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Recommendations for point-of-care home International Normalized Ratio testing in children on vitamin K antagonist therapy

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Capillary point-of-care (POC) International Normalized Ratio (INR) measurement within the home is a feasible method of INR testing and is associated with non-inferior warfarin/INR control when compared with traditional approaches [1,2]. Owing to the lack of studies providing evidence for guidance in POC INR Home Testing (PIHT), consensus recommendations have been developed for use in the pediatric community. Vitamin K antagonist therapy which includes all coumarin preparations (VKA-C) is monitored using the prothrombin time expressed as an INR, and conventional management consists of attending a laboratory for venipuncture. The POC INR meter requires a minimal blood sample, produces an immediate INR result and can be performed at the patients' convenience thereby eliminating the need for laboratory attendance [3,4]. Laboratory attendance interrupts school and parent professional engagement potentially impacting adherence [5]. The convenience of PIHT facilitates more frequent INR testing which is necessary in children on VKA-C as a result of additional special challenges compared with adults [4].

The level of evidence in POC INR monitoring pediatric trials is weak owing to the methodological limitations inherent in most study designs employed. The incidence of major clinical complications is the best method for quality assessment but requires large patient numbers and is not feasible in pediatrics [1]. Minor complications are complex to evaluate and often not reported. Time in target therapeutic range (TTR) is commonly used as a surrogate measure for safety and efficacy of VKA-C therapy [6]; however, varied statistical methodologies are employed in pediatrics studies which may not be interchangeable. Children's reported laboratory TTR is

approximately 50% [4]; however, previous studies have demonstrated that PIHT results in better control (TTR 60–84%) [1].

Currently, vitamin K antagonists will probably remain the most common oral anticoagulant used in children. Although novel oral anticoagulants are being tested in adults, pharmacokinetic studies in pediatrics are still in their infancy and necessary to guide pediatric dosing.

Recommendations and discussion

PIHT testing can be performed accurately, has been demonstrated to be non-inferior to laboratory monitoring and is associated with patient preference [7,8], and possibly improved the health-related quality of life [1,9] This position paper recommends that PIHT be considered for children prescribed long-term VKA-C therapy (>3 months) such as children with prothrombotic conditions or in children with acquired or congenital heart disease requiring thromboprophylaxis.

PIHT programs

PIHT programs have been conducted within dedicated pediatric anticoagulant clinics. Studies evaluating PIHT are largely cohort studies with only one randomized control trial (RCT) and are reviewed by Christensen *et al.* [1]. Further limitations to study design include sample size and the low number of warfarin patient-years reported.

Two models exist, patient self-testing and patient self-management, described below.

1 Patient self-testing is when a child/parent performs an INR test at home and the result is reported to a health care provider. The health care provider recommends a VKA-C dosing plan with a follow-up testing interval. Patient Self Testing (PST) has been investigated in several studies ranging from 14 to 80 patients (mean 23) [1] with various indications for VKA-C, predominately case series design. The mean follow-up was 16 months and the TTR (63.0–83.9%) compared favorably with

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laboratory monitoring (50%) [4]. Patients who become adept and comfortable with PST will often transition to patient self-management over time.

2 Patient self-management is when the patient takes an active role in his/her own treatment by performing a POC INR and self-adjusting the warfarin dose. This model is built upon standardized and comprehensive education, and requires the health care provider support during the 'learning phase', when dosing decisions are unclear to the patient/family, and for very low or high INRs. Patient self-management has been assessed in seven studies [1] using case series designs except in a single RTC where children were randomized to continue patient self-testing or commence patient self-management [10] In the randomized control trial, TTR was similar in both groups at 83%, with the patient self-management group reporting higher health-related quality of life and satisfaction with therapy [10,11]

Considerations for developing point-of-care INR home testing programs

Successful implementation of a PIHT program can be achieved through a clearly articulated plan incorporating quality assurance, education and training, maintenance and evaluation processes. A strategic approach to program development ensures that all requisite elements for success are considered and accommodated. There is no minimum number of patients required to initiate PIHT INR monitoring. PIHT can be established for one patient if the recommendations in this manuscript are adhered to. Educational information can be acquired from the manufacturers or other pediatric centers. Characteristics that preclude PIHT have not been identified in a systematic way in either adults or children. Until these characteristics are identified the health care provider and family should agree on the feasibility of this method of management. Time in target therapeutic range is demonstrated to increase in children using PIHT [1]. Therefore, children attending the laboratory with low TTR would be eligible and benefit from PIHT.

