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ORIGINAL ARTICLE *Clinical haemophilia*

FEIBA in the treatment of acquired haemophilia A: Results from the prospective multicentre French 'FEIBA dans l'hémophilie A acquise' (FEIBHAC) registry

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Summary. Factor VIII inhibitor bypass activity (FEIBA) is a recommended first-line bypassing agent for bleeding episodes in patients with acquired haemophilia A (AHA). Due to the low incidence of AHA, available clinical data on FEIBA treatment are limited. The study aim was to delineate practice patterns in FEIBA treatment of AHA patients, the haemostatic efficacy of FEIBA, including criteria for its assessment, and safety. A prospective registry was established of AHA patients receiving FEIBA for bleeding episodes or prophylaxis at the time of invasive procedures. Data were collected at 16 participating centres in France. Patients were followed up for 3 months. Haemostatic efficacy, FEIBA regimen and FEIBA-related adverse events were documented. Thirty-four patients averaging 81.8 years old with standard deviation (SD) 8.1 years were included in the study: 33 for acute bleeding and one for haematoma evacuation. The mean initial dose of FEIBA for acute bleeding was 75.4 U kg^{-1} (SD, 7.7 U kg^{-1}), most often administered twice daily, and the median duration of FEIBA treatment was 4.0 days (interquartile range, 2.2–8.0 days). FEIBA was effective in managing 88.0% of bleeding episodes (95% confidence interval, 75.8–94.5%). No baseline variables influencing treatment response could be identified. The sensitivity and specificity of an objective haemostatic efficacy scale in predicting sequential investigator assessments of haemostatic efficacy were 45.3% and 84.1% respectively. Four patients experienced a total of six serious adverse events possibly related to FEIBA. In the first prospective study specifically focused on FEIBA treatment of patients with AHA, 88.0% of bleeding episodes were effectively managed.

Keywords: acquired haemophilia A, blood coagulation factor inhibitors, factor VIII inhibitor bypass activity, FEIBA, haemorrhage

Introduction

Acquired haemophilia A (AHA) is a bleeding disorder caused by autoantibodies directed against functional epitopes of coagulation factor VIII (FVIII) [1–5]. AHA is rare, with an estimated yearly incidence of 1.4 cases per million reported for the UK surveillance study, and increases with age [6]. In the UK surveillance study [6] and the European Acquired Haemophilia (EACH2) registry [7], the two largest available cohorts, the median ages of diagnosed patients were 78 and 74 years respectively. In this elderly population, prognosis may be related to interconnected causes and mechanisms including bleeding, specific or advanced age-related co-morbidities or iatrogenic complications as shown by an analysis of 121 deaths associated with AHA in France [8].

Bleeding at presentation is usually severe and can be life-threatening [1,4,6,7,9,10]. The use of bypassing agents, such as activated prothrombin complex concentrate (FEIBA) and recombinant activated factor VII

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(rFVIIa) to treat severe bleeds has been recommended by an international consensus group [11].

The use of FEIBA therapy for controlling bleeding episodes in AHA patients has been reported in several small studies and two registries [4,7,12–15], but more information on factors that influence FEIBA as a treatment choice and the haemostatic response to FEIBA would be of value to clinicians. The French prospective multicentre 'FEIBA dans l'hémophilie A acquise' (FEIBHAC) registry under the sponsorship of Baxter S.A.S. was designed to determine reasons for initiating haemostatic treatment, FEIBA posology, haemostatic response, potential factors affecting outcome and thrombotic complications.

Materials and methods

Study design

Clinicians in France at either haemophilia treatment centres or in haemostasis and internal medicine departments were recruited to participate in the registry at scientific meetings and through direct mailing. Of 31 centres invited 16 (52%) participated, and data were collected from November 2008 until November 2011. At 11 of the centres, the investigators included specialists in both internal medicine and haemostasis, while only haemostasis specialists were involved at the other five centres.

This was a non-interventional study. Accordingly, informed consent was not required. Nevertheless, subjects meeting the eligibility criteria for the study received verbal information and a written patient information sheet from their clinician, informing them about the objectives of the registry and policies for collecting data with strict confidentiality and anonymity. Patients were informed about their rights of access and correction with regard to their personal data.

