Author’s response to reviews

Title: Circumcision in hemophilia using low quantity of Factor Concentrates: Experience from Dakar, Senegal

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Author’s response to reviews:

Answers letter

Dear Editorial board

Thank you for all your comments to improve the paper. Please receive below the corrections/comments following remarks from the reviewers. I also put all the edited sections in red in the manuscript

Best regards
Reviewer #1:

1- Data on the quantity of factors used are given in Table 4 (added) and in the abstract page 2, lines 41 and 42

2- Outcome measure were more defined and the statistical tests were detailed: page 6, line 142 to 146

3- Hemostatic control during surgery was reported in the surgery protocol: page 7, line 129 to 134

Other comments

Background

1- The sentence has been reworded: page 3, lines 69 and 70

2- The reference was provided on page 3, line 73 (reference 18)

Methods

1- The reference was provided: page 4, line 79

2- The definition of hemophilia A by FVIII <30% is used in reference 1.

3- The answers concerning inclusion criteria were given on page 4, line 85 to 87

4- The answers concerning consent statements or ethics consideration for this study were given on page 4, line 94 to 96

5- Doses of FEIBA or rFVIIa were reported in page 5, lines 103 to 105

6- Oxacillin and paracetamol were administered orally, page 5, lines 108 to 110

7- Healing time is defined by the period from the beginning of circumcision to healing. page 6, line 134

8- Bleeding event is any haemorrhage that occurs since the release of hemophiliacs in the operating room until healed. Page 6, lines 134 to 136

9- The data collected at the start of the study are presented in Table 1

10- The response to patient follow-up and inhibitor dosing is presented on page 6, lines 137 to 139
The dosage of FVIII was monitored only before circumcision. It was not considered necessary to repeat the FVIII assay since the severity of all hemophiliacs is already known.

Statistics

1- The statistical tests were presented and explained on the pages 6 and 7, lines 141 to 146

Results

1- Definitions:

Severe hemophilia is defined as a factor VIII level of less than 1%.

Moderate hemophilia is defined as a FVIII level between 1% and 5%

Mild hemophilia is defined as a FVIII level between 6% and 30%

The term minor was changed to mild.

2- Page 7, line 154: “low titer inhibitor” instead of "low responder".

3- No haemophiliac had prophylactic treatment. page 4, line 84

4- Perioperative Control of bleeding was explained on surgical protocol section. page 7, lines 123 to 129

5- Table 2 comparing outcome according to age was deleted

6- "bleeding event" is defined at page 6, line 134 to 136

7- Minor bleeding was defined as any bleeding that stops after local application of tranexamic acid

8- All patients systematically received the first three doses. Additional doses were administered to the hemophiliacs who had bleeding and during dressings (see Table 4 added)

9- Mean doses of FVIII concentrate administered are calculated. page 8, lines 177 to 184 and presented in Table 4
10- Details for the treatment in patients with inhibitors are reported : page 5, lines 103 to 105 and page 8, lines 180 to 184

11- Mean time to occurrence of bleeding was not calculated in the study. What was important to us was to note the occurrence or not of bleeding.

Discussion

1- "Substitution therapy consisted to raise FVIII levels around 60% for three days" is the protocol of the study

2- Amount of factor used in this study is compare with other protocols: page 9, lines 197 à 207.

3- Necessary corrections have been made in Table 1, 2. Table 2 is corrected but no percentage has been set to avoid overloading the table

4- No hemophiliacs had a prophylaxis treatment

Reviewer #2:

1. Corrections have been made at all the declarations (page 11 and 12, lines 246 to 282

2. These are Muslim and non-Muslim patients in the cohort. The fact that circumcision was performed late in some patients is explained by unavailability of FVIII concentrates. If we have not enough products, we always prioritize treating bleeding events instead of performing circumcision