Primary prophylaxis and inhibitor development in patients with severe Hemophilia A and B

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Introduction and objectives: Approximately 30% of individuals with severe hemophilia A and 3% with severe hemophilia B develop alloantibodies (inhibitors) to FVIII and to FIX, respectively. Recent studies have shown a protective effect of prophylaxis against the development of inhibitors. In 2010 our Center started, for the first time, primary prophylaxis (PP). Our objective is to determine among these patients how many developed inhibitors during PP.

Patients and methods: Data were raised from the charts of patients with severe hemophilia A and B registered in Hemorio, submitted to PP from November 2010 to 31 June 2015. The protocol used was the Canadian dose tailored prophylaxis modified. The first 12 patients with hemophilia A received plasma derived factor VIII (pdFVIII). In March 2012 they switched to recombinant FVIII (rFVIII). After this date, all patients with hemophilia A included in PP received rFVIII. Patients were evaluated for alarm signals (surgery, trauma, severe bleeding, infection, etc) associated with factor concentrate replacement.

Results: Thirty six patients were included. Twenty six (72%) had hemophilia A and 10 (28%) hemophilia B. The ages at the beginning of PP ranged from 8 months to 3 years. Five (14%) patients developed inhibitors, all with hemophilia A. Three inhibitors were high titer (12 UB, 5,7 UB, 1126 UB) diagnosed at 10, 34, 10 exposure days (ED), respectively, and two were transient inhibitor (one diagnosed before switch). No family history of inhibitor was described. Eight (22%) patients (2 with hemophilia B and 6 with hemophilia A) presented alarm signals associated with factor concentrate replacement. Four patients with inhibitor were included in this group and 3 of them had switched to rFVIII before the inhibitor's diagnosis.

Hemophilia	Number (n)	Inhibitor	Switch	Danger Signals	Danger signals and inhibitor	Switch and inhibitor
A	26	5	12	6	4	4**
B	10	0	0	2	0	0
TOTAL	36	5*	12	8	4	4

Table: Characteristic features of the study
* 3 cases switched before the inhibitor
** 3 cases presented danger signals

Conclusion: These findings support the RODIN study that high dose intensive treatment in association with danger signal are risk factor for inhibitor development. Even though there is no evidence that switching factor concentrate has any significant effect on development of inhibitor, four patients (80%) with inhibitor switched from pdFVIII to rFVIII .

References:
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