The impact of implementing WMTAC towards anticoagulation treatment in Dungun Hospital

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ABSTRACT

Objective: The main objective of this study is to compare patients' outcome in anticoagulation treatment before and after Warfarin Medication Therapy Adherence Clinic (WMTAC). The study compares the cost of INR test between usual care (UC) and WMTAC. The study also determines factors affecting International Normalized Ratio (INR) level among WMTAC patients.

Methods: A retrospective study involving WMTAC patients was conducted by trained pharmacists at Dungun Hospital. Patients were reviewed by UC for 4 months and continuously followed up by WMTAC for another 4 months were included in this study. Patients who passed away, transferred out and defaulted were excluded from the study. The data were derived from Patient Medical Record and recorded in Warfarin Data Collection Form for analyze.

Results: The time in therapeutic range (TTR) was 73.46% for WMTAC and 45.58% for UC ($p < 0.001$). The expanded TTR for WMTAC was 90.37% and 61.88% for UC ($p < 0.001$). The percentage of time INR level < 1.5 were 0.57% for WMTAC patients and 7.92% for UC patients, while 5.28% UC patients had INR level > 5 . The total reagent costs of INR test were MYR 341.04 for WMTAC and MYR 519.40 for UC. The known factors affecting INR level in WMTAC patients were diet (55%), missed dose (36%) and drug interaction (9%).

Conclusion: According to this study, the WMTAC implementation significantly improved anticoagulation treatment. Besides that, it also beneficial for our reagent cost expenses.

Keywords: Cost, Expanded TTR, INR, TTR, WMTAC

INTRODUCTION

Oral anticoagulant (OAC) is commonly used despite its narrow therapeutic index, thus it is vital to maintain INR within targeted range [1–3]. It is such a successful agent for the medical management commonly used in the management, for the prevention of stroke and systemic embolism in adults, involving patients who are having either atrial fibrillation (AF), deep vein thrombosis (DVT), pulmonary embolism (PE), prevention of recurrent DVT or recurrent PE [1,2,4,5] . Hence pharmacist-managed Warfarin Medication Therapy Adherence Clinic (WMTAC) being established in most countries. Implementation of the pharmacist-managed anticoagulation clinic (ACC) had positive impact on patient care [6–8]. In Malaysia, Warfarin MTAC was introduced in 2004 as part of the clinical pharmacy services in the Ambulatory Clinic System which emphasizes on medication management to improve on quality, safety and cost effectiveness of patient care [9].

Warfarin Medication Therapy Adherence Clinic (WMTAC) was implemented at Dungun Hospital since 18 February 2013. Pharmacist-managed WMTAC is collaborating with Medical Officer in the management of patients with anticoagulation therapy by providing medication counseling services. The aim of WMTAC was to provide service continuity and enhance patient care for patients on anticoagulation therapy through education, frequent monitoring, and close follow-up. The continuity of patient care will maximize the benefits of anticoagulation therapy and minimize the adverse effect and complications resulting from OAC therapy. WMTAC also provides consultative services to healthcare providers on anticoagulant drug management and related issues [9].

Many studies have demonstrated good INR level in WMTAC patients. Another study stated that WMTAC patients were found to have better International Normalized Ratio (INR) control compared to patients who received intervention by usual care (UC). Patients who were receiving treatment by UC, their INR result were reviewed by the doctors then received any adjustment that will be made based on the result. There is no specific dosing nomogram was utilized but based on doctors' management and practices. Nevertheless, it is still important that joint cooperation between physicians, pharmacists, and nurses should exist in order to achieve desired therapeutic outcomes. [10].

Evidence has shown that there is an improvement in Time in Therapeutic Range (TTR) and clinical outcomes in patients managed by trained staff using standardized procedures and dosing decision support tools. Study by Van De Ham et al conclude that INR patterns of patients can predict the clinical outcomes over TTR, and this also can help us to identify patients who need additional OAC monitoring [11].

Many similar studies were conducted in Malaysia and found that WMTAC had achieved better INR level compared to UC. Since WMTAC has been established at Dungun Hospital from 2013, we decided to carry out the study to measure the importance and needs of WMTAC service among our population. The objective of this study is to compare anticoagulation control before and after WMTAC care. In addition, from this study we were able to determine the effectiveness of WMTAC service in Dungun Hospital.

METHODOLOGY

Selection and description of participants

A retrospective study was conducted from June to July 2016 in WMTAC and Outpatient Department (OPD) at Dungun Hospital, Terengganu. All data for 81 patients in WMTAC were derived from patient medical record from 2013 to 2015. The patients who has met the inclusion criteria were included in the study as participants. Those participants who were selected has been reviewed by UC for 4 months and followed by WMTAC for another 4 months. We chose a total of 8 months because that is the longest and most complete data that we can retrieved from the patient medical record. During the treatment under UC, the participants received standard care from medical officers and no algorithm or protocol used. In the followed-up session by WMTAC, the same standard care with some additional services such as medication counselling and close drug therapy monitoring were given to the participants by trained pharmacist. On the other hand, participants who had at least two INR values not more than 6 weeks apart were also included in the study. Patients with incomplete data, passed way and transferred out were excluded from this study. Flow of the study was shown in.

