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CLINICAL REPORT

Thromboelastometry during intraoperative transfusion of fresh frozen plasma in pediatric neurosurgery

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Abstract Normal blood coagulation is essential in pediatric neurosurgery because of the risk of abundant bleeding, and therefore it is important to avoid transfusion of fluids that might interfere negatively with the coagulation process. There is a lack of transfusion guidelines in massive bleeding with pediatric neurosurgical patients, and early use of blood compounds is partly controversial. We describe two pediatric patients for whom fresh frozen plasma (FFP) infusion was started at the early phase of brain tumor surgery to prevent intraoperative coagulopathy and hypovolemia. In addition to the traditional laboratory testing, modified thromboelastometry analyses were used to detect possible disturbances in coagulation. Early transfusion of FFP and red blood cells preserved the whole blood coagulation capacity. Even with continuous FFP infusion, fibrin clot firmness was near to critical value at the end of surgery despite increased preoperative values. By using FFP instead of large amounts of crystalloids and colloids when major blood loss is expected, blood coagulation is probably less likely to be impaired. Our results indicate, however, that the capacity of FFP to correct fibrinogen deficit is limited.

Keywords Fluid therapy · Transfusion · Fresh frozen plasma · Red blood cells · Brain tumor · Pediatric neurosurgery

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Introduction

In pediatric brain tumor surgery, the patient is often at risk for abundant bleeding. Normal blood coagulation is essential, and transfusion of fluids must not disturb this homeostasis. All artificial colloids and mannitol, in addition to their dilutional effects, decrease whole blood clot strength, predisposing patients to bleeding [1–3].

Transfusion protocols in massive bleeding are well documented in adult populations [4–6]. Pediatric patient guidelines are, however, scarce, and those for adults are not directly transferable to children [7]. We describe two cases in which an early fresh frozen plasma (FFP) infusion was used in brain tumor surgery to prevent intraoperative coagulopathy and hypovolemia. In addition to traditional laboratory testing, we used modified thromboelastometry analyses to trace possible blood coagulation disturbances.

Case report

Patient 1

A previously healthy 10-month-old boy (height 78 cm, weight 9.9 kg) had a richly vascularized left parieto-occipital tumor. The tumor extended to the mesencephalon and hypothalamus, causing a midline shift and hydrocephalus.

After induction, anesthesia was maintained with propofol and remifentanil infusions. The surgery took place with the patient in a sitting position. After a left paramedian parieto-occipital craniotomy, an occipital interhemispheric fissure was used to approach the tumor. After tumor debulking, the anaplastic meningioma was gradually dissected from the surrounding neurovascular structures and completely removed.

Addition to Ringer acetate solution, FFP infusion at the rate of 20 ml/h was started after anesthesia induction. 50 ml mannitol (150 mg/ml) was administered. Blood loss during surgery was 750 ml (300 ml within 25 min), and the patient received a total of 500 ml red blood cells (RBC) during surgery and another 60 ml in the intensive care unit (ICU), with no need for platelet transfer. The total amount of fluids infused during surgery (blood compounds and crystalloids) was 1,504 ml, and fluid loss (blood and urine) was 1,090 ml. The patient woke up and was extubated without complications 120 min after the operation.

Patient 2

A 5-month-old boy (height 67 cm, weight 7 kg) developed symptoms of increased intracranial pressure. Magnetic resonance imaging (MRI) study revealed a massive tumor in the left pontocerebellar area causing pressure to the brainstem.

Propofol and remifentanil infusions maintained the anesthesia. Surgery took place with the patient in a park bench position with head attached to the Mayfield device.

The neurosurgeon performed a left suboccipital craniotomy. After tumor debulking, he dissected and completely removed the lesion from the surrounding cerebrovascular structures. The tumor was ependymoma gradus II–III.

Together with 0.9 % sodium chloride solution with 5 % glucose (20 ml/h), FFP infusion was started after induction (240 ml in total). 25 ml mannitol (150 mg/ml) was given. Intraoperative blood loss was 380 ml, and the patient received a total of 250 ml RBC during surgery and another 60 ml in the ICU, with no need for platelet transfer. The total amount of fluids infused during surgery (blood compounds and crystalloids) was 870 ml and fluid loss (blood and urine) 960 ml. Two 250-mg boluses of tranexamic acid were given during surgery. The patient was kept sedated in controlled ventilation in the ICU until the first postoperative morning.

Laboratory analyses

The results of laboratory tests are given in Table 1. Both patients had mild anemia and abnormally high platelet count, but thromboplastin time values (PT-%, normal 70–130 %) fell within normal limits.

Four different thromboelastometry tracings were used: Intem® (intrinsic pathway), Extem® (extrinsic pathway), Fibtem® (platelet function inhibition by cytochalasin D), and Aptem® (added aprotinin to detect hyperfibrinolysis).

