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ORIGINAL ARTICLE

Utility of a Dedicated Pediatric Cardiac Anticoagulation Program: The Boston Children's Hospital Experience

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Abstract Congenital heart disease is the leading cause of stroke in children. Warfarin therapy can be difficult to manage safely in this population because of its narrow therapeutic index, multiple drug and dietary interactions, small patient size, high-risk cardiac indications, and lack of data to support anticoagulation recommendations. We sought to describe our institution's effort to develop a dedicated cardiac anticoagulation service to address the special needs of this population and to review the literature. In 2009, in response to Joint Commission National Patient Safety Goals for Anticoagulation, Boston Children's Hospital created a dedicated pediatric Cardiac Anticoagulation Monitoring Program (CAMP). The primary purpose was to provide centralized management of outpatient anticoagulation to cardiac patients, to serve as a disease-specific resource to families and providers, and to devise strategies to evolve clinical care with rapidly emerging trends in anticoagulation care. Over 5 years the CAMP Service, staffed by a primary pediatric cardiology attending, a full-time nurse practitioner, and administrative assistant with dedicated support from pharmacy and nutrition, has enrolled over 240 patients ranging in age from 5 months to 55 years. The most common indications include a prosthetic valve (34 %), Fontan prophylaxis (20 %), atrial arrhythmias (11 %), cardiomyopathy (10 %), Kawasaki disease (7 %), and a ventricular assist device (2 %). A patient-centered multi-disciplinary cardiac anticoagulation clinic was created in 2012. Overall program international normalized ratio (INR) time in therapeutic range (TTR) is favorable at 67 % (81 % with a 0.2 margin) and has improved steadily over 5 years. Pediatric-specific guidelines for VKOR1 and CYP2C9 pharmacogenomics testing, procedural bridging with enoxaparin, novel anticoagulant use, and quality metrics have been developed. Program satisfaction is rated highly among families and providers. A dedicated pediatric cardiac anticoagulation program offers a safe and effective strategy to standardize anticoagulation care for pediatric cardiology patients, is

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associated with high patient and provider satisfaction, and is capable of evolving care strategies with emerging trends in anticoagulation.

Keywords Congential heart disease (CHD) · Anticoagulation · Time in therapeutic range (TTR) · International normalized ratio (INR) · Cerebrovascular accident · Thrombosis

Introduction

In young patients with congenital or acquired heart disease, thromboembolism can result in serious or life-threatening illnesses such as stroke, pulmonary embolism, limb loss, and death [12, 17–19, 25]. In fact, recent studies suggest congenital heart disease (CHD) may be one of the leading cause of stroke in children worldwide [12]. More commonly, thromboembolism may be associated with a variety of non-life-threatening problems, such as blood vessel narrowing or occlusion (e.g., following cardiac catheterization), central line obstruction, or spontaneous Fontan fenestration closure, which may require specific treatment such as anticoagulants or thrombolytics and sometimes hospitalization [30]. Anticoagulants such as warfarin are prescribed routinely for primary prevention of venous and/or arterial thromboembolism for specific conditions such as a prosthetic heart valves, Fontan palliation, recurrent atrial arrhythmias, or Kawasaki disease with giant coronary aneurysms [30]. Regardless of the indication, anticoagulants such as warfarin are widely recognized as posing a major threat to patient safety because of their narrow therapeutic index, complex dosing, need for routine laboratory monitoring, and inconsistent patient adherence.

