Major Surgical Interventions in Childhood Factor VII Deficiency

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Introduction

Factor VII (FVII) deficiency is not rare in our country where consanguineous marriages are common. Guidelines and papers exist on surgical interventions for haemophilic individuals. The same does not apply to FVII deficiency. The number of patients is limited and the registries are relatively unsystematic compared to those for haemophilia patients. The few reports are about adult patients. Most of the individuals with FVII deficiency are diagnosed by pre-operative testing. Factor VII deficiency patients with prolonged PT may cause concern in surgery and anaesthesia teams. It is the task of primarily the haematology clinic to perform a relevant assessment on the patient prior to surgery, to plan necessary replacement therapies and to ensure that the surgical team can perform their procedures safely. Presence of bleeding history in the individual or in his/her family and/or presence of factors that may affect haemostasis, and comorbidities are important. Comorbidities may be of degrees that might contribute to the risk of bleeding and thrombosis.

The present article intends to report the major surgical procedures for patients with FVII deficiency being monitored by our centre since 1990.

Materials and Method

Our study retrospectively reviewed 24 major surgical interventions to 23 patients who were selected to receive surgical intervention among childrens with FVII deficiency monitored and treated by our clinic between1990 and 2013. Information of 17 (73.9%) male and 6 (26.1%) female patients with an age range of 3-19 years (mean 10.8 ± 6.2) were retrieved from patient records. Patient characteristics, age at presentation and the causes of surgical intervention, preparation to surgery, pre-operative replacement therapies, information on the surgical process as a whole and post-operative bleeding outcomes, transfusion needs and surgical wound healing information were recorded. Patients' clinical phenotyping was based on the data of the European Network of Rare Bleeding Disorders (EN-RBD) group. FFP and rFVIIa had been used for surgical intervention of FVII patients. All of the factor preparations were administered as bolus via the peripheral vein. No catheters were used. Tranexamic acid was used as the antifibrinolytic agent. Whether the patient achieved post-surgical haemostasis was confirmed by physical examinations, whole blood count and haemostasis tests. Post-operative factor activity and inhibitor tests were performed on need basis.

Results

Of the patients who underwent major surgery, 17 (73.9%) were asymptomatic and 6 (26.1%) symptomatic. All asymptomatic patients were diagnosed before surgical intervention. Six of the cases had hernioplasty, three had adenotonsillectomy, three had adenoidectomy, three had undescended testicle, two had tonsillectomy and seven had other surgical procedures. Recombinant FVIIa was used for 7, FFP for 2 and FFP and rFVIIa was co-administered in one intervention. No replacement therapy was administered in 14 interventions (58.3%). Recombinant FVIIa was used at 15-35mcg/kg for 3-83 times and in 4-12 hour intervals. In two interventions antifibrinolytic agents were used also. Bleeding during and after surgical procedures was not observed. Transfusion was not needed. Thrombotic events were not observed. Antibody occurrence was not detected in these patients. No delay in surgical wound healing was noted. Patient information is presented in table 1. Major surgeries and replacement therapies are presented in Table 2.

Table 1: Patient characteristics

Characteristic	n	%
Patients	23	-
Gender		
Male	17	73.9
Female	6	26.1
F:C		
< 5%	4	17.4
5-30%	6	26.1
30-50%	13	56.5
Clinical Phenotype		
Asymptomatic	17	73.9
Symptomatic	6	26.1
Grade I	-	-
Grade II	2	33.3
Grade III	4	66.7
Replecament therapy	10	41.7
rFVIIa	7	70
FFP	2	20
rFVIIa+FFP	1	10
No therapy	14	58.3
Post op bleeding	-	-
Transfusion need	-	-
Use of Anti-fibrinolytics	2	8.3

