Prophylactic use of desmopressin in surgery of six patients with symptomatic heterozygous factor XI deficiency

From January 1998 to March 1999, we followed 6 symptomatic heterozygous factor XI (FXI) deficient patients undergoing surgery. There were 4 males and 2 females. Their mean age was 39.8 years (range 6-67 years). Three of the 6 patients were members of the same family. The investigation of additional coagulation abnormalities (e.g. bleeding time, platelet aggregation, other clotting factors levels and von Willebrand factor level) was negative in all 6 patients. This report shows that desmopressin can be used successfully to prevent surgical bleeding in these patients.

Sir,

Patient #1 was a 56-year old female undergoing endoscopic cholecystectomy. Her mother had died at the age of 61 of a post-cholecystectomy hemorrhage. The patient had suffered severe bleeding, which required multiple blood transfusions, after a tonsillectomy at the age of 10. She had had 2 pregnancies, 1 with severe post-partum hemorrhage. At the age of 42 the patient underwent a total hysterectomy and was successfully treated with fresh frozen plasma in order to avoid hemorrhagic complications.

Patient #2, a 65-year old male, the first patient’s brother, was transfused aged 60 because of hemorrhagic complications after a prostatectomy.

Patient #3, a 29-year old male, the second patient’s son, had received blood transfusions for haemorrhagic complications following splenectomy after road accident trauma. Patients #2 and #3 were scheduled for arthroscopic reconstruction of knee ligaments.

Patient #4, a 67-year old nulliparous female, was to undergo right leg saphenectomy. This patient had suffered from menorrhagia and reported bleeding complications during left leg saphenectomy 2 years previously.

Patient #5, a 6-year old male child, had received blood transfusions for haemorrhagic complications following splenectomy after road accident trauma. Patients #2 and #3 were scheduled for arthroscopic reconstruction of knee ligaments.

Patient #6, a 16-year old male, suffered from excessive and prolonged bleeding after two dental extractions. He was undergoing hydrocele surgery.

Before surgery, each patient was tested for the response to a subcutaneously injected dose of 0.3 µg/kg of DDAVP. In all patients the desmopressin injection led to normalization of the APTT, a slight increase in FXI activity (mean 12.0 U/dL; range 9-14 U/dL), a marked increase in FVIII:C (mean 147.8 U/dL; range 132-162 U/dL), WF:Ag (mean 89.3 U/dL; range 68-123 U/dL) and WF:Ricof (mean

<table>
<thead>
<tr>
<th>Patients</th>
<th>Before DDAVP</th>
<th>60 minutes after DDAVP</th>
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<tbody>
<tr>
<td></td>
<td>APTT (ratio)</td>
<td>FXI:C (U/dL)</td>
</tr>
<tr>
<td>Patient #1</td>
<td>1.34</td>
<td>32</td>
</tr>
<tr>
<td>Patient #2</td>
<td>1.25</td>
<td>42</td>
</tr>
<tr>
<td>Patient #3</td>
<td>1.28</td>
<td>40</td>
</tr>
<tr>
<td>Patient #4</td>
<td>1.19</td>
<td>45</td>
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<td>Patient #5</td>
<td>1.35</td>
<td>36</td>
</tr>
<tr>
<td>Patient #6</td>
<td>1.32</td>
<td>34</td>
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</tbody>
</table>

Normal range: APTT = 0.8-1.15 (ratio); FXI:C = 60-140 U/dL; FVIII:C 50-150 U/dL; WF:Ag = 60-150 U/dL; WF:Ricof = 50-145 U/dL.
to the hemostatic efficacy of DDAVP in such patients. But significant increase in FXI activity may contribute to concomitant, DDAVP-dependent increases of FVIII:C, the slight though the observed APTT normalization is probably due to the marked increase in FVIII:C. The slight increase in FXI activity and a marked increase in FVI-C are rather unlikely as Castaman et al. have previously demonstrated parallel degrees of increase in both FVIII:C and FXI:C after administration of DDAVP.

Recent reports indicate that DDAVP has been used successfully to prevent surgical bleeding in FXI deficient patients. Our case reports confirm these findings: we first tested and then utilized subcutaneous desmopressin (0.3 µg/kg s.c.) 12 hourly for 5 days to the remaining patients, starting on the day of the operation. All patients received tranexamic acid (10 mg/kg thrice daily i.v. for 5 days). Serum electrolytes were monitored regularly.

DDAVP therapy was well tolerated and no hemorrhagic complications occurred during or after surgery.

FXI deficiency is a rare inherited coagulation disorder characterized by rarity of spontaneous bleeding but the risk of severe hemorrhagic complications after trauma or surgery. There is often little direct correlation between the tendency to bleed and the severity of the disease itself, so it is extremely difficult to predict hemorrhagic complications after surgery in patients with mild disease.1-3 Currently available therapeutic products for the treatment of bleeding in FXI deficient patients include fresh frozen plasma and virus-inactivated FXI concentrates: the former may carry blood-borne viruses, the latter, although the first choice treatment in patients with severe FXI deficiency, should be used cautiously because of its thrombotic risk.4-6

References

Comparison between radial immunodiffusion and flow cytometry techniques for detecting antiplatelet antibodies

The aim of our work was to compare radial immunodiffusion (RI) (in use for years) versus flow cytometry (FC) (a new technique). The discrepancies of the results in our patient population indicate that both techniques are valuable tools to understand the pathogenesis of thrombocytopenia.

Sir,

To evaluate the clinical use of RI and FC for detecting antiplatelet antibodies, we analyzed platelet samples from 39 patients. The samples were grouped according to the etiology of the thrombocytopenia into: group A (n=12): immune thrombocytopenic purpura (ITP) (Table 1), group B (n=19): conditions associated to bone marrow failure or malignancy (Table 2) and group C (n=8): unexplained mild thrombocytopenia.

Surface platelet associated IgG (PALg) was assayed by FC using the procedure described by Lin et al. and total (PALg) by RI using the procedure described by M orse et al. We observed significant positive correlations between both methods when all 39 cases were examined (r=0.44, p=0.006). The main contribution to this significant positive correlation was given by group A results (r=0.8, p=0.0018).