

Initiation of warfarin therapy in children: a new safe and practical clinical algorithm

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Purpose: Managing vitamin-K antagonist therapy is challenging in children. We developed a simple weight-adapted warfarin algorithm (target INR, 2.0-3.0) for starting warfarin therapy in children in order to reduce the frequency of over-anticoagulation and the time required to obtain the maintenance dose. To build this initiation warfarin regimen, we used a derivation cohort from 2009 to 2012. In this cohort, the loading dose was chosen according to the CHEST recommendation (0.2 mg/kg whatever the age). The observation of this cohort allowed us to create an empirical regimen in a validation cohort from 2012. In this regimen, the initial fixed warfarin dose was weight-dependent according to three growth periods. The two cohorts are independent.

Methods: Sixty-one children (median age 7.1 years; from 0.1 to 17.9 years) were included in the derivation cohort. In our warfarin regimen, the induction dose was adapted to three weight sub-groups: <20kg; 20 to 30 kg and > 30kg with respectively 2, 3 and 5 mg/day during 2 consecutive days. The day 3 daily dose was predicted from the INR value obtained the day after the second intake. To validate this algorithm, we used prospectively this regimen in consecutively hospitalized children between 2012 and 2017. This validation cohort included 66 consecutively children (median age 5.6 years; from 0.3 to 18 years) who had a target INR of 2.0 to 3.0.

Results: The time to achieve a therapeutic INR was 5 days in both cohorts (derivation, [3-8]; range, 3-24 days vs validation [4-6]; range, 3-11 days, p 0.82) but only 3 patients of the validation cohort had an INR > 5 versus 7 in the derivation cohort. No major bleeding was recorded in this validation cohort. Finally, the time to achieve the maintenance dose was significantly shorter in the validation cohort than in the derivation cohort (11 days ([8-15]; range, 6-35 days) vs 14 days ([11-30]; range, 7-82 days), p 0.00012).

Conclusion: Our warfarin induction regimen is simple, practical, safe, and accurate in predicting the daily maintenance warfarin dose in children. It reduces the frequency of over-anticoagulation and the time required to achieve the maintenance dose.