Patients

Inclusion criteria were a diagnosis of AHA based on isolated, prolonged activated partial thromboplastin time (aPTT), inhibitor titre > 1 Bethesda unit (BU) and FVIII coagulation activity < 20%; an initial or recurrent bleed and/or an invasive procedure such as surgery; need for first- or second-line FEIBA therapy; and age > 18 years. The FVIII cut-off for inclusion was adopted on the premise that FVIII concentrate or desmopressin would be preferred for treatment of patients with FVIII levels ≥ 20%. A recurrent bleed was defined as exacerbation of bleeding at an existing site or appearance of bleeding at a new site. Exclusion criteria were congenital haemophilia or an international normalised ratio > 4.5 following an overdose of vitamin K antagonist.

FEIBA treatment

The FEIBA regimen was chosen at the discretion of the attending physician and in accordance with the national Summary of Product Characteristics.

Assessments

Patients were evaluated at baseline, in recommended intervals of every 12 h over the course of FEIBA therapy and during a follow-up period of 3 months. Baseline laboratory tests included haemoglobin levels, haematocrit, blood cell counts (white, red and platelet), aPTT, prothrombin time, fibrinogen levels, residual FVIII levels and inhibitor titres. Laboratory parameters recorded as baseline could have been determined up to 1 month prior to study inclusion. Data on the use of tranexamic acid were not captured.

Periodically determined laboratory parameters during the treatment and follow-up periods were haemoglobin and FVIII levels, aPTT and inhibitor titres. After the baseline determination, inhibitor titre measurements were recommended after 10 ± 2, 30 ± 7 and 90 ± 7 days employing the original Bethesda assay or the modified Nijmegen method. Severity-of-bleeding scores were calculated according to criteria described in Table 1. This novel numerical score was devised *a priori* by the study investigators, allowing the relationship between bleeding severity and the haemostatic efficacy of FEIBA to be quantitatively characterized. Blood samples were collected as part of the usual follow-up for patients with AHA and were not required according to a specific schedule.

Investigators were to record all adverse events (AEs) related to FEIBA, both serious and non-serious. The relationship of FEIBA to the AE was judged independently by both the investigator and the study sponsor. AEs were reported on standardized forms. Serious AEs were defined as events meeting one or more of

Table 1. Calculation of bleeding severity score.

Finding	Points to add for each
Type of bleeding	
Intracerebral	8
Retroperitoneal, GI or other major haemorrhage	6
Haematuria or genital	3
Muscular haematoma, multiple haemarthroses or diffuse ecchymoses	2
Single haemarthrosis, localized ecchymoses, epistaxis or gingival	1
Haemoglobin level (g dL^{-1})	
<6	4
6–8	3
>8 and <11	1
Other	
Need for transfusion or increased extent of bleeding	3

GI, gastrointestinal.

the following criteria [16]: (i) either fatal or life-threatening, (ii) prompting or prolonging hospitalization, (iii) manifested as a defect or congenital malformation, (iv) causing disability or permanent incapacity or (v) judged medically important.

Patients routinely received immunosuppressive therapy. The outcome of that therapy was scored as: (i) failure, if the inhibitor titre after therapy equalled or exceeded the titre at study enrollment, (ii) partial response, if the inhibitor titre was ≥0.6 BU and below that present at study enrollment and/or FVIII levels were less than 50% and (iii) complete response, if the inhibitor titre was <0.6 BU and FVIII levels were >50% or missing. Data on AEs related to immunosuppressive therapy were not collected as part of the study.

Endpoints

The primary study endpoint was the sequential physician assessment of haemostatic efficacy at recommended intervals of every 12 h during FEIBA therapy. At each assessment, the physician rated the response to FEIBA as exacerbation, stabilization or improvement. An objective standardized haemostatic efficacy scale score was also assigned at each sequential assessment during FEIBA treatment (Fig. 1). In addition, an overall assessment of haemostatic efficacy for the entire bleeding episode was recorded. FEIBA was scored as effective in the treatment of a bleeding episode if either (i) cessation of bleeding was documented during sequential assessments or (ii) resolution of the episode was recorded by the investigator at the time FEIBA treatment was discontinued.