Figure 1: Flow of the study

Technical information

The primary outcome of this study is to measure the percentage of time patients' INR within the recommended TTR, to determine the percentage of TTR within ± 0.2 units of the recommended therapeutic range ('expanded therapeutic range') and to measure the percentage of time the INR was above 5.0 or below 1.5. TTR is a percent of days where INR is between targeted therapeutic range. TTR of INR between targeted range is very important not only for safety but also for effectiveness of warfarin anticoagulation in patients [13]. Expanded TTR is the percentage of TTR of INR within ± 0.2 units of the recommended therapeutic range [9].

The secondary outcome was to compare the INR cost test between WMTAC and UC. The cost involved was only the reagent used per patient. The tertiary outcome was to determine factors affecting INR level among patients under WMTAC care.

The data were derived from Patient Medical Record, including patient's demographic, indication for warfarin, INR target, duration of therapy and risk factor (bleeding or thromboembolic events). INR results and weekly dose recommended also were taken into account. All the data that have been collected will be recorded in Warfarin Data Collection Form. This study was approved by Medical Review and Ethical Committee of Ministry of Health (MOH) and registered with National Medical Research Registry (NMRR) NMRR-16-2089-30772.

Statistical Analysis

Statistical analyses were done by using IBM Statistical Package for Social Science (SPSS) Version 21.0. Means and standard deviations were calculated for continuous data whilst frequency and percentage were tabulated for categorical data. TTR was calculated using a modification of the Rosendaal linear interpolation method [12]. This method of calculating TTR examines the amount of time between INR results to determine how long the patient may have been within therapeutic range. Paired t-test was used to compare adequacy of anticoagulation before and after WMTAC care. All statistical assessments were conducted at 5% significance level with its 95% confident interval.

RESULT

A total of 41 participants were included in this study. The median age is 48 years old and 63.4% of patients are female. The most common indications for warfarin were atrial fibrillation and mechanical heart valves which are 51% and 44% respectively.

Table 1: Sociodemographic characteristic of WMTAC patients at Hospital Dungun (n=41)

Variables	n (%)
Age in years, median	
Male	63
Female	48
Gender	
Male	15 (36.6)
Female	26 (63.4)
Indication for anticoagulation	
Atrial Fibrillation	21 (51.2)
Mechanical Heart Valve	18 (43.9)
PE ^a	1 (2.4)
CVA ^b	1 (2.4)
MI ^c /ACS ^d	1 (2.4)
Target INR range (Based on individualized target)	
2.0-3.0	27 (65.9)
2.0-2.5	1 (2.4)
2.5-3.0	3 (7.3)
2.5-3.5	10 (24.4)
Risk Factor for thromboembolism or bleeding	
Hypertension	19 (46.3)
Stroke history	6 (14.6)
Diabetes	2 (4.9)
Age > 65	6 (14.6)
Renal disease	1 (2.4)
Antiplatelet	7 (17.1)

^aPE: Pulmonary embolism; ^bCVA: cardiovascular accident; ^cMI: myocardial infarction; ^dACS: Acute coronary syndrome

The number of INR test per patient within 4 months in the WMTAC and UC group was 4 and 6, respectively. The number of INR tests per patient greater than 4 weeks apart in WMTAC and UC group was 1 and 0 respectively.

Table 2: Frequency of INR testing among warfarin patient (n=41)

Variables	Warfarin MTAC	Usual Care
Total number of INR test	174	265
Number of INR test per patient	4	6
INR tests >4 weeks apart, n	58	14
Number of INR test >4 weeks apart per patient	1	0
Number of withhold session	8	23
Number of withhold session per patient	0	1
Number of adjustment dose	39	108
Number of adjustment dose per patient	1	3

The WMTAC group spent significantly more time than the UC group in the therapeutic range TTR: 73.46% versus 45.58%; $p < 0.001$, as well as in the expanded TTR: 90.37% versus 61.88%; $p < 0.001$.

The percentage of time that the patients INR <1.5 and >5.0 in WMTAC group is less than the UC group (0.57% versus 7.92% & 0.00% versus 5.28%) respectively.

Table 3: Anticoagulation control among warfarin patients

Variables	WMTAC	UC	p-value ^a
Percentage of Time INR in Range			
Therapeutic range (TTR) ^b	73.46	45.58	p<0.001
Expanded range (Expanded TTR) ^c	90.37	61.88	p<0.001
<1.5	0.57	7.92	
>5.0	0.00	5.28	

^a Paired t-test; ^b Therapeutic range: 2.0-3.0, 2.0-2.5, 2.5-3.0 or 2.5-3.5; ^c expanded therapeutic range $\pm 0.2^{6,12,1}$

There is a significant association between number of INR test, number of adjustment dose and number of withhold session with TTR in UC group (p<0.001, p=0.002 and p=0.001) respectively. While there is no significant association between number of INR test, number of adjustment dose and number of withhold session with TTR in WMTAC group (p=0.376, p=0.641 and p=0.976) respectively.