To address this risk, in 2008, the Joint Commission established a National Patient Safety Goal (NPSG) to reduce patient harm associated with anticoagulant therapy through a set of broad-based clinical recommendations [31]. These recommendations, or elements of performance (EP), include using standardized dosing algorithms for warfarin, performing a baseline assessment [e.g., international normalized ratio (INR)], educational and nutritional evaluation prior to initiation of warfarin—using authoritative sources to manage food and drug interactions—and systematically evaluating and measuring anticoagulation safety practices (Table 1) [31]. Rapid adoption of these national patient safety EP has been facilitated in adult cardiology practice by the widespread proliferation of large hospital-based centralized anticoagulation programs [37]. While dedicated centralized pediatric programs have been developed at many leading pediatric institutions [3, 23, 39–41], to our knowledge, no pediatric program has been developed specifically for pediatric cardiology patients whose anticoagulation care is complicated by a variety of unique challenges. These include extremes of patient age and size (e.g., a 2-year old with a prosthetic mitral valve vs. 32-year old with complex CHD and pulmonary hypertension), significant heterogeneity in types of heart disease due to a variety of morphologic subtypes, a diversity of clotting risk factors which often co-exist (e.g., fenestrated Fontan with atrial arrhythmias and poor ventricular function), and a general lack of evidence to support anticoagulation recommendations in patients with CHD [18, 28, 30]. These challenges exist in the context of several rapidly evolving trends in adult cardiology anticoagulation practice, including the use of pharmacogenomics-based dosing algorithms for warfarin [24, 26, 27, 34], the proliferation of novel oral anticoagulants particularly for atrial fibrillation [8, 9, 21, 32], growing national consensus around the percent INR time in the therapeutic range (TTR) for quality benchmarking for warfarin therapy [33, 43], and shifting clinical practices related to procedural bridging driven by a variety of recent studies [6, 10, 11, 13, 14, 20, 22, 29, 42]. Therefore the purpose of this report is to describe our institutional experience creating a centralized pediatric cardiac anticoagulation program to support patients and providers alike at a large academic children's hospital and to review the literature related to the challenges of managing safely systemic anticoagulation in patients with cardiac disease (Table 2).

Methods

Program Development

In response to the 2008 Joint Commission NPSGs for anticoagulation, the Heart Center at Boston Children's Hospital created the Cardiac Anticoagulation Monitoring Program (CAMP) to centralize warfarin management for the estimated 100–120 patients receiving warfarin followed by roughly three dozen of the cardiology faculty at Boston Children's Hospital. While patients receiving warfarin were found across all cardiology divisions and sections, electrophysiology, the Boston Adults with Congenital Heart Disease (BACH) Program, Heart Failure/Transplant/Mechanical Support, and Outpatient Cardiology Program, including the Kawasaki Disease Program, accounted for the largest numbers of patients enrolled into the CAMP Service. The Committee on Clinical Investigation, Boston Children's Hospital, approved the protocol.

CAMP Service Structure, Scope and Patient Eligibility

Original Program Scope

The CAMP Service was originally tasked with centralizing outpatient warfarin management for an estimated 100–120

Table 1 Joint Commission National Patient Safety Goals for Anticoagulation Elements of Performance (2012 update)

(1) Use only oral unit-dose products, pre-filled syringes, or pre-mixed infusion bags when these types of products are available. Note for pediatric patients, pre-filled syringe products should be used only if specifically designed for children
(2) Use approved protocols for the initiation and maintenance of anticoagulant therapy
(3) Before starting a patient on warfarin, assess the patient's baseline coagulation status; for all patients receiving warfarin therapy, use a current international normalized ratio (INR) to adjust this therapy. The baseline status and current INR are documented in the medical record. Note: The patient's baseline coagulation status can be assessed in a number of ways, including through a laboratory test or by identifying risk factors such as age, weight, bleeding tendency, and genetic factors
(4) Use authoritative resources to manage potential food and drug interactions for patients receiving warfarin.
(5) When heparin is administer intravenously and continuously, use programmable pumps in order to provide consistent and accurate dosing
(6) A written policy addresses baseline and ongoing laboratory tests that are required for anticoagulants
(7) Provide education regarding anticoagulant therapy to prescribers, staff, patients, and families. Patient/family education includes the following: (1) the importance of follow-up monitoring, (2) adherence, (3) drug-food interactions, and (4) the potential for adverse drug reactions and interactions
(8) Evaluate anticoagulation safety practices, take action to improve practices, and measure the effectiveness of those actions in a time frame determined by the organization

From http://www.jointcommision.org/assets/1/18/NPSG_Chapter_Jan2013_HAP.pdf

Table 2 Challenges specific to anticoagulation management in children with cardiac disease