Statistical analysis

In order to attain a target enrollment of approximately 40–50 patients, a study duration of 3 years was estimated to be necessary based on the incidence of AHA in France and the anticipated frequency of FEIBA treatment for bleeding episodes. Data were analysed using SAS version 9.0 (SAS Institute Inc., Cary, North Carolina, USA) and R version 3.0.2 (The R Foundation for Statistical Computing, Vienna, Austria) statistical software. Haemostatic efficacy and the sensitivity and specificity of the haemostatic efficacy scale in predicting investigator assessments of haemostatic efficacy were analysed by mixed effects logistic regression.

Results

Patients

The selection and disposition of patients are detailed in Fig. 2. Fifty patients were assessed for eligibility and 34 patients were included in the study. Of the 16 patients who were assessed but not included, 8 required no antihaemorrhagic treatment, while 4 received a non-FEIBA bypassing agent. Six included patients died, and 26 were followed up for the complete planned study period of 3 months. In both of the two patients treated at the centre in Caen FVIII level was measured by the modified Nijmegen method, while the original Bethesda assay was used in all other patients at all other centres.

Of the 34 patients included in the registry, 33 were included for treatment of a bleeding episode and one was included to prevent bleeding during and after an invasive procedure to evacuate a haematoma. Their characteristics are listed in Table 2. The average age of the cohort was 81.8 years (SD, 8.1 years), and the majority (61.8%) were women. The median baseline residual FVIII level was 1.6% and median inhibitor titre 20.8 BU. Of the index bleeds, 76% arose spontaneously and manifested primarily as muscle haematomas or ecchymosis. Two-thirds of the patients had thrombotic risk factors, namely, hypertension, smoking, hypercholesterolaemia, elevated glycated haemoglobin (≥8%) or type 1 diabetes, and almost a quarter had a history of thrombotic events.

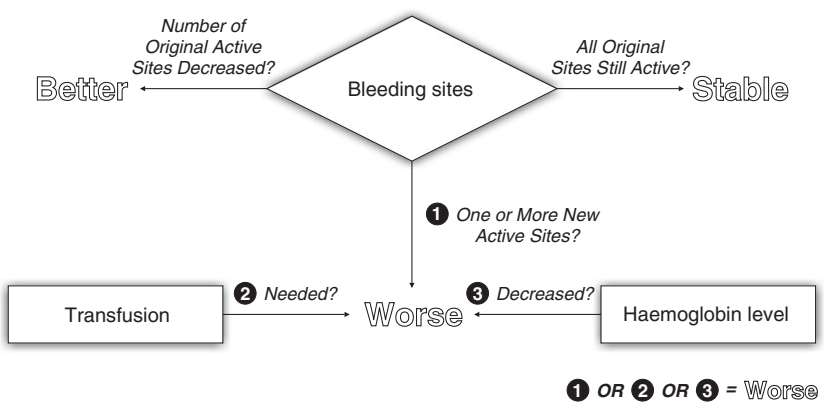

Fig. 1. Assignment of haemostatic efficacy scale with possible categories of better, stable or worse.

