

Implementation of In-Patient Anticoagulation Service in Malaysia

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Abstract

Background: Anticoagulants are extensively used in the in-patient setting for the prevention and treatment of Venous Thromboembolism (VTE) and stroke prevention for Atrial Fibrillation. They are high-risk medications associated with a significant rate of medication errors among hospitalized patients. The Pharmacy Department in collaboration with Medical Department in Hospital Tengku Ampuan Afzan (HTAA) is seeking to expand anticoagulation services and standardize care by implementing an In-Patient Anticoagulation Service (IPACs) providing daily surveillance and dosing consultation for patients receiving Anticoagulant Therapy (ACT). The team comprises of consultant hematologist, pharmacists, general physician and medical officers. The objectives of this study are to describe the implementation and outcomes of an IPACs and identifying the issues in the management of ACT. The use of anticoagulant was retrospectively collected from IPACs data during the period February 2017 to December 2018.

Results: 320 patients were referred to IPAC, with 59% of them were female. Of 303 patients seen by IPACs team, 52.5% patients used for acute VTE, 19.5% were referred for anticoagulant reversal and 3.3% for recurrent VTE. Almost two-third (72.3%) of patients used warfarin followed by 20.5% used direct oral anticoagulant and 7.2% used either low molecular weight or heparin. Of 159 patients referred for acute VTE, only 33% of them received VTE prophylaxis. Issues that were identified were the inappropriate dose of Vitamin K for over-warfarinization and underutilisation of prothrombin complex concentrate in the setting of prolonged International Normalized Ratio (INR) with severe bleeding as well as doing daily INR leading to improper titration of warfarin. Unsupervised and improper dose of heparin infusion and patients discharged with longer appointment for INR monitoring are the main issues encountered in IPACs.

Conclusion: With the IPACs, the awareness of VTE prophylaxis and the issues that related to ACT were resolved. This service appears to enhance quality of patient care in ACT.

Keywords: Anticoagulant therapy; In Patients AntiCoagulant Service (IPACS); Warfarin, Direct oral anticoagulant; Heparin

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Background

Anticoagulants are extensively used for the prevention and treatment of Venous Thrombosis (VTE) and prevention of stroke in atrial fibrillation. However, anticoagulants are high risk medications associated with a significant rate of medication errors due to the complex dosing nature, insufficient monitoring and inconsistent patient compliance [1]. Medication error related to anticoagulant often cause serious or fatal events. In particular, when patients were transferred from in-patient to outpatient setting [2].

In the out-patient setting, pharmacist-managed anticoagulation

has been shown to decrease bleeding and thromboembolic events, as well as increasing the likelihood of a therapeutic international normalized ratio (INR) for patients on warfarin [3]. In Malaysia, pharmacist-managed Warfarin Medication Therapy Adherence Clinic (W-MTAC) was started since 2005 and already implemented in all major hospitals since 2010 [4]. Currently the service has not been started in the in-patient setting. The implementation of in-patient anticoagulation services in hospitals has been proven to help patients achieve their INR [5]. Target or activated Partial Thromboplastin Time (aPTT) goal in a shorter amount of time and decrease critical INR values during titration of warfarin dosing [6,7].

Introduction and Description of the Service

Hospital Tengku Ampuan Afzan (HTAA) is an 823-bed hospital and is one of major hospitals in Malaysia. The hospital's pharmacy department employs 108 full time pharmacists. W-MTAC was implemented in March 2008 and currently managing approximately 1050 patients. Pharmacist-managed services were extended for consultations for in-patient anticoagulation management from February 2017. The In-Patient Anticoagulation Service (IPACs) served as one stop center for all departments in HTAA to standardize the practice of Anticoagulant Therapy (ACT) and provided consultative services for healthcare providers on anticoagulant management and related issues. The IPACs collaborated with consultant hematologist, general physician and medical officers. Seven IPACs pharmacists undergone two weeks of anticoagulant training program under Pharmaceutical Service Division (PSD) Ministry of Health (MOH) Malaysia. The training was conducted at training hospital and this is to assure all IPAC pharmacists have good competency in conducting ACT. To maintain the competency, they need to be credentialed by PSD MOH Malaysia. Patients who had problems and issues related with ACT were referred to the IPACs team through phone calls. The cases were reviewed by medical officer together with pharmacists and were discussed with consultant hematologist during grand ward round in weekly basis. Daily review was done by scheduled pharmacists to assess the accuracy of prescribed ACT (e.g., INR target based on indication, renal and liver functions, drug interactions, duration of ACT) (**Figure 1**). Due to manpower constraints, the IPACs were available only for working days from 8.00 am to 5.00 pm. Consultation through phone call can be made during weekends and public holidays.