(1) Demographic—large numbers of small children (e.g., under age 5 years)
(a) Behavioral limitations to stable vitamin K intake ('picky eaters')
(b) Limited understanding of need for frequent blood draws
(c) No liquid preparation for warfarin requiring pill or pill fragments to be used to approximate intended dose
(d) Frequency of antibiotics use (e.g., ear infections) leading to INR instability
(e) Frequency of gastro-intestinal illness leading to INR instability
(f) Age-appropriate activity level—prone to bumps and falls including head trauma
(2) Indications for warfarin therapy
(a) High-risk indications common (e.g., prosthetic mitral or aortic valve, Kawasaki disease with giant coronary aneurysms, miniaturized ventricular assist devices)
(b) Duration of therapy often indefinite
(c) Unique circumstances surrounding indications (e.g., placement of a 19 mm St. Jude valve in the supra-annular position of a toddler)
(d) Limited evidence to support anticoagulation recommendations (e.g., single-ventricle patients) leading to conflicting recommendations
(e) Uncertainty related to anticoagulation intensity for common combinations of risk factors (e.g., adult failing Fontan with atrial arrhythmias)
(3) Comorbidities—high prevalence of right-sided congenital heart disease associated with liver dysfunction (e.g., Fontan failure)
(4) Drug interactions with medications frequently prescribed in cardiac patients (amiodarone, omeprazole)
(5) Social/insurance—insurance approval for home INR monitors often difficult for pediatric indications for warfarin (Fontan prophylaxis)
(6) Limited data regarding safe and effective procedural bridging guidelines for children

pediatric cardiology patients distributed across roughly three-dozen cardiologists at Boston Children's Hospital. Prior to the program's creation, cardiologists and/or nurse practitioners (NPs) followed an average of 1–15 patients receiving warfarin, used a variety of different warfarin dosing algorithms and testing frequencies (ranging from weekly to bi-annually), and tracked patient INRs in separate databases, some of which were paper-based, making INR data inaccessible to other clinical providers, most notably off-hours, and for program-wide analyses of quality and outcome.

Program Initiation and Centralized Database

During a 12-month period beginning in 2008, each primary cardiology team transferred their group of warfarin patients to the CAMP Service, while retaining primary control over all non-warfarin related cardiology care. Each patient was then entered into a centralized coagulation database (Standing Stone's CoagClinic, Westport, CT) designed specifically to track and monitor INR visits for patients receiving warfarin; software that was adopted jointly by the

CAMP Service and the Boston Children's Hospital Thrombosis and Anticoagulation Program.

CAMP Service Patient Eligibility

To be eligible for the CAMP Service, a patient needs (1) to have a primary cardiac indication for warfarin therapy with a prescribed INR target range identified, (2) to be followed actively by a member of the Boston Children's Hospital cardiology faculty at least once per year, and (3) to sign, or have an appropriate family member sign, a patient safety contract outlining program expectations regarding adherence and criteria for dismissal. Adult patients with a significant non-adherence history may be dismissed from the program if a standardized protocol of serial warning letters do not improve patient adherence.

Expansion of Services

Although originally conceived as a virtual outpatient warfarin program without a physical clinic, it became apparent early on that the success of the outpatient program was dependent on adequate family preparation, education, and planning prior to hospital discharge and periodically after hospital discharge. Thus, CAMP activities were also expanded from the outpatient to the inpatient setting, initially around warfarin teaching and discharge planning, but later to include direct management of inpatient INRs for non-intensive care unit patients, including all durable Ventricular Assist Device (VAD) patients. In addition to consultative activities for patients enrolled in the CAMP Service, an inpatient screening for all hospitalized patients prescribed long-term anticoagulation with warfarin, enoxaparin, or a novel anticoagulant is completed as recommended by the Joint Commission's NPSGs.

Other inpatient activities including staff in-service training and overseeing Heart Center adherence with NPSGs for anticoagulation. Enoxaparin was added to the CAMP formulary in 2010, and a multi-disciplinary pediatric Cardiac Anticoagulation Clinic opened at Boston Children's Hospital in 2012 to provide ongoing support to patients and families after hospital discharge.

CAMP Service Staffing

The CAMP Service is staffed by a multi-disciplinary team comprised a medical director (cardiology attending), a full-time NP, full-time administrative assistant, with dedicated support from a registered nurse, two clinical pharmacists, and a dietician. Under the supervision of the medical director, the CAMP NP assumes primary responsibility for day-to-day clinical management of INR's working closely with the administrative assistant to coordinate INR testing and follow-up appointments in the community, coordinate CAMP clinic appointments and maintain a monthly program performance dashboard that is reviewed at monthly operational meetings. Overnight and on weekends, the CAMP pager is covered by the on-call cardiology fellow with back-up from the CAMP attending. To avoid the safety concern of tracking down random INR's on nights and weekends, CAMP INR appointments are intentionally clustered toward the beginning of the workweek during business hours. Other staffing models were also considered, including multiple part-time nurse or NP models; however, an internal review by the Hospital's Program for Patient Safety and Quality felt that assigning a primary team of clinicians could minimize medical errors and foster team learning and development and program memory over time.

