CARDIAC SURGERY IN HAEMOPHILIACS : REPORT OF 14 CONSECUTIVE CASES

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INTRODUCTION

Advances in management of haemophilia and improved safety of therapeutic products are leading to an increased life expectancy of haemophiliac patients. Therefore, cardiovascular diseases become more prevalent in these patients, occasionally requiring cardiac surgery. However, guidelines for replacement therapy do not exist yet in these major surgical procedures.

AIM OF THE STUDY

This study reports a retrospective cohort of 13 haemophilia patients undergoing 14 open heart surgery procedures performed in 3 University Hospitals in France. Details are provided on concomitant disorders, operative strategies, management of replacement therapy and relevant outcomes.

PATIENTS AND METHODS

Thirteen haemophilia A and B patients (12 adults and 1 infant) underwent 14 surgical procedures : one case in 1982 and 13 cases over the period from 1997 to 2011. None of the patients had a previous history of inhibitor. Myocardial revascularization, valve replacement and congenital heart disease surgery were performed : off-pump technique was chosen in 3 cases whereas conventional extracorporeal circulation was performed in 11 cases (systemic heparinisation 300 IU.kg^{-1} monitored with activated clotting time [ACT > 400 seconds], intraoperative use of aprotinin or tranexamic acid according to local institutional guidelines, protamine reversal).

RESULTS

Patient characteristics and replacement therapy regimen are shown in Table 1.
Plasma-derived or recombinant FVIII / IX concentrate was administrated 1 h prior to surgery through a central line to achieve a target level of 80-100%. A second bolus was infused at the end of the procedure. Bolus infusions were repeated twice or less frequently once daily (daily monitoring of FVIII/IX level : trough level 80 % D1-4, then 50 % until usually D 10-14). Continuous infusion (CI) was used in one single case (patient 7). Total factor concentrate consumption reflects the severity of haemophilia and the individual patient's recovery as well as the duration of replacement therapy which varied widely from 2 to 30 days, related to clinical outcome and complications (Table 2). Postoperative thromboprophylaxis, mainly low molecular weight heparin (LMWH), was individually tailored over a treatment period ranging from for 4 to 21 days. Postoperative mortality predicted by logistic euroscore was unfavourable in patient 7.

Patients	Age (years)	FVIII / IX level	Type of intervention	Number of cardio-vascular risk factors	BMI	Logistic euroscore (%)	Duration of factor replacement (days)	Total factor consumption
1*	51	FVIII < 1%	CABG	3	28	0,88	11	1 031 IU / kg
2	58	FVIII 14 %	CABG	1	27	1,33	5	170 IU / kg
3	68	FVIII 23 %	CABG	3	29	4,86	2	68 IU / kg
4	70	FVIII 24 %	CABG	3	25	1,82	4	122 IU / kg
5	70	FIX 2 %	CABG + AVR	3	32	3,44	30	1 420 IU / kg
6	56	FIX 5 %	CABG + ascending aorta replacement	4	28	4,37	21	1 560 IU / kg
7*	63	FVIII < 1%	AVR	3	29	20,7	13	846 IU / kg
8	70	FVIII 16 %	AVR	4	28	4,61	17	787 IU / kg
9	58	FVIII 26 %	AVR	1	30	2,3	9	350 IU / kg
10	63	FIX 3 %	AVR	3	24	1,96	21	1 949 IU / kg
11	53	FVIII 16 %	OPCAB	2	26	0,88	14	409 IU / kg
12	45	FVIII 33 %	OPCAB	4	20	5,11	3	100 IU/kg
13	78	FIX 3 %	OPCAB	3	27	ND	15	1 417 IU/kg
14	4 months	FVIII 2%	ventricular septal defect repair	NA	NA	NA	15	1 660 IU/kg

Table 1. Patient characteristics and replacement therapy regimen

* same patient
CABG: coronary artery bypass grafting, **AVR**: aortic valve replacement (all biological valves)
OPCAB: off-pump coronary artery bypass **BMI** : body mass index
Cardiovascular risk factors : hypertension, diabetes, hypercholesterolemia, smoking

Patient	Postoperative complications
3	pneumopathy
5	cutaneous infection at venous access site (drainage)
6	non hemorrhagic pleural effusion (drainage)
8	symptomatic heparin-induced thrombocytopenia (HIT) (deep venous thrombosis and stroke)
12	hemorrhagic pericardial and pleural effusion (re-operation)

Table 2. Postoperative complications

Replacement therapy was very short (2 and 3 days) in patients 3 and 12 (persistent high FVIII level postoperatively), but was prolonged in patients 5 and 6 (30 and 21 days) because of delayed complications requiring re-operation. Patient 8 developed heparin-induced thrombocytopenia after 5 exposure days to heparin and was subsequently treated by lepirudin for 5 days followed by fluindione for 3 months without any bleeding event. Bleeding in patient 12 was not related to an insufficient FVIII level (FVIII = 76%).
As expected in the 4 month-old boy (patient 14), significant high factor VIII concentrate consumption was necessary in order to maintain optimal FVIII level.
Except the HIT patient (8), no patient developed a thrombo-embolic event postoperatively. No patient developed inhibitor.

DISCUSSION AND CONCLUSION

Bolus infusions of FVIII/IX were used in most cases of this series. One patient was operated on 2 occasions first using bolus infusion and secondly using CI; we observed reduced consumption when CI was used. Further studies are needed in order to evaluate CI in cardiac surgery in terms of safety, cost effectiveness, practicability. The need for thromboprophylaxis remains controversial, however all patients in our cohort except one (patient 1) received LWMH and were treated with low dose aspirin if indicated.
Our study confirms that major cardiac surgery can be performed safely in haemophilia patients. We conclude that each situation should be discussed on an individual basis in order to manage factor replacement and antithrombotic treatment. The outcome of cardiac surgery depends on the collaboration of a well-informed and multidisciplinary team.

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