1 Quality assurance

In general, POC INR meters authorized for use have demonstrated accuracy and reliability and are considered adequate for monitoring of VKA-C therapy in adults and children [1,6,9,12]. There a number of meters available on the market with the CoaguChek meter (Roche Diagnostics, Basel Switzerland) being the most studied in children [7,12,13]. Point of care meters have been demonstrated to be accurate and precise for use in children prescribed VKA-C therapy [7] with an average difference between the meter and laboratory INR of 0.13–0.67 [12].

Recommendations strongly encourage POC INR and laboratory comparisons to be performed prior to clinical implementation of a meter both institutionally and in each patient with repeated comparisons every 12 months to confirm meter function, integrity of test strip thromboplastin and user proficiency in testing [1,6,9,12].

2 Self-Testing Models: processes for reporting results are described above (see Patient self-testing and Patient self-management).

3 Mobile health programs are available with some having been evaluated to support patients with INR reminders, logging INRs, resources and with dose adjustments [8,14].

4 Staff and patient education

1 Training/education equips staff with skills to train others in PIHT. Patient training is successfully achieved when health care providers who train patients are trained in the management of VKA-C therapy and are proficient in PIHT [1,6,15]. Proficiency in PIHT improves INR meter accuracy ($r^2 = 0.92$) [16] compared with unqualified users ($r^2 = 0.87$) [17]. Training should include theoretical and pharmaceutical aspects of anticoagulation, use of equipment, reporting of INRs and a practical session.

2 Child and family education should be family centered and focus on knowledge of VKA-C action as well as proficiency in PIHT (see reference 19 for educational tools). Comprehensive standardized education that is interactive and incorporates proven learning techniques, including the use of sight, sound, touch and colour, accelerates the learners' acquisition of knowledge and skills [18]. Oral and written education should present the following key concepts [3,19]:

1 Clarify PIHT follow-up expectations for the patient/family for example performing INRs when recommended and calling results to the health care provider for VKA-C dosing instructions.

2 Information on blood coagulation.

3 Indication for VKA-C therapy.

4 VKA-C mechanism of action, interactions with other medications and other influences on patient's clinical response to VKA-C (i.e. diet and viral infections).

5 Potential adverse effects, safety issues: bleeding that does not stop with application of 10 min of firm pressure should be discussed with the health care provider at the time of the event. One of the advantages of PIHT is that immediacy of the INR result which can be responded to quickly.

6 Practical skills of PIHT include testing proficiency, meter storage and test strip stability [6,9].

7 Importance of adherence: non-reported INRs must be followed up by the health care provider. Should

this non-adherence to recommendations persist, the health care provider should work with the patient/family to promote adherence [5].

Pediatric PIHT programs should provide access to participants for queries at pre-specified times and 24-h availability for exceptional INR results, and in case of emergencies.

5 Funding implications

Funding of PIHT varies depending on the country and specific institution. Each institution should be aware of this aspect of program support prior to embarking on program development.

Future directions

PIHT of VKA-C therapy in children affords considerable advantages, including ease of blood collection, immediacy of results, patient preference for PIHT and non-inferior if not better warfarin control. Given the current level of evidence for PIHT, well-designed studies are required to further evaluate PIHT-associated quality of life and long-term VKA-C control in patients performing PIHT [1].

Disclosure of Conflict of Interest

The authors state that they have no conflict of interest.

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