

SURGERY & INVASIVE PROCEDURE WITH BYPASSING AGENTS IN HEMOPHILIC PATIENTS WITH INHIBITORS : A SINGLE CENTER EXPERIENCE

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Introduction

Inhibitory antibodies to factor VIII (FVIII) or factor IX (FIX) are one of the most important complications of managing patients with hemophilia A and B. For hemophiliacs with inhibitors, recent advances in the use of bypassing agents such as recombinant activated factor VII (rFVIIa) and activated prothrombin complex concentrates (APCC) have enabled them to aggressively manage their diseases in emergency or elective surgery. Hemostatic control in these patients with hemophilia with inhibitors can be challenging, and is especially risky in those undergoing surgical interventions.

We report here the findings of our single center experience in patients with hemophilia and inhibitors undergoing invasive procedure and surgery using bypassing agents-APCC or rFVIIa as hemostatic cover. The aim of this study was to identify possibility of surgical intervention in hemophilic patients with inhibitors by using bypassing agents under the thorough inspection of hematologists.

Methods

We reviewed the charts of the hemophilia patients with inhibitor and performed retrospective study in a single center of Kyung Hee University Hospital at Gangdong, Seoul, South Korea. Between May 2008 and July 2013, a total 32 cases of surgery in 16 patients were identified.

All patients presented in this article required hospitalization and received hemostatic therapy as accepted in our medical institution and according to accepted reports for treating hemophilia patients in our country.

Characteristics of subjects were collected : age, gender, weight, type of hemophilia, factor level, titer of inhibitors, previous medical history, type of surgery, initial single agent used, initial treatment regimen and whether the prophylactic treatment was performed before the episodes.

Follow-up after surgery occurred once a month for 1 month, once every 6 months for the following first year, once every 1 years during the second and third years after surgery.

Results

Table 1. Types of surgery included in this study

Types of surgery	n
Orthopedic surgery	
Total knee replacement	9
Total hip replacement	1
Arthroscopic synovectomy	8
Amputation of leg	1
Closed reduction of ankle dislocation	1
Device removal from leg	1
Finger tenotomy	1
Open reduction of femur fracture with internal fixation	1
Other surgery	
ICH removal and craniectomy	1
Polypectomy of colon	1
Exploratory thoracotomy	1
Miringotomy with insertion of tube	1
Segmental resection of small bowel	1
Circumcision	1
Catheter insertion (PICC, chemoport)	2
Arterial embolization	1
total	32

Table 2. Demographics and details of patients included in this study

Number of patients, n (sex)	16 (male 16, female 0)
Number of procedures evaluated, n	32 (orthopedic 23, others* 9)
Median age, year (range)	30.5 (7-52)
Type of hemophilia, n (%)	A 14 (87.5%) B 2 (12.5%)
Severity of hemophilia, n	Severe(< 1%) 16
Titer of inhibitors at procedures	
median titer, BU (range)	15 BU (0.7-1900), <i>except borderline and negative after ITT</i>
low titer (<5 BU), n (%)	12 (37.5%)
high titer (≥ 5 BU), n (%)	17 (53.1%)

The progress after use of bypassing agent in patients with inhibitors

Efficacy of bypassing agents at various surgeries and procedures, based on final patient outcome, was 93.8% (30/32). Two deaths occurred at emergency condition as a result of hypovolemic shock secondary to intracranial hemorrhage or retroperitoneal bleeding.

Table 3. Bleeding response and patient outcome in inhibitor patients undergoing surgery

Median duration of hospitalization, days (range)	14 (1-58)
Initial hemostatic cover, n	
FVIII concentrates	2
APCC	21
rFVIIa	9
Changes of medication, n	
Total	32
Yes	11
Sequential	5
No	21
Patient outcome, n (%)	
Good (Discharge)	30
Death	2

The use of bypassing agent at emergency conditions

There were 4 cases which occurred to patients with inhibitors the use of bypassing agent at emergency conditions. As we mentioned above, the results of two deaths fell under in these situations. In two cases, sequential therapy was performed and bleeding control was handled well.

Table 4. At emergency conditions

Cas e	Age (Yr.)	Diagnosis	Names of operation	Sequential therapy	Results
1	41	Small bowel ischemia	Segmental resection of small bowel	Y	Discharge
2	42	Intracranial	ICH removal and craniectomy		Expired
3	15	hemorrhage	Exploratory thoracotomy	Y	Discharge
4	43	Hemothorax	Angiography and arterial embolization		Expired

Conclusion

Good control of hemostasis can be achieved with bypassing agents in hemophilia patients with inhibitors undergoing surgery. If surgery would perform at emergency condition, more active and aggressive management should be needed. The use of bypassing agents in peri-operative period can allow surgery to be safe and successful in hemophilic patients with inhibitors.

