Prevalence of inhibitor antibodies in the Mazandaran(North of Iran) haemophilia A population.

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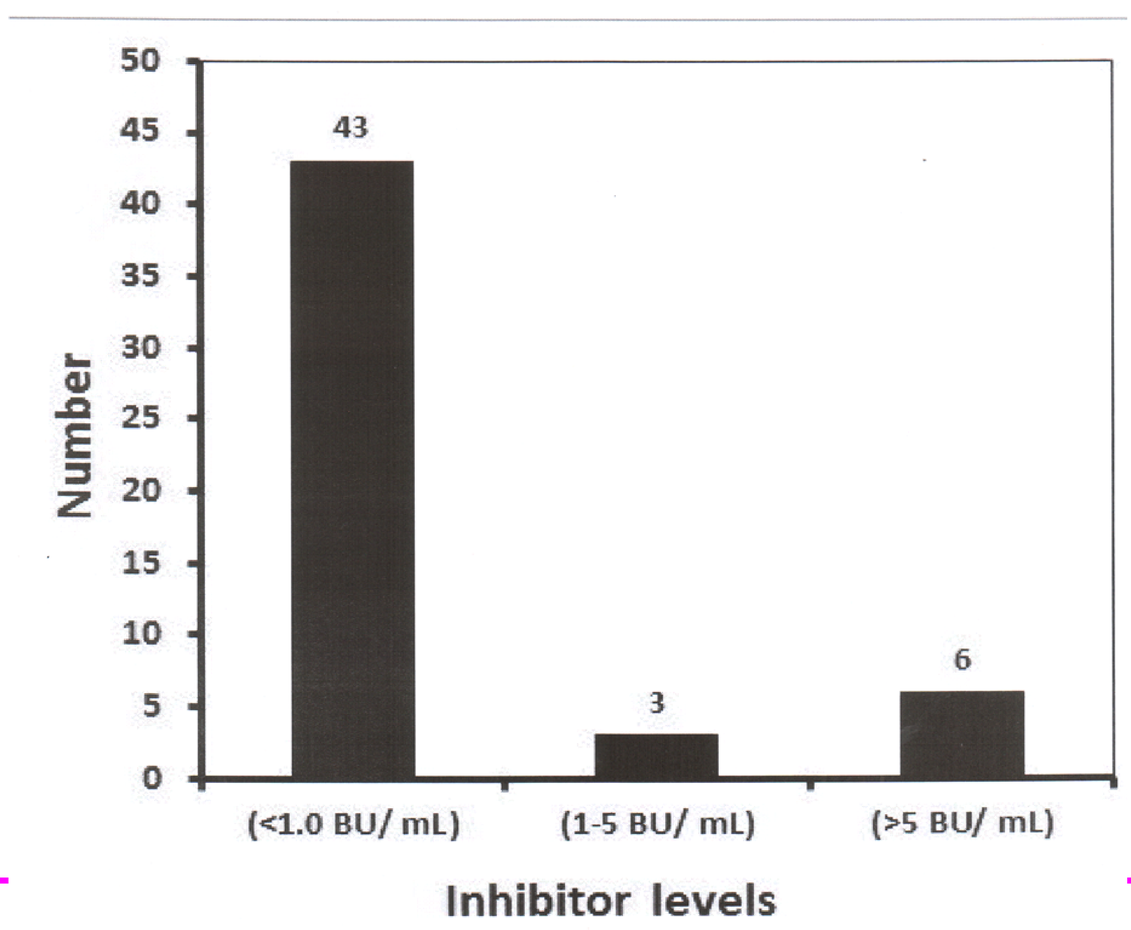
OBJECTIVES

Hemophilia A is the most common type of hemophilia(1). Prophylaxis has long been used but not universally adopted because of medical, psychosocial, and cost controversies. Inhibitory antibodies to exogenous FVIII are a major complication of haemophilia treatment (2). Clinical hallmark of inhibitor development is failure to respond to routine replacement therapy(3-4).Some study showed, the risk of inhibitor development is higher in patients treated with rFVIII than in patients treated with pFVIII(5). Several data suggest that prophylaxis initiated at the early age may increase the risk of inhibitor formation (6) . However some studies showed that early exposure to factor VIII was not directly associated with higher incidence of inhibitor(7).The titer of antibody may be less than 5 Bthesda units (low responders) or excess of 5 Bthesda units (high responders). The clinical approach is different for these two groups (8-9) .We performed a study to assess the patients with inhibitors directed against FVIII.

METHODS

This descriptive analytic study was done in our teaching center from May 2010 to May 2011. Data were collected from all eligible children attending in our hemophilia Care Center. Consecutive patients with severe hemophilia A (FVIII ≤1 IU/ mL) were included. Patients were treated with either a plasma-derived or recombinant FVIII (rFVIII) product. First monitoring for inhibitory antibodies was performed at the time of study with a mixing study. In every patient with abnormal mixing study antibody against FVIII has been measured. Our laboratory used the Bethesda assay and a significant inhibitor titer was defined as being ≥1.0 BU/ mL on at least two consecutive measurements. High titer inhibitors were defined as having a titer of >5 BU/ mL at any time. Data were collected for each patient on family history of inhibitor development, date of first exposure to exogenous FVIII, the age of the patient at inhibitor development and the number of joint involvement were recorded. Analysis of the parameters was performed using SPSS 18 with chi-squared testing. All analyses were performed using a significance P value of < 0.05.



RESULTS

In our study 52 severe hemophilia patients recruited. All of them were male at age 4-60 years (mean=22.33±1.99 years). All these patients had hemophilia A and a FVIII level of ≤1 IU/ mL and had commenced treatment between 1995 and 2010. The overall prevalence of inhibitor development (≥1.0 BU/ mL) in this study was 9 of 52 (17.3%; CI=95%, 7%-28%). In 6 patients (11.5%) inhibitor levels were more than 5 Bethesda units. Minimum levels of inhibitors were 2.3 Bethesda units and maximum levels of inhibitors were 29 Bethesda units. Mean age of patients with inhibitors was 10.89 months and mean age of patients without inhibitors was 24.60 months (p.value:0.008). The children in the younger patients received their first treatment during the first month of life while older patients were treated at the time of bleeding. The older patients have irregular treatment. Patients without inhibitors suffered from at least one joint deformity more than patients without inhibitors [3 of 9(33%) versus 25 of 43(58%)] respectively.

CONCLUSIONS

Conclusion:

Our study showed that the prevalence of inhibitors in our population is similar to other population (10-11).But it is more than that has been showed by Klukowska and et al(12). The product that has been used in this study was Octanate. So we need to be more familiar for this product. Our study showed that the production of inhibitors in our population, in recent decade, is more than that was previous decades. It may be due to use of exogenous FVIII as prophylaxis in some new hemophilia A patients and use of exogenous FVIII on demand in old hemophilia A patients at the last decades or may be due to difference in type of concentrate that were used (13).Conversely, Ociepa and his coworkers showed that undisputable is that prophylaxis of haemophilia is associated with a lower risk of inhibitor development than on-demand therapy(7). Mauser and et.al believed, risk of inhibitor development in mild haemophilia A is increased with age (14).Although other studies did not show this problem(15-16). It may be such as other study that has announced; initial treatment with recombinant FVIII and the presence of a major molecular defect was the most important variables affecting inhibitor development(17-18). We should consider both inhibitor antibodies formation and joint bleeding in hemophilia A for managing of hemophilia patients.

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