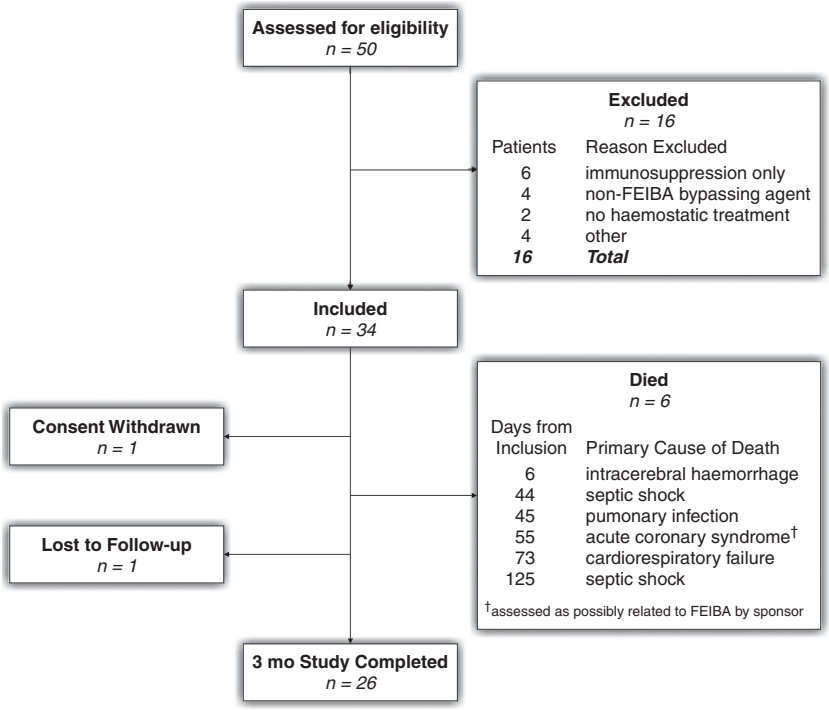

Fig. 2. Patient selection and disposition.

FEIBA regimen

The mean initial FEIBA dose per infusion was 75.4 U kg^{-1} with standard deviation (SD) 7.7 U kg^{-1}, while the mean total daily dose was 155 U kg^{-1} (SD, 52 U kg^{-1}). The most common initial dosing interval was 12 h, which was employed in 52% of the patients. Twenty percent of the patients received once daily dosing, whereas 28% received FEIBA three times daily. The median duration of FEIBA treatment was 4.0 days with interquartile range (IQR) 2.2–8.0 days. The median number of FEIBA infusions for each bleeding episode was 7.5 (IQR, 3.0–11.8).

Three patients discontinued FEIBA treatment and switched to rFVIIa during the study. The reason for the switch was in one patient each: lack of efficacy, disseminated intravascular coagulation (DIC) and need for an invasive procedure.

All patients were treated with immunosuppressive agents to eradicate the inhibitors. Combination treatment with corticosteroids + rituximab ± other immunosuppressors was used most frequently, in 14 patients, while 10 patients received corticosteroids + oral cyclophosphamide and 9 corticosteroids alone. Rituximab monotherapy was administered in one patient.

Bleeding episodes

Of the 33 patients included for acute bleeding, 28 (85%) received FEIBA as first-line and 5 (15%) as second-line therapy. Of those 33 patients, 21 experienced a single bleeding episode prompting FEIBA treatment during the course of the study, 7 two episodes and 5 three episodes, for a total of 50 evaluable bleeds. In 36 of the 50 bleeds (72%), the investigators indicated that a single type of bleed prompted the initiation of haemostatic therapy. In these single types of bleeding episodes, the primary bleeding types were muscle haematomas and ecchymoses, accounting for 52% of all bleeding episodes treated with FEIBA. Multiple types of bleeds were present in 12 (24%) bleeding episodes, with 7 of these involving both muscle haematoma and ecchymosis.

Of other factors that may have prompted or influenced the initiation of haemostatic therapy, haemoglobin levels and FVIII levels were each specified by the investigators for 70% of the bleeding episodes, a perceived risk of increased bleeding for 68%, advice of a specialist for 56%, a recent fall in haemoglobin for 54% and inhibitor titre for 52%. An increased extent of bleeding and a need for transfusion were chosen for 46% and 44% of episodes respectively. A recent fall in haematocrit was only indicated as a reason for treatment in 26% of the bleeding episodes.

Major reasons indicated by investigators as to why FEIBA was specifically chosen to treat a bleeding episode included staff convenience (66%), experience of the department (58%), rapid action of FEIBA (50%), severity of bleeding (48%) and availability at the hospital (42%). Tolerability of the treatment schedule and prior successful treatment were each selected in 36% of the 50 bleeds.

Table 2. Demographic and baseline laboratory data.

