintained with 1.5–2.5% sevoflurane and 66% nitrous oxide in oxygen. Group GA received no i.v. analgesics during surgery.

Whole blood was obtained by antecubital venepuncture before tourniquet inflation, 30 and 90 min after tourniquet inflation, and 5 min after tourniquet deflation. Tourniquet deflation occurred soon after 90 min (table 1). Whole blood (360 \( \mu l \)) was placed in the Thrombelastogram (TEG) C-3000

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(Haemoscope, Glenview, IL, USA) immediately after sampling, and a few drops of mineral oil were spread over the blood surface to prevent evaporation of blood. The TEG records the activity of whole blood coagulation, including cellular and humoral elements, such as interactions of red blood cells, platelets, coagulation factors and calcium. The following variables were measured (fig. 1): reaction time (min); coagulation time (min); maximum amplitude (MA, mm) (which reflects coagulability); and fibrinolytic rate \( \left( \frac{MA - A_{60}}{MA} \right) \times 100 \) (A\(_{60}\) = amplitude 60 min after MA).

Arterial pressure and heart rate were measured every 5 min during anaesthesia and the mean of all measurements calculated. Data are expressed as mean (SD) and comparisons were made using the unpaired, two-tailed t test or one-factor analysis of variance with Fisher’s test. In all comparisons, \( P < 0.05 \) was considered significant.

Results

The two groups were comparable in age, sex, weight, height and duration of anaesthesia and surgery, and also in duration of tourniquet inflation (table 1). There were no differences in haemodynamic variables during operation or in the amount of postoperative bleeding for 24 h between the two groups.

Changes in TEG parameters are shown in figure 2. None of the parameters before tourniquet inflation differed significantly between groups EA and GA. Reaction time in group GA was reduced after tourniquet inflation (19%); it did not change during the same period in group EA (fig. 2A). There was a significant difference between groups at 90 min after tourniquet inflation \( (P < 0.05) \). After tourniquet deflation, reaction times increased significantly (20% and 37% in groups FA and GA, respectively) \( (P < 0.05) \). There was no significant difference between groups at this time. Coagulation time in group EA did not change significantly (fig. 2B). In group GA, coagulation time was reduced significantly (39%) after tourniquet deflation \( (P < 0.05) \), and there was a significant difference between groups at this time \( (P < 0.05) \). Similar to the changes in reaction time, maximum amplitude in group GA increased after tourniquet inflation (11%), whereas in group EA it did not change (fig. 2C). After tourniquet deflation, maximum amplitude increased significantly (by 10% and 20% in groups EA and GA, respectively) \( (P < 0.05) \). There were significant differences between groups at 90 min after tourniquet inflation and at 5 min after tourniquet deflation \( (P < 0.05) \). Fibrinolytic rates did not change in both groups during tourniquet inflation (fig. 2D), and after tourniquet deflation, it increased significantly (160%) in both groups \( (P < 0.05) \); there were no significant differences between groups.

Discussion

Using TEG, we have shown that the reaction time in group GA was reduced and maximum amplitude increased, whereas these values did not change in group EA during tourniquet inflation. In general, blood coagulability is accelerated during surgery. Surgical trauma increases plasma concentrations of coagulation factors, decreases concentrations of coagulation inhibitors and enhances platelet activity at the site of vascular damage. Simultaneously, surgical pain, including tourniquet pain, provokes the release of catecholamines and serotonin intravascularly, leading to increased blood coagulability. Therefore, the increase in blood coagulability in group GA during tourniquet inflation seemed to depend on surgical/tourniquet pain. Fibrinolytic rates did not change in both groups during tourniquet inflation. Surgical stress also causes release of plasmin at the site of vascular damage, leading to fibrinolysis. Therefore, we can conclude that surgical or tourniquet pain per se had no effect on systemic blood fibrinolysis. The anaesthetic technique may have an effect on coagulability and fibrinolysis. However, sevoflurane is reported to inhibit blood coagulability in vivo.

**Table 1** Patient characteristics and operation data. Values are mean (range). There were no significant differences between the groups for any variable. GA = General anaesthesia, EA = extradural anaesthesia

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group GA (n = 11)</th>
<th>Group EA (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (F/M)</td>
<td>8/3</td>
<td>8/3</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>67 (57–72)</td>
<td>65 (55–76)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73 (58–92)</td>
<td>72 (58–89)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>156 (146–172)</td>
<td>152 (140–175)</td>
</tr>
<tr>
<td>Heart rate during operation (beat min(^{-1}))</td>
<td>67 (54–102)</td>
<td>78 (52–95)</td>
</tr>
<tr>
<td>Arterial pressure during operation (mm Hg)</td>
<td>118/74</td>
<td>114/68</td>
</tr>
<tr>
<td>Duration of anaesthesia (min)</td>
<td>171 (137–198)</td>
<td>175 (129–195)</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>111 (97–135)</td>
<td>117 (95–143)</td>
</tr>
<tr>
<td>Duration of tourniquet inflation (min)</td>
<td>103 (91–135)</td>
<td>100 (91–125)</td>
</tr>
<tr>
<td>Postoperative blood loss (ml)</td>
<td>240 (83–420)</td>
<td>265 (76–580)</td>
</tr>
</tbody>
</table>

**Figure 1** Typical recording of thrombelastogram and measured parameters. Normal ranges: reaction time 7–14 min; coagulation time 3–7 min; maximum amplitude (MA) 40–60 mm; and fibrinolytic rate < 10%. Fibrinolytic rate is defined as \( \frac{MA - A_{60}}{MA} \times 100 \) (A\(_{60}\) = amplitude 60 min after MA).
and lidocaine (used in group EA) is reported to have little effect on blood coagulability in clinical doses.\textsuperscript{13} Therefore, the difference in anaesthetic techniques is not likely to have had an effect on the differences in blood coagulability and fibrinolysis in this study.

After tourniquet deflation, blood coagulability increased significantly with fibrinolysis in both groups. These changes in blood coagulability–fibrinolysis produced by tourniquet deflation could be caused by release of clotting and anti-clotting factors from the surgical site. However, the degree of blood coagulability in group GA was significantly higher than that in group EA, even after tourniquet deflation. Mean maximum amplitude in group GA was outside the normal range, indicating hypercoagulability. This could be a result of the surgical/tourniquet pain-induced coagulability seen in group GA during tourniquet inflation.

Blood hypercoagulability is thought to lead to thrombotic complications.\textsuperscript{2,5,11} Regional anaesthesia has been reported to reduce perioperative morbidity and mortality compared with general anaesthesia.\textsuperscript{5} Rosenfeld and colleagues reported that extradural anaesthesia inhibited coagulation and prohibited the development of arterial thrombosis.\textsuperscript{14} Our study is the first to demonstrate the role of pain in intraoperative blood coagulability and fibrinolysis under conditions where the regional effects of surgery are excluded.

In summary, surgical/tourniquet pain increased blood coagulability during surgery and this was not accompanied by changes in fibrinolysis. Extradural anaesthesia inhibited the acceleration of blood coagulability compared with general anaesthesia.

**References**