CAMP Multi-disciplinary Clinic

In 2012, the CAMP Service opened a multi-disciplinary cardiac anticoagulation clinic at Boston Children's Hospital after extensive consultation with established pediatric thrombosis clinics within Boston Children's Hospital Hematology Division, and Stollery Children's Hospital in Edmonton, Canada (KIDCLOT® Program). The CAMP clinic, which is offered bi-monthly, includes a private or small group warfarin education session by one of two CAMP clinical pharmacists, a nutritional consultation, and history and physical assessment with the CAMP NP and cardiology attending. Currently patients enrolled in the CAMP Service are seen annually in the clinic if their TTR (with a 0.2 INR unit shoulder) is <70 % and bi-annually if their TTR is ≥ 70 %. The CAMP clinic also sees pediatric cardiology patients not followed by the CAMP team on a referral basis.

Feedback from patients and families through anonymous patient satisfaction surveys suggest program satisfaction is high. Among 43 consecutive patients and/or families surveyed in clinic: (1) 84 % rated the quality of care provided by the CAMP Service to be excellent, 11 % very good and 5 % good (0 % fair and/or poor); (2) 72 % rated their educational experience as excellent, 19 % as very good and 9 % as good; (3) 76 % rated their nutrition education as excellent, 16 % very good and 8 % good. Among 39 of 43 patients and/or families who responded, 100 % of patients indicated they would recommend the CAMP Service to family and friends. Verbal feedback from individual cardiologists and staff at Boston Children's Hospital and referring cardiologists was similarly positive, and led to a successful department campaign to recognize one CAMP staff member as the Hospital employee of the month.

Collaboration with Hematology

The CAMP Service works in close collaboration with the Division of Hematology's Anticoagulation Service and

Thrombosis Program. Opportunities for collaboration have included the development of guidelines for warfarin and heparin dosing, development of guidelines for procedural bridging, joint research projects including an NIH-funded pharmacogenomics-based warfarin dosing project in children, quality improvement studies evaluating the safety of home INR monitoring and enoxaparin procedural bridging in children, joint hemostasis and thrombosis meetings, and ample opportunities for collaborative discussion/consultation for difficult cases. Although the primary CAMP office is located physically within the Heart Center, the CAMP office is adjacent to the Division of Hematology's Anticoagulation and Thrombosis Program, which serves to facilitate communication and collaboration between programs.

Census and Performance Metrics

Over the past 5 years, the CAMP Service has enrolled more than 240 patients in total, ranging in age from 5 months to 55 years. Of these, 212 patients (88 %) were enrolled primarily for warfarin management, whereas 28 patients (12 %) were enrolled primarily for enoxaparin management. In addition to the 28 patients enrolled for longer-term enoxaparin management, 29 patients were prescribed enoxaparin as a short-term bridge anticoagulant surrounding a procedure or because of an unexpected subtherapeutic INR value in a patient considered to be at high risk for thrombosis (e.g., mitral valve replacement). Since 2009, the number of active patients annually has nearly doubled from 81 in 2009 to more than 150 patients in 2013 (Fig. 1). Similarly, the total number of patient-days on warfarin therapy has increased sixfold from 7,275 patient-days in 2009 to 50,148 patient-days in 2013. The median duration of warfarin therapy for CAMP patients was 730 days.

The most common primary indications for warfarin in the CAMP Service are outlined in Fig. 2. These include a prosthetic valve (34 %, equally divided between mitral and aortic valves), Fontan prophylaxis (20 %), atrial arrhythmias (11 %), heart failure/cardiomyopathy (10 %), Kawasaki disease with giant aneurysms (7 %), and a VAD (2 %). Patients receiving warfarin prophylaxis for Fontan palliation represent the group with the largest relative growth over the past 5 years.

