

Immune tolerance induction in adult patients with severe haemophilia A and long lasting inhibitors

Introduction and objective: The development of anti-factor VIII(FVIII) neutralizing antibodies (inhibitors) is the most serious treatment-related complication in patients with haemophilia A. Inhibitors occur in approximately 30% of severely affected (baseline FVIII:C<1IU/dl) patients, usually during the first 50 exposure days to FVIII concentrates. Immune tolerance induction (ITI) which consists in regular intravenous injections of FVIII may lead to eradication of inhibitors. It is recommended to start ITI at a younger age, as quickly as possible after inhibitor appearance for two reasons: success rate of ITI in children is high (approx.70%) and costs of ITI are reduced (low body weight). **Materials and methods.** This prospective study comprised 23 patients with severe haemophilia A and inhibitors toward FVIII, in whom ITI was initiated at the age of 19-59 years. The time interval from inhibitor diagnosis to ITI start was between 5-40 years. Inhibitor titre was measured with Bethesda assay in Nijmegen modification. **Results.** Historical inhibitor titre was in range 8-819 BU/ml and starting titre was between 0.6-90BU/ml. All patients received plasma derived FVIII containing von Willebrand factor concentrates (pdFVIII/VWF) at a dose 50-100IU/kg once daily. The lowest peak inhibitor titre during ITI was 2 BU/ml and the highest 24576 BU/ml. The significant increase in the number of bleeding episodes at the beginning of ITI was observed in most cases and the treatment with by-passing agents was necessary in majority of patients. Inhibitor became negative (<0.5 BU/ml) in 9 patients and everyone achieved good clinical response to FVIII infusions (ITI success) after 4-48 months (median 25). ITI failed in 11 patients after 6-68 months (median 16) and 3 other patients resigned from the treatment for various reasons. All patients with ITI success continue exposure to FVIII (prophylaxis) thrice weekly. **Conclusion.** ITI in adults is less effective and very costly compared to children. Nevertheless, in some patients with long-lasting inhibitors, mainly those with severe bleeding phenotype, low historical inhibitor titre and good compliance, ITI can be successful and therefore should be recommended.



Poster
Presented at:

DOI: 10.3232/ajco.2016.20.6

Hemophilia - clinical
Anna Buczma

88--PP-T

9T0ZHM