Patient	Age (y)	Sex	Weight (kg)	BMI ($kg \cdot m^{-2}$)	FVIII (%)	Hb ($g \cdot dL^{-1}$)	Inhibitor Titre (BU)
0101	74	F	60	22.6	<10	9.2	93.0
0301	83	F	70	28.0	<10	10.1	–*
0302	75	F	90	35.2	0.9	9.9	47.0
0401	87	F	60	22.0	2.0	6.3	6.0
0402	84	M	83	26.2	1.0	7.9	4.0
0403	86	F	60	23.4	6.0	6.0	14.0
0404	76	F	70	25.7	1.0	10.4	13.0
0405	59	F	40	17.8	1.0	9.7	11.0
0406	72	F	52	21.6	1.0	11.3	8.0
0407	93	F	56	22.2	7.0	5.2	24.0
0408	81	F	67	29.8	1.0	6.1	110
0409	79	M	94	29.0	3.0	8.6	35.0
0501	88	F	47	18.1	1.0	12.9	42.0
0502	79	F	75	28.6	< 10	8.2	140
0503	84	F	57	23.4	2.0	8.0	52.0
0504	88	F	50	–	3.0	7.7	2.2
0601	97	F	64	25.6	1.0	12.9	2.4
0602	81	M	65	25.4	6.0	13.4	18.5
0701	85	F	58	24.1	< 10	10.2	1000
0801	72	F	43	15.8	1.0	12.3	14.0
0901	95	F	43	21.9	7.0	≤ 6	2.0
0902	81	M	60	20.5	1.0	9.0	23.0
0903	73	M	68	23.5	3.0	12.2	5.0
0904	90	F	65	27.1	1.0	10.3	148
1001	90	M	77	–	4.8	7.2	64.0
1101	83	M	57	19.3	3.0	13.3	2.6
1201	88	M	65	24.2	1.0	9.7	100
1202	80	M	70	–	< 10	7.4	60.0
1301	75	F	80	33.3	3.0	12.5	3.8
1401	84	M	67	23.0	3.0	11.5	14.9
1601	76	M	70	23.7	1.6	14.2	10.0
2001	89	F	47	20.3	4.0	9.5	–*
2002	87	M	70	22.9	0.5	10.4	80.0
2101	68	M	63	23.4	0.0	8.1	2250

*All patients satisfied the eligibility criteria, specifically including inhibitor titre >1 BU. However, inhibitor measurements supporting the diagnosis of AHA could have been performed prior to study inclusion, and baseline inhibitor determinations at the time of inclusion were not a prerequisite for eligibility. Such baseline data were not available for two patients.
AHA, acquired haemophilia A; BMI, body mass index; BU, Bethesda unit; FVIII, factor VIII; Hb, haemoglobin.

Overall efficacy

The overall efficacy of FEIBA in resolving the bleeding episodes was 88.0% (95% confidence interval, 75.8–94.5%), as indicated in Fig. 3. None of the evaluated baseline variables, namely prior AHA diagnosis, cause of bleeding, bleeding severity score, inhibitor titre and residual FVIII levels, significantly affected bleeding resolution (Fig. 3).

Sequential assessments

A total of 243 sequential assessments were performed during the 50 bleeding episodes (Table 3). The median number of assessments per bleeding episode was 4 (IQR, 2–6), with the median time between assessments of 18 h (IQR, 13–23 h). Haemoglobin levels increased or were unchanged in 51.4% of the assessments, decreased in 14.0% and unspecified in 34.6%. Diagnostic imaging was reported in 4.1% of assessments and transfusion in 10.7%. Investigators judged the bleeding to be better or stable in 218 (89.7%) of the assessments.

Investigators judged the bleeding to have improved in 50% of the 243 assessments, whereas improvement was indicated by the haemostatic efficacy scale in 20% of assessments (Table 3). In an analysis for the sensitivity and specificity of the haemostatic efficacy scale combining better or stable ratings and comparing with worse ratings, sensitivity was 45.3% and specificity 84.1%.

Inhibitor titre

The median inhibitor titre decreased from 20.8 BU at baseline to 5.5 and 2.0 at 1 and 3 months respectively (Fig. 4). FVIII levels increased over the study period. At baseline, median FVIII levels were 1.6%. By 1 month median levels had risen to 14.5% and by 3 months 107%.