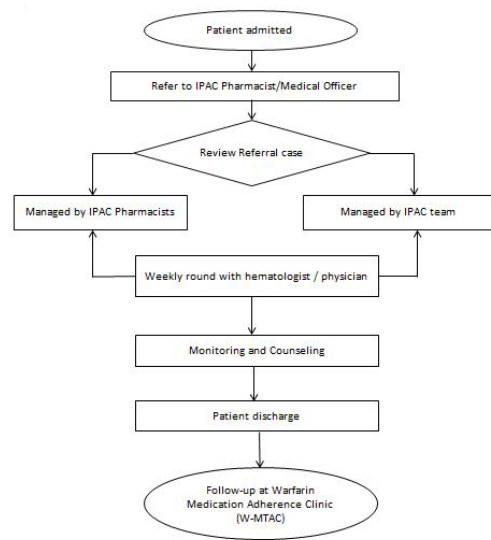


Figure 1: In-patient anticoagulation (IPAC) service workflow.

Pharmacists also assess patients' eligibility for Direct Oral Anticoagulants (DOACs). Laboratory results were reviewed to ensure patients were closely monitored while they are on ACT. Patient newly started on anticoagulants will be counseled with related issues (e.g., INR target, dose, frequency, duration of treatment, side effects, adherence, drug and food interaction, signs and symptoms of bleeding) pertaining to ACT. Interventions and recommendations were documented in the standard clerking sheet. The cases were followed up until patients were discharged. Upon discharge, IPACs pharmacists ensure patients have proper follow up appointments at W-MTAC and the correct dose of anticoagulant as well as properly counseled regarding ACT. The objectives of this study are to define the implementation and outcomes of an IPACs and identifying the issues in the management of ACT.

Materials and Methods

As part of a Clinical pharmacy to improve the management of ACT, an IPACs comprising a pharmacist's daily advice on ACT for in-patients, was started in HTAA. This was a single-center cohort study. In-patient hospitalization data for patients treated with ACT, which referred to IPACs between February 1, 2017, and December 31, 2018, were retrospectively evaluated. Before the implementation of the IPACs, the standard management cohort was managed separately by each department. Anticoagulation such as warfarin and heparin dosing were based on the doctors' experience without any nomograms or standard dosing guidelines.

Results

This study was approved by NMMR ethic committee. Total number of 303 cases were reviewed with 53% were female. Almost two-third (72.3%) of patients used warfarin followed by 20.6% used DOACs and 7.2% used either low molecular weight (LMWH) or heparin. The patient's characteristics are described in **Figure 2**.

Characteristics	n (%)
Age, Mean \pm SD	65.36 \pm 10.25
Gender	
Female	161 (53)
Male	142 (47)
Type of Anticoagulant	
Warfarin	219 (72.3)
DOAC	62 (20.5)
Rivaroxaban	52 (17.3)
Dabigatran	5 (1.6)
Apixaban	5 (1.6)
Low Molecular Weight Heparin / Heparin	22 (7.2)
Indication	
Pulmonary Embolism (PE)	88 (29.0)
Deep Vein Thrombosis (DVT)	80 (26.4)
Atrial Fibrillation (AF)	54 (17.8)
Heart Valve Replacement (HVR)	16 (5.3)
Left Ventricular Clot (LV Clot)	12 (4.0)
Sinus Thrombosis	5 (1.7)
Recurrent DVT/PE	5 (1.7)
Deep Vein Thrombosis Prophylaxis	2 (0.7)
Others	41 (13.5)

Figure 2: Patients' characteristics.

Although the interventions are not significant, the IPAC service has also identified the gaps in treatment related to transition of care from in-patient to out-patient setting. Previously, improper documentation was encountered in warfarin book when patients were discharged to W-MTAC. Patients who newly started on warfarin or DOACs were also not properly counseled and discharged with insufficient history of ACT

Besides that, non-standardization of heparin infusion monitoring aPTT vs. Prothrombin Time (PT) ratio has been used in this hospital. This issue caused improper dose of heparin infusion dose which led to failure on achieving aPTT or PT ratio target. Patients who received heparin infusion usually need closed monitoring to ensure they achieved the desired target to avoid bleeding or thrombosis. The IPAC team managed to standardize the heparin infusion monitoring using aPTT by developing new heparin protocol that needed to be used in HTAA.