In Extem® and Fibtem® analyses, coagulation time (CT), clot formation time (CFT), alpha-angle, and maximum clot firmness (MCF) were within normal reference ranges before the surgery, but both patients had increased fibrin MCF preoperatively (Fibtem®). Maximum lysis (ML), indicative of fibrinolytic activity, was 21 % (normal <15 %) in both patients in preoperative Extem® analysis. However, MCF was comparable between Aptem® and Extem® analyses.

Clot formation time was longer in all samples in comparison with the preoperative values (Fig. 1). MCF was slightly decreased in Intem® and Extem® analyses in comparison with preoperative values (Fig. 2). Decrease in MCF in Fibtem® analysis was more profound and reached a critical value of 8 mm at the end of surgery in patient 2 (Fig. 3). Maximum lysis (ML) diminished gradually in both patients, showing least activity at 2 h after the surgery in patient 1 (ML 1 %).

Thromboelastometry analyses in the first postoperative morning were similar to preoperative values. Fibrin clot firmness was increased in both patients, i.e., leaning slightly toward hypercoagulopathy. Maximum lyses (ML) were within normal reference ranges.

Discussion

Both patients were preoperatively considered to have a significant risk of major blood loss during neurosurgery.

Table 1 Results of laboratory and standard coagulation tests

	Hb (g/dl)		Hct (%)		Platelets (E^9/l)		PT (%)	
	P1	P2	P1	P2	P1	P2	P1	P2
Baseline	9.1	10.1	28	31	656	560	122	136
Intraoperative 10.59	8.3	8.5	25	24	633	316		
Intraoperative 12.20	12.3		35		436		93	
End of surgery 13.32	10.7		30		327			93
3 h after operation	9.4		26		292		103	
5 h after operation		12.6		35		220		
9 h after operation	8.5		24		279			
First postoperative day	9.8	11.9	27	34	301	236	120	102

Hb hemoglobin, *Hct* hematocrit, *Eryt* erythrocytes, *PT* prothrombin time, *P1* patient 1, *P2* patient 2

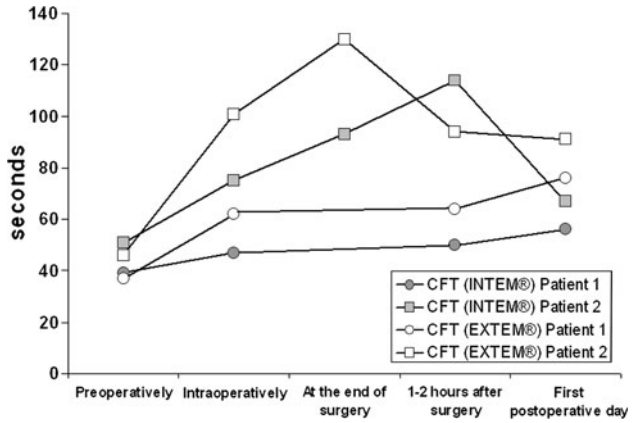

Fig. 1 Clot formation time (*CFT*) in Intem® (normal reference range, 30–110 s) and Extem (34–159 s) analyses

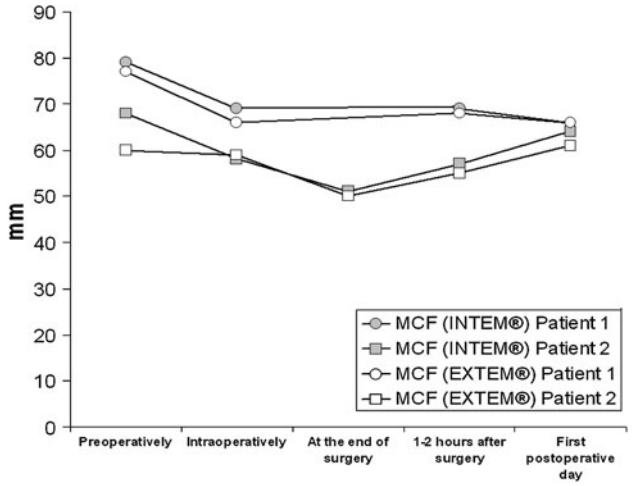

Fig. 2 Maximum clot firmness (*MCF*) in Intem® (normal reference range, 50–72 mm) and Extem (50–72 mm) analyses