Table 4: Relation between Interventions and TTR

Group	Interventions	TTR ^a	p-value ^b
WMTAC	No. of INR test number of adjustment dose	73.46	p=0.376
	No. of adjustment dose	73.46	p=0.641
	No. of withhold session	73.46	p=0.976
UC	No. of INR test	45.58	p<0.001
	No. of adjustment dose	45.58	p=0.002
	No. of withhold session	45.58	p<0.001

^a Therapeutic range: 2.0-3.0, 2.0-2.5, 2.5-3.0 or 2.5-3.5; ^b Simple Linear Regression test

The total number of INR test in UC group was 265 which totaled to MYR 519.40. While the total cost of INR test under WMTAC was MYR 341 which involved 174 INR test. Thus, there is 34% of cost reduction when referred to WMTAC.

Table 5: Total reagent cost of INR test under UC and WMTAC

Variables	Usual care (UC) (4 months)	Warfarin MTAC (4 months)
Total number of INR test	265	174
Total cost of INR test (MYR)	519.40	341.04
Average number of INR test per patient	6.5	4.2
Average cost of INR test (MYR) per patient	12.74	8.23

Note: Cost per INR test is MYR 1.96

The largest contributing factors affecting INR among WMTAC patients was diet which 55% followed by missed dose, 36% and drug interaction, 9%. From 55% of diet, the type of diet that involves was fruit (about 50%) then followed by green leafy and nuts.

Figure 2: Factors affecting INR level under Warfarin MTAC

DISCUSSION

The result demonstrated that participants in the WMTAC group spent more time in both the TTR and the expanded TTR compared to the UC group and these differences were statistically significant. This result was well supported by a study conducted by You J.H.S. *et al.*, where patients in the pharmacist-managed group spent a higher percentage of time in both the therapeutic INR range and expanded therapeutic range than those in the physician-managed group [64% (n=112) versus 59% (n=109), $p < 0.001$] and [78% versus 76% $p < 0.001$] respectively [14]. The study conducted in Canada showed patients managed by the anticoagulation clinics were within the TTR and expanded therapeutic range more than patients managed by family physicians (73% versus 65%, $p < 0.0001$) and 91% versus 85%, $p < 0.0001$) as in accordingly [12]. This finding also supported by other study done by Hassan SS. *et al*, Saokaew S. *et al* and Thanimalai S. *et al* [10, 15, 16]

The percentage of time patients' INR was < 1.5 and > 5 is lower in WMTAC group compared to UC group respectively. This finding was supported by one of the studies conducted by Wilson S.J. *et al.* presented high risk INR values (< 1.5 or > 5.0) were more often observed in patients managed by family physicians (40%) than in patients managed by anticoagulation clinics (30%, $p = 0.001$) [17]. The other study conducted by Young S. *et al.* found the percentage of time INR values was < 1.5 and > 5 were lower for both pharmacist care (PC) compared to usual care (UC) [0.7% (n=112) versus 1.9% (n=81) $p < 0.0001$] and [0.3% versus 0.1% $p < 0.0001$] respectively [12].

Our study only indicates a significant difference in UC group when comparing TTR with number of INR test, number of adjustment dose and number of withhold session. While TTR of WMTAC group did not have any influence in those third variables. This finding reflected on how each group intervene the patients in each their INR visits. The WMTAC group used warfarin dosage adjustment algorithms, assessed patients for factors that would affect the result and/or the subsequent recommendation for examples changes in medications or diet, sign and symptoms of hemorrhagic or thromboembolic events, missed dose and illnesses and provide education/counselling [11, 13].

The total cost of INR test was lower in WMTAC group compared to UC group. Chan *et al* found that the cost per patient per months was lower in the pharmacist-managed group (76 +/- US dollar) (43 +/- 53 British pound) compare to physician-managed group (98 +/- 158 US dollar) (55 +/- 89 British pound) [18]. Another study found that the direct anticoagulation care cost

was 35,465 US dollar versus 111,586 US dollar and the overall medical care cost was 754,191 US dollar versus 1,480,661 US dollar for the anticoagulation service group versus the usual care group [19].

The limitation of this study was inconsistent WMTAC follow up, which may affect the continuity management of INR control. Thus, data from patient medical record will be missing. Patient with incomplete data would only produce limited data and they were excluded from the study. As the result we managed to get small sample size.

CONCLUSIONS

WMTAC resulted in a significantly better anticoagulation control. The WMTAC compared to usual care achieved significantly better INR control as measured by the percentage of time patient's INR values were kept in both therapeutic and expanded range. Besides that it also showed benefit in our reagent cost expenses.

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CONFLICT OF INTEREST

The author has none to declare.

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