




Trombosi ed emostasi in età pediatrica

# QUALITY AND SAFETY OF VITAMIN K ANTAGONIST TREATMENT IN PEDIATRIC PATIENTS: A RETROSPECTIVE CLINICAL AUDIT FROM A SINGLE CENTRE

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**Background and aims.** The knowledge of quality and safety of vitamin K antagonists in pediatric patients is limited. In children the time-in-therapeutic-range (TTR) achievement has been reported between 39% and 81%, while warfarin-related major bleeding rates ranging from 0.5% to 1.7% per year.

**Methods.** A retrospective clinical audit has been conducted to evaluate the characteristics and rates of bleeding in long term follow up and identify possible hemorrhagic risk factors. All patients used a point-of-care device for INR determination. The TTR is calculated using the Rosendaal method. TTR > 65% has been considered optimal. Major bleeding refers to the ISTH definition. Patients are in anticoagulation for mechanical valve replacement (group A, 8 patients), other post-surgical congenital cardiopathies, mainly Fontan surgery (group B, 48 patients) and thrombotic disease (group C, 3 patients). Grade 1,2 and 3 types of bleeding according to the CTCAE classification occurred in our population. No grade 4 and 5 events were observed. We evaluated: age, suboptimal TTR, indication for anticoagulation in relation to quality of INR control and type of bleeding. Among grade 3 bleeds, only two could be classified as major. Associations between categorical variables were assessed using Pearson's chi-square test. All statistical analyses were performed using SPSS version 21.0 (IBM Corporation), and a two-tailed p-value < 0.05 was considered statistically significant.

**Results.** Included were 59 consecutive patients (45 male, 14 female, median age 11), actively in follow up at our outpatient service for vitamin K antagonists (VKA) monitoring. Median duration of follow up was 6 years (range 10-0.5). Median TTR percentage was 63.3% and mean value 65.1%. Nine patients received pediatric formulations of warfarin; 3 patients received acenocumarol while 47 commercial tablets of warfarin. There were 8 cases with at least one grade 1 bleeding event, 8 cases with grade 2 and 8 with grade 3 bleeding events. With a total follow-up of 375 person-years, the incidence rate of all hemorrhagic events was 0.064 per person-year (6.4% per year). Major bleeding events rate was 0.005 per person-year (0.5% per year). No significant correlation has been found between TTR and age; grade 1 and grade 2 bleeding and age, non-optimal TTR, type of indication; grade 3 events and age, non-optimal TTR. Group B indication correlates to less probability of grade 3 bleeding (p=0.014), while patients with prosthetic heart valve replacement have higher risk of grade 3 bleedings (P=0.034) despite a median TTR of 83%.

**Conclusions.** Our data confirm good INR control when considering TTR and incidence of major bleeding among pediatric patients. Among all types of haemorrhage, the highest risk of events requiring medical intervention was observed in patients with mechanical prosthetic heart valve.