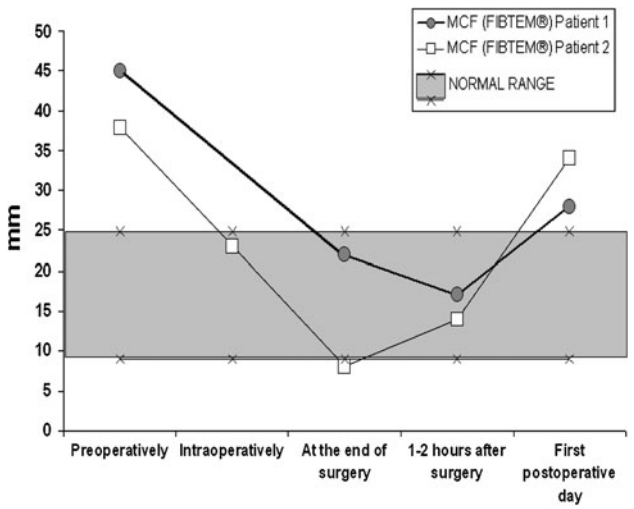

Fig. 3 Maximum clot firmness (*MCF*) in Fibtem® analysis

Thromboelastometry analysis showed that early transfusion therapy with FFP and RBC preserved the whole blood coagulation capacity. Interestingly, fibrin clot firmness was near the critical value at the end of surgery, despite increased preoperative fibrin clot firmness.

Transfusion guidelines concerning pediatric patients address very little intraoperative fluid management during excessive blood loss. The emphasis is more on critically ill patients and patients suffering from a chronic coagulation deficit [8–10]. Although transfusion guidelines for adults in massive bleeding are leaning toward the use of an increased ratio of FFP and platelets in relationship to red blood cells [11], the general view with pediatric patients still is that crystalloids are the first-line solutions and different blood compounds should only be administered when coagulation deficit, revealed by laboratory testing, has developed [8, 9]. This is a challenge when treating pediatric neurosurgical patients. Hypovolemia may develop quickly because of the patient's low blood volume. Second, abrupt massive bleeding is possible, in which situation laboratory testing and thromboelastometry analysis are too slow to guide transfusion of fluids.

To prevent the development of coagulation disturbance and hypovolemia intraoperatively, we started FFP infusion at the beginning of the surgery before major bleeding could occur. Even with continuous FFP infusion, a decrease in PT-% was evident with both patients (25–29 % percentage points during surgery). However, relatively minor changes in CT and CFT values in Intem® and Extem® analysis indicate that a marked deficit of coagulation factors did not developed during surgery. Our results suggest that without an early FFP infusion, or with crystalloid or colloid infusions, a clinically relevant lack of coagulation factors would have occurred during the operations.

Efficacy of FFP to correct fibrinogen deficit is limited. Decrease in clot firmness in Fibtem® analyses was also evident in both our cases, which suggests that our patients would probably have benefited from increment of fibrinogen if surgical hemostasis would not have been satisfactory. Haas and co-workers [12] showed that the administration of fibrinogen during craniosynostosis repair avoided the need for FFP transfusion; instead, colloids were used to compensate blood loss. Use of colloids in massive bleeding, however, is not unambiguously supported, because of their negative interference with blood coagulation [13], especially with mannitol [2]. We gave patient 2 tranexamic acid because of the increased maximum lysis (21 %) preoperatively and positive in vitro effect of aprotinin (Aptem®) on clot strength in the intraoperative analysis. A single bolus of tranexamic acid also reduces bleeding and the need for red blood cell transfusion without extreme fibrinolytic activity in craniosynostosis operations [14].

A postoperative hypercoagulable state is a common finding in children undergoing brain surgery [15], and enhanced coagulation in thromboelastometry analysis is seen after relatively minor blood loss during craniotomy [15]. The specific definition of hypercoagulability and its effect on the risks of either thrombosis, or bleeding, are still unclear in craniotomy patients [16]. Our patients had increased MCF in Fibtem® analyses preoperatively, but in Extem® analyses MCF were within the normal reference range. Hypercoagulability, i.e., increased MCF in Fibtem®, however, decreased during the operations, and the critical values for fibrin clot firmness were almost reached at the end of surgery. A decrease in clot strength is associated with bleeding complications [13].

Thromboelastometry (ROTEM®) allows a dynamic evaluation of the entire coagulation process and distinguishes intrinsic and extrinsic coagulation pathways from pure fibrin formation. The use of thromboelastometry analysis in pediatric surgical patients is well documented [14, 17, 18]. Recent Cochrane analysis states, however, that there is still a lack of evidence that use of ROTEM® would decrease morbidity or mortality [19].

Allergic reactions, transfusion-related acute lung injury (TRALI), and infections are the major concerns related to transfusion of FFP and other blood components [20]. Virus inactivation and reduction of HLA and other antibodies by pooling have led to reduced risks of transfusion-related adverse effects. Instead of traditional FFP, we used Octaplas®, which is a pharmaceutical product that has gone through solvent-detergent treatment and is pooled from approximately 1,000 donors.

Perioperative fluid administration should be planned in advance when treating pediatric neurosurgical patients, and possible detected disturbances in blood coagulation should be handled before surgery. The excessive use of crystalloids and colloids in itself disturbs blood coagulation, and therefore early use of FFP is a noteworthy option when major blood loss is expected. Thromboelastometry offers an additional tool to observe possible disturbances in blood coagulation and to guide administration of fibrinogen or tranexamic acid.

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