Immunosuppression

By day 10 after study inclusion, 26 of 30 patients (86.7%) showed a partial response to immunosuppressive therapy, but none a complete response. By 30 days, almost a quarter of the evaluable 31 patients (22.6%) had achieved a full response. At 90 days, data were available for 26 patients. A complete response was achieved in 13 patients and a partial response in 11, while immunosuppressive therapy failed in 2.

Safety

Five patients experienced an AE related to FEIBA: four patients experienced six serious AEs and one patient experienced a non-serious AE. All of these were judged to be possibly related to FEIBA; no AE was judged to be probably related. All AEs were thrombosis-related or indicative of a potentially hypercoagulable state. The six serious AEs consisted of biological DIC in two patients, deep distal vein thrombosis and superficial thrombophlebitis in one patient and reduced fibrinogen twice in one patient. Two of these AEs prompted discontinuation of FEIBA treatment. The single non-serious AE was reduced fibrinogen.

The two patients developing biological DIC were both elderly men receiving 5000 U FEIBA twice daily. In both cases, fibrin degradation products measured in the 40–80 $\mu g\ mL^{-1}$ range, but clinical symptoms of DIC were not noted. One of the patients was switched to rFVIIa, and in the other patient FEIBA dosage was reduced to 5000 U once daily. The biological DIC of both patients resolved fully.

The patient with deep distal vein thrombosis and superficial thrombophlebitis was an elderly female. In addition to advanced age, risk factors present in that

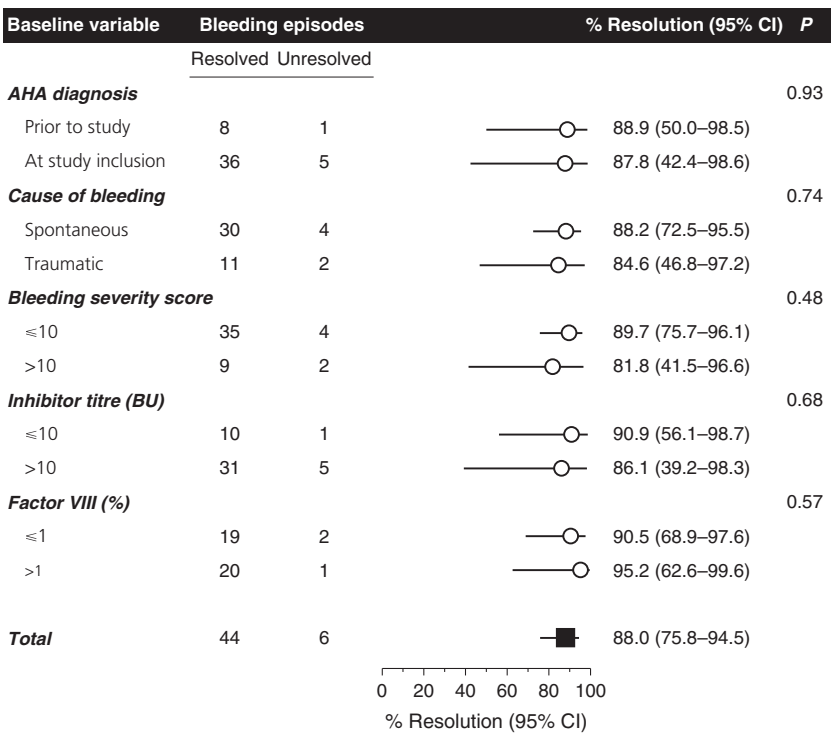

Fig. 3. Haemostatic efficacy of FEIBA in the treatment of bleeding episodes. AHA, acquired haemophilia A; 95% CI, 95% confidence interval.