Discussion

This study is the first evaluation of the outcomes of the IPACs in Malaysia. It provided critical information to the anticoagulation IPAC team for consideration of quality-improvement efforts. For example, many of the interventions were clinically important since they were related to inappropriate dosing and inappropriate selection of anticoagulants which can lead to bleeding or thrombosis. IPACs identified and resolved medication errors as well as optimized ACT through development of guidelines and protocols such as heparin protocol and warfarin dosing initiation and INR monitoring. A meta-analysis conducted by Hammond et al. in 2003 reviewed 54 separate studies that compared traditional drug management by physicians to inpatient drug management that had a pharmacist involved [8]. This meta-analysis found that 85% of the studies showed improvements in patient care when a pharmacist was added to the team compared to usual care management. These improvements included improved effectiveness, efficiency, and safety of the patient's drug therapy.⁸ Most of the studies had shown that in-patient anticoagulation care and outcomes were significantly improved by a pharmacist-managed anticoagulation service [6,9-11]. Currently, more studies had proven that pharmacist-managed in-patient anticoagulation care produced better outcomes [9,10,12]. Furthermore, although it was not significant, fewer adverse drug reactions and less supra-therapeutic INR were seen in pharmacists-managed than physician-managed care [13].

However, as a new service started in Malaysia, there are some challenges and barriers when implementing this new service. Compared to outpatient anticoagulation service (W-MTAC), IPACs is more challenging to do dose adjustment of warfarin when dealing with acutely ill patients with unstable conditions especially when there is a deterioration of renal and liver function during hospitalization. Some patients need lower initiation dose when antibiotics were given to treat infections. Bridging of anticoagulant before and after some procedures are time consuming and requires expert knowledge as the patients are highly at risk for thrombosis as well as bleeding.

Lack of awareness in initiating ACT for DVT prophylaxis was one of the reasons why patients develop PE and DVT especially in cancer and immobilized patients. Almost 80% of patients received prophylaxis after three to five days of hospital admissions. For Provoke DVT, the duration of ACT was three to six months [14,15]. unless for Cancer-Associated Thrombosis (CAT) which required longer duration of ACT. VTE was higher in cancer patients. It is currently estimated that the annual incidence of VTE in patients with cancer was estimated 0.5% compared to 0.1% in the general population. In CAT, active cancer accounts for 20% of the overall incidence of VTE.¹⁶ The recommendation duration of anticoagulation after a CAT episode is still debatable. Most guidelines suggested that the minimum duration of ACT for at least 6 months after the acute thrombotic event in cancer [16-20]. The extended duration of anticoagulation therapy after a CAT episode must be reevaluated in active cancer, metastatic disease or chemotherapy use patients because the risk factor for VTE recurrence is still present after the initial 6 months [16,17]. Many guidelines recommended the use of LMWH or DOAC for CAT. Nevertheless, despite guideline recommendations, the use of these ACT for CAT treatment is not easily done. DOACs are recommended over warfarin for treatment of non-cancer associated VTE and for stroke prevention in non-valvular atrial fibrillation by the American College of Chest Physicians (CHEST) [15,16]. However, budget constraint was the barrier in this service to use DOAC. Nevertheless, for patients who are eligible for DOAC, patient was suggested to self-purchase DOAC if the duration of treatment was less than six months. Unfortunately, higher costs and low patient adherence because of local pain due to the method of LMWH administration was another barrier. Also, both LMWH and DOAC should be avoided in renal impaired patients because the elimination of these drugs is via the kidneys, so the use of these ACT in patients with renal impairment requires more clinical attention. However, it is safe to be used in stable renal function but monitoring for bleeding complications and changes in renal function is still required [16-21].

Inadequate care transitions led to adverse outcomes especially when patients have complex or chronic medical conditions, including those on high risk anticoagulation therapy [22]. Thus, IPACs help to assure appropriate care transitions from in-patient to out-patient or other settings for patients receiving ACT. Documentation regarding ACT includes warfarin dosing and INR value during ward stay, INR target, duration for ACT and current dose were recorded in patient's warfarin book prior to leaving the hospital. The collaboration of IPAC service with the W-MTAC has led to improved transitions of care. IPACs have identified and solved the issues on patients who have difficulty getting ACT information after discharged. Counselling related to ACT and follow-up date was arranged prior to discharge. Pharmacists who managed IPACs also see patients at WMTAC, which has opportunity to provide more information for a better understanding of in-patient issues. With this IPAC service, the team is able to bridge the gap and provide the appropriate patient education as well as facilitate patient transfer to his preferred health clinic for anticoagulant monitoring.

Conclusion

Implementation of IPAC service identified and addressed issues related to ACT. Overall, IPACs appears to enhance quality of patient care in anticoagulation management which improves in-patient anticoagulation management, improves transitions of care and enhanced interdisciplinary practices.

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Declaration of Conflicting Interests

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