Quality Performance Measures: Time in the Therapeutic Range (TTR)

For the CAMP Service as a whole, the INR time in the therapeutic range (TTR), excluding the 2-week loading phase but inclusive of a 0.2 unit INR margin on either side of the target range where the dose is typically left unchanged, has hovered in the low 80 % range (Fig. 3) using the linear interpolation method described by Rosendaal [36]. This is similar to the only other TTR experience in pediatrics published from the Edmonton group (82 %) [3] where a similar methodology was used (personal communication [2]). By contrast, the overall TTR for the exact INR range within the CAMP service was 67 % in 2013 which has improved considerably since the program began (Fig. 3), and compares favorably with published national benchmarks for adult patients (60–70 %) released

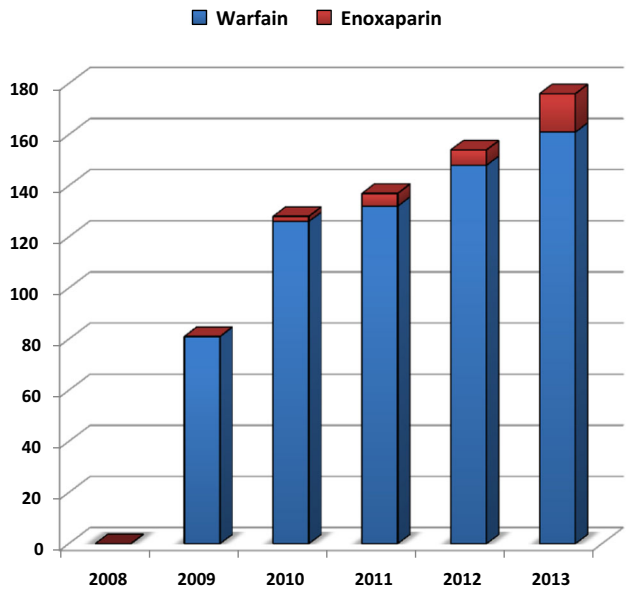

Fig. 1 Cumulative number of cardiology patients enrolled in the Boston Children's Hospital Cardiac Anticoagulation Monitoring Program by year and primary anticoagulant

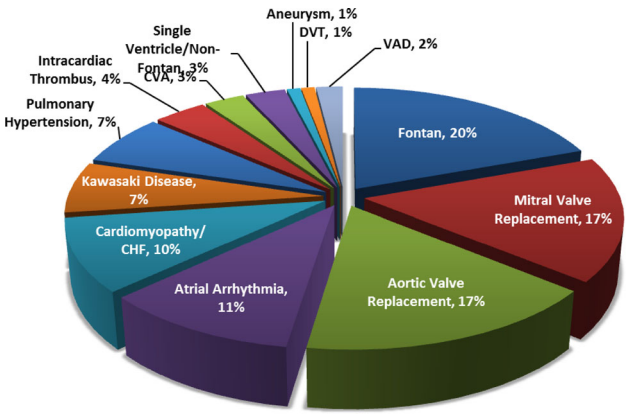

Fig. 2 Primary indication for warfarin among cardiology patients in the Cardiology Anticoagulation Monitoring Program at Boston Children's Hospital as of 2013 ($N = 151$) *CHF* congestive heart failure, *CVA* cerebrovascular accident (including transient ischemic attack), *DVT* deep venous thrombosis, *KD* Kawasaki disease

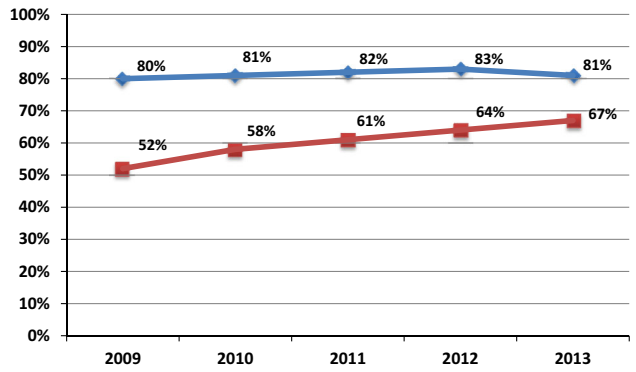

Fig. 3 Percentage time in therapeutic range (TTR) for patients enrolled in the Cardiac Anticoagulation Monitoring Program, by year. TTR is calculated using the linear interpolation method, as described by Rosendaal, as the percentage of patient-time in which the patient's INR values fall within the exact target range (depicted in *red*) and within the target range ± at 0.2 INR units (depicted in *blue*). The latter reflects the INR range where warfarin dosing may not be changed despite the INR falling outside the exact range

by the Department of Health and Human Service's Agency for Health Care Research and Quality [33]. However, it is important to note that pediatric-specific and pediatric cardiology-specific benchmarks for TTR have not been developed making it difficult to interpret a single number. This is important because it has been well established that TTR varies considerably by patient population; however, current risk-adjustment methodologies for TTR do not take into account pediatric covariates [35], which may impact INR control, such as age <2 years, or non-adherence effects common among adolescents. Efforts to develop risk-adjusted TTR models for pediatric patients would be helpful for better understanding INR control in children.