Table 3. Sequential clinical and laboratory assessments during FEIBA treatment

Parameter	Summary statistics (n = 243)
Total assessments per bleeding episode; *n* (%*)	
1	4 (8.0)
2	10 (20.0)
3–5	20 (40.0)
6–10	14 (28.0)
>10	2 (4.0)
Time between assessments (h); median (IQR)	18 (13–23)
Haemoglobin levels at each assessment; *n* (%)	
Increased	53 (21.8)
Unchanged	72 (29.6)
Decreased	34 (14.0)
Unspecified	84 (34.6)
Diagnostic imaging performed; *n* (%)	10 (4.1)
Transfusion needed; *n* (%)	26 (10.7)†
Investigator assessment of bleeding; *n* (%)	
Better	122 (50.2)
Stable	96 (39.5)
Worse	25 (10.3)
Haemostatic efficacy scale; *n* (%)	
Better	42 (20.2)
Stable	152 (62.6)
Worse	49 (17.3)

*Denominator of 50 bleeding episodes for this percentage computation. For all other percentage computations in this table denominator was 243 sequential assessments.
†On a per patient basis, 19 of 33 patients included for acute bleeding (57.6%) required transfusion.
IQR, interquartile range.

patient were moderate hypertension and exposure to rFVIIa immediately prior to the onset of FEIBA treatment.

The patient with serious fibrinogen decreases, a 68-year-old male with acute leukaemia, received three FEIBA treatment courses. Isolated decreases in fibrinogen levels from 3.5 g L^{-1} to the 1.25–1.5 g L^{-1} range occurred during the first treatment course for an iliac haematoma and from 2.64 g L^{-1} to 1.35 g L^{-1} during the third treatment course for a thoracic haematoma. No remedial treatment for the decreased fibrinogen levels was required. The patient was concurrently being treated with rituximab, which has been reported to reduce fibrinogen concentration [17].

During the 3-month follow-up, six patients died. The primary causes of death are indicated in Fig. 2. No death was judged by the investigator to be FEIBA-related; however, the death of one patient from an acute coronary syndrome was assessed as possibly associated by the study sponsor. That 84-year-old female patient received FEIBA over 5 days for treatment of gastrointestinal bleeding. FEIBA was discontinued when the bleeding episode resolved. The patient died from acute coronary syndrome almost 2 months thereafter. Advanced age and hypertension at study inclusion were risk factors for coronary syndrome in this patient.

Discussion

This is the first prospective study focused specifically on the use of FEIBA in AHA and provides detailed information on the types, numbers and clinical courses of bleeding episodes prompting FEIBA treatment in an

elderly population often presenting with thrombotic risk factors. The FEIBHAC registry population, with a median age of 83 years (IQR, 76–88 years) and five patients in their 90s, was older than that of other studies involving FEIBA use in AHA. Median age in an earlier French study was 72 years (range, 43–86 years) [13], in an American study 57.5 years (range, 26–82 years) [14] and in the EACH2 registry 76.5 years (IQR, 24–92 years) [7].

Treatment efficacy in the FEIBHAC registry was comparable to that in other studies of FEIBA use for AHA. FEIBA treatment was effective in managing 88.0% of the 50 bleeding episodes that occurred in 33 patients. In the earlier EACH2 registry, which was conducted from 2003 to 2008 and included data from 13 European countries, FEIBA was used as first-line therapy in 60 patients and achieved a 93.3% bleeding control rate [7]. In propensity score-matched samples, the haemostatic efficacy as the first-line haemostatic agent was the same for FEIBA and rFVIIa [7]. While the 2-year national surveillance study of AHA in the United Kingdom determined the frequency of FEIBA use, data were not collected on the haemostatic response to treatment [6].