Table 2: Major surgeries and replacement therapies

Procedure	Gender	Age	F:C	Clinical Phenotype	RT	RT dose	Dose interval	Number of doses	Anti-fibrinolytics
VP shunt	M	10	0	G-III	rFVIIa	15-35mcg kg	4-12 hours	83	-
VP shunt valve replacement	M	10	0	G-III	rFVIIa	15-35mcg/kg	4-12 hours	60	-
Undescended testicle	M	19	47	A	rFVIIa	20 mcg/kg	4 hours	3	-
Adeno-tonsillectomy	F	8	0.1	G-III	rFVIIa	20 mcg/kg	4-6 hours	4	Yes
Tonsillectomy	M	8	29	G-II	rFVIIa	20 mcg/kg	4 hours	3	Yes
Adenoidectomy	F	7	48.6	A	rFVIIa	20 mcg/kg	4 hours	3	-
Hernioplasty	M	13	4	A	rFVIIa	20 mcg/kg	4 hours	4	-
Hernioplasty	M	14	42	G-II	FFP rFVIIa	20ml/kg 20 mcg/kg	12 hours 4 hours	9 4	-
Splenectomy	F	17	47	A	FFP	20ml/kg	-	1	-
Subdural haematoma discharge	F	8	4.9	G-III	FFP	20ml/kg	4-12 hours	7	-
Fracture repositioning	F	7	48.6	A	-	-	-	-	-
Hernioplasty	M	11	27	A	-	-	-	-	-
Hernioplasty	M	5	27.4	A	-	-	-	-	-
Hernioplasty	M	13	45.8	A	-	-	-		-
Hernioplasty	M	10	34.1	A					
Adeno-tonsillectomy	M	7	32.1	A	-	-	-	-	-
Tonsillectomy	M	16	17	A	-	-	-	-	-
Adeno-tonsillectomy	M	13	45.8	A	-	-	-	-	-
Adenoidectomy	M	19	36.6	A	-	-	-	-	-
Adenoidectomy	F	11	24.5	A	-	-	-	-	-
Undescended testicle	M	10	38	A	-	-	-	-	-
Undescended testicle	M	5	32.9	A	-	-	-	-	-
Hydrocele	M	3	24.5	G-II	-	-	-	-	-
Appendectomy	M	16	39.2	A	-	-	-	-	-

Discussion

Optimal replacement therapy for surgical interventions to patients with FVII deficiency is not clear. rFVIIa was administered as bolus in the surgical procedures of our patients with FVII deficiency. The most frequent treatment reported in the literature is in 4-6 hour intervals in the form of bolus. There are authors who recommend that rFVIIa should be given as continuous infusion. It is reported that less factor is consumed with this approach. Although there are articles reporting that co-administration of tranexamic acid and rFVIIa was safe, care has been taken to leave at least one hour between the administrations of the two agents. In major surgeries, tranexamic acid was added to the therapy during one adenotonsillectomy and one tonsillectomy operations.

It is known that this factor affects FVII activity and that patients with decreased activity tend not to bleed whilst some patients with relatively higher values develop bleeding attacks. Because FVII:C may fluctuate, it is also recommended that the activity be checked prior to major surgeries. The French FVII working group suggests an algorithm for pre-operational assessment (Sheth S. et al.Expert Review of Hematology. 2012) The recommendation to abstain from replacement treatment in patients with factor activity over 20% and without bleeding history may be problematic in young children in particular. Our experience indicates that caution should be exercised even in the presence of marginal FVII deficiencies in children with no bleeding history. It should, however, be borne in mind that FVII-deficient patients with marginal/normal activity has the risk of bleeding.

Whether the intended surgical intervention is major or minor as well as the site of intervention and bleeding and fibrinolytic activity characteristics of the surgical site should also be taken into account. Patient's haemostasis tests and F:C values are also guiding in pre-operative assessment. Especially for interventions which are desired to be performed without prior replacement, it would be necessary to persuade the surgical and anaesthesia teams who would otherwise like to see normal haemostasis results. The specific factor should be determined based on the individual patients with FVII deficiency or on the nature of the surgical intervention beforehand and they should be made available prior to the surgical intervention . Fulfilling these may help perform an unproblematic surgery.

In conclusion, surgical interventions to FVII deficient patients, which represent a population with varying characteristics, should be performed in hospitals with experienced haematology centres. Patients as well as the surgery and anaesthesia teams should be prepared and encouraged prior to the intervention.