Program Development/Areas of Special Focus

Bridging Anticoagulation

Patients on chronic warfarin therapy often require interruption of warfarin therapy around procedures that carry a high risk of bleeding. In adult cardiology practice, the approach to bridging anticoagulation has evolved significantly over the past 10 years [4, 13, 14, 16, 20, 22, 29, 30, 42]. Trends include a higher threshold for actively bridging patients with short-term anticoagulants like heparin (e.g., for ICD placement) [4, 16], a preference for using low-molecular weight rather than unfractionated heparins enabling patients to be bridged at home rather than in-hospital, and the need to adapt bridging guidelines for patients receiving novel anticoagulants, such as Dabigatran®, Rivaroxaban®, and Apixaban®. Unfortunately, it is not clear how well-evolving adult guidelines apply to children in part because pediatric patients are physically smaller with smaller cardiovascular structures, require smaller-sized artificial valves (which may need to be implanted in a supra-annular position), and suffer from conditions, such as Kawasaki disease, where there are scant data on the absolute risk of thrombosis during warfarin interruption; data that play an important role in driving adult bridging recommendations.

To address these issues, the CAMP Service is in the process of finalizing standardized pediatric guidelines for warfarin bridging around procedures that have been adapted from the most recent AHA/ACC, CHEST, and European Heart guidelines. Adaptations to adult guidelines include (1) addition of pediatric-specific indications for warfarin such as Kawasaki disease with giant aneurysms and Fontan physiology that are frequently encountered in pediatric discussions of bridging anticoagulation, (2) preliminary guidance on classifying the thrombotic risk of pediatric conditions similar to adult guidelines, and (3) guidance on classifying patients with common combinations of risk factors (e.g., Fontan with atrial arrhythmias, aortic valve replacement in a failing Fontan). Once finalized, the guidelines, which were developed in conjunction with the Hematology Service at Boston Children's Hospital, will be circulated to other centers for review in hopes of initiating a multi-center data collection to characterize the safety and efficacy of various bridging strategies. The Standardized Clinical Assessment and Management Plan (SCAMP) Program is a very appealing mechanism to achieve a multi-center collaboration and data collection.

Ventricular Assist Device Program

Stroke, device-related thromboembolism, and bleeding are by far the most feared complication associated with use of pediatric VAD in children [1, 5, 7, 15, 38]. Recent studies suggest the risk of stroke is as high as 29 %, and the leading cause of death, for children supported with the Berlin Heart EXCOR® Pediatric VAD, the most commonly used pediatric VAD in US children today [1, 15]. Because this risk is significantly higher than the 6–12 % risk reported for the most commonly used adult VADs like the HeartWare® HVAD® (HeartWare Inc. Framingham, MA) and Heartmate II® (Thoratec Corp. Pleasanton,CA), the anti-thrombotic protocol is more complex and involves three anti-thrombotic agents: one anticoagulant such as warfarin or enoxaparin, and two platelet inhibitors such as aspirin and dipyridamole [15]. Anti-thrombotic agents are titrated carefully using both conventional clotting assays and data from Thromboelastography with Platelet Mapping (TEG-PM) (Haemonetics®, Inc, Braintree, MA), a hemostatic test that provides global information on hemostasis and specific information on platelet function, however, is

not easy to interpret, leading to variable interpretations among providers.

To address these challenges, the CAMP Service has assumed primary responsibility for anti-thrombotic therapy for pediatric VAD patients beyond the immediate post-operative setting, which has allowed for greater standardization of practices and an opportunity to improve the quality of care and learn from clinical events. The CAMP Service has also played an important role in the education of residents, fellows, and staff regarding the anti-thrombotic protocol and Thromboelastography and Platelet Mapping interpretation through the lectures, and the development of education materials such as a VAD Anti-thrombotic Therapy "reference card."