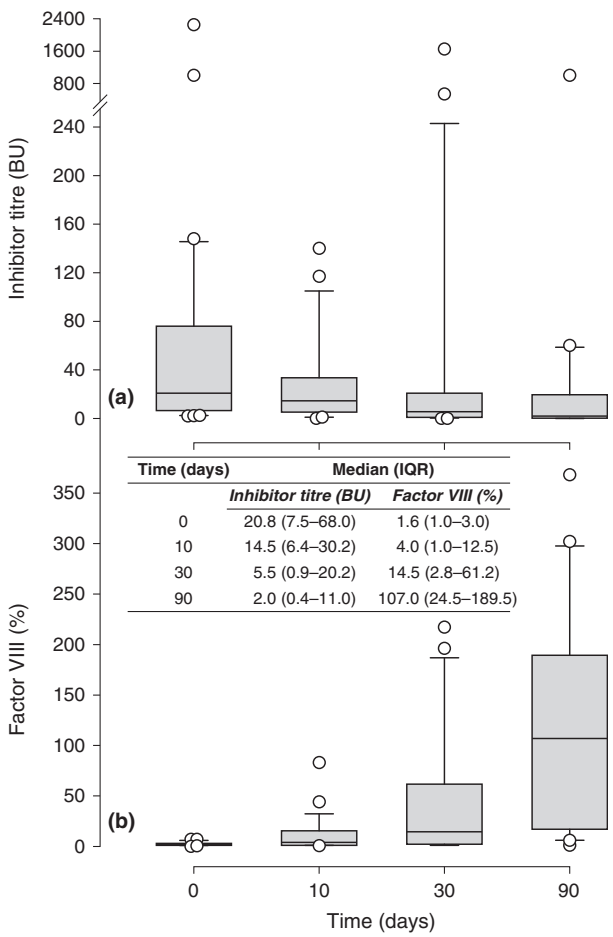

Fig. 4. Longitudinal changes in (a) inhibitor titre and (b) residual factor VIII level over the course of the study. Boxes extend from the 25th to 75th percentiles and error bars from the 10th to 90th percentiles. Median values shown by horizontal lines bisecting the boxes. BU, Bethesda units; IQR, interquartile range.

FEIBA efficacy in other AHA studies was also consistent with that of the FEIBHAC and EACH2 registries. In a retrospective French study of 19 AHA patients treated from 1990 to 2001, FEIBA efficacy was judged excellent or good in 89% of bleeds [13]. In a retrospective American study of 34 patients, a complete response was reported in 76% of severe and 100% of moderate bleeding episodes, for an overall response rate of 85.3% [14]. Five patients experiencing five acute bleeding episodes and undergoing three surgical procedures received FEIBA, and the treatment response was judged to be excellent in all instances [15]. In a recent prospective French registry report, complete resolution or improvement of bleeding was achieved in all six patients receiving FEIBA [4].

In this study, two-thirds of the patients had thrombotic risk factors and almost a quarter had a history of thrombotic events. However, only one patient experienced an overt thrombosis during treatment, an 86-year-old woman who developed a deep distal vein thrombosis in the internal soleus vein and superficial thrombophlebitis in the right forearm. The patient was treated for a total of 9 days and received the recommended maximum daily dose of FEIBA (240 IU kg^{-1}). Two other patients were diagnosed with biological DIC, and one displayed a decrease in fibrinogen levels on two occasions that was considered serious. The EACH2 registry was the only prior study in AHA to report thrombotic events associated with FEIBA use. Thrombotic events were observed in 3 of 63 patients (4.8%) treated with FEIBA as first- or second-line therapy, which was not significantly different from the 2.9% rate associated with rFVIIa use [7]. In EACH2, thrombotic events were significantly associated with greater mean age (79.4 vs. 68.3 years). It is difficult to compare the rate of thrombotic events in the present study with EACH2, because laboratory evidence of hypercoagulation was not reported in the EACH2 registry.

Since many AHA patients present with thrombotic risk factors, steps to mitigate the risk may be warranted when using bypassing agents such as FEIBA. For some patients such steps might include caution in dose selection and monitoring for early laboratory signs of thrombosis through the use of fibrin degradation product or fibrinogen assays.

Several limitations of this study should be noted. With 34 included patients, the study population was smaller than the target sample of 40–50 patients. This limited the precision with which haemostatic efficacy rate and the frequency of AEs could be assessed. While the participation of all AHA treatment centres in France was solicited, it is possible that the AHA case mix among the 16 participating centres was not a

representative of the entire universe of French centres or of non-referral hospitals with respect to clinical presentation, natural history and outcome of AHA treatment.

Conclusion

With a demonstrated haemostatic efficacy rate of 88.0%, this study further supports the role of FEIBA as a first-line treatment for bleeding episodes in AHA. The potential for thrombotic AEs and risk profile of AHA patients should be carefully considered during treatment with bypassing agents such as FEIBA.

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Disclosures

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