Novel Anticoagulants

In the USA, there has been tremendous growth in the use novel anticoagulants, such as Dabigatran (Pradaxa®), Rivaroxaban (Xarelto®), and Apixaban (Eliquis®), instead of warfarin, in adults with non-valvar atrial fibrillation to reduce the risk of stroke [8, 21, 32]. Because novel anticoagulants do not require routine blood monitoring like warfarin does, and large adult studies have found their safety and efficacy profiles to be at least equivalent to warfarin, their use in children and adults with CHD has begun to rise even as their role and safety and efficacy profile are not fully known. As of 2013 at Boston Children's Hospital, more than 30 patients have been prescribed a novel anticoagulant since 2007, with the most common indication being adult CHD with atrial arrhythmias and/or Fontan palliation. The rise of novel anticoagulant use in children raises important questions for providers and families regarding safe administration, and perhaps most notably, what the acute medical response should be to a life-threatening bleeding given no reversal agent is available [44–46]. Over the past several years, the CAMP Service has worked with the cardiology providers, the Hematology Program, Pharmacy Department and Cardiac Anesthesia groups to develop guidelines for urgent management of bleeding in children treated with novel anticoagulants adopted from adult guidelines [44–46]. The CAMP Service has also begun to collect safety data on BCH patients receiving novel anticoagulants, and providing guidance around procedural bridging adapted from adult recommendations.

Pharmacogenomics

There are few areas in clinical medicine where pharmacogenomics testing currently plays a greater role in clinical practice than in the management of adult warfarin patients [24, 26, 27]. This is because warfarin has a narrow therapeutic index, and there is enormous individual variation in warfarin metabolism, and therefore dose needed to achieve a stable INR. Adult studies suggest that prospective knowledge of specific polymorphisms in genes encoding vitamin K oxide reductase complex (VKORC1) and cytochrome P-450 2C9 (CYP2C9) can reduce the time to achieve a therapeutic INR during the loading phase, improve overall INR TTR, and reduce clinical adverse events. While cost and laboratory turn-around time remain a significant hurdles to more widespread use, many in the pediatric community believe pharmacogenomics-based dosing may be able to improve outcomes in children, too, while also reducing the total number of blood draws necessary to achieve a stable INR. The CAMP Service has worked in conjunction with the Department of Pharmacy and Hematology Service to bring warfarin pharmacogenomics clinical testing on-line at Boston Children's Hospital as of the fall of 2013. While turn-around time is currently 5–7 days, plans are underway to reduce the turn-around time to less than 48 h, consistent with the decision timeframe for most children who are beginning warfarin therapy. Multi-center studies are underway to validate the currently available pediatric dosing algorithm for warfarin.

Conclusion

In summary, warfarin anticoagulation in children with cardiac disease is complicated by a variety of factors related to the drug's narrow therapeutic index as well as factors unique to the population of children with cardiac disease. To address these safety challenges, we created a dedicated pediatric cardiac anticoagulation program to provide centralized management of outpatient anticoagulation to cardiac patients and to serve as a disease-specific resource to families and providers. Over 5 years there has been significant growth in the number of patients followed by the CAMP team and the services offered, including creation of a dedicated cardiac anticoagulation clinic staffed by a multi-disciplinary group of providers. It is unclear precisely why patient numbers increased after the Department's initial panel of patients was enrolled. We speculate that several factors may contribute, including (1) a greater appreciation among providers of the morbidity and mortality associated with thromboembolic disease in pediatric cardiology patients which may translate into a greater tendency to prescribe anticoagulants over platelet inhibitors in situations where both agents are considered accepted therapy (e.g., single-ventricle patients); (2) a tendency to underestimate the total number of patients actually receiving warfarin therapy who might be eligible to be followed in a centralized program, and (3) high program satisfaction among patients as measured by patient satisfaction survey and verbal feedback from providers prompting additional referrals by regional providers.

Still, it should be expected that resources devoted to the program, including clinical and clerical staff and clinic space, may need to be scaled upward during the first few years to meet the latent demand.

Centralization of care has facilitated institution-specific guidelines for pharmacogenomic testing, procedural bridging, quality metrics and novel anticoagulant usage in patients with cardiac disease, consistent with emerging trends in adult anticoagulation. A 5-year review of program performance suggests favorable INR control that is improving steadily, consistent with national benchmarks and enjoys high program satisfaction among patients and providers. Future challenges include the need to develop multi-center networks to study anticoagulation in children with cardiac disease and to support robust studies characterizing the safety and efficacy of novel anticoagulants in high-risk populations such as children with single-ventricle circulations and children with ventricular dysfunction requiring mechanical circulatory support.

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