Evaluation of Anticoagulant Therapy for Atrial Fibrillation in Babylon.

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الخلاصة

المقدمة: رجفان الأذينين هي من أمراض اضطراب تناسق ضربات القلب الواسعة الانتشار وتعتبر من عوامل الخطورة للأصابة بالخثر الهاجرة وخاصة الطارئة الوعائية الدماغية. إن أدوية مضادات التخثر هي من أهم الأدوية الوقائية المستخدمة لمنع مضاعفات فرفرة الأذينين في الوقت الحاضر.

لهدف من الدراسة تقييم مدى وصول علاج مضادات التخثر لمرضى فرفرة الأذينين في محافظة بابل ومدى الوصول للأهداف المرجوة من العلاج.

الطرق والأدوات: لقد تم أخذ 236 مريضا مصابا بفرفرة الأذينين المزمنة أو الحادة المتكررة ممن راجعوا أو رقدوا في مستشفى الحلة التعليمي للفترة من الأول من كانون الثاني 2008 ولغاية الأول من كانون الثاني 2010. وتم اجراء فحص النسبة العالمية الموحدة للتخثر لجميع المرضى وتم اعتبارها مطابقة للأهداف المرجوة للعلاج اذا كانت بضمن الحدود المتفق عليها في أكثر من نصف عدد التحاليل المنجزة كما وتم دراسة مدى تطابق المرضى لتوصيات الكلية الأمريكية لأطباء الصدر لعام 2005.

النتائج: وجدنا أن 38,6 % (91 مريض من أصل 236) من مرضى هذه الدراسة يتبعون توصيات الكلية الأمريكية لأطباء الصدر وان 43,1 %(56 مريض من أصل 130) من المرضى الذين يستحقون العلاج بمضادات التخثر يستعملون هذا العلاج واقعا.

كما وجدنا ان 41,7 % (25 مريض من أصل 60 مريض) من المرضى الذين يستعملون مضادات التخثر هم يحققون النسب المطلوبة للعلاج.

الاستنتاج: أن هناك قصور في استعمال علاج مضادات التخثر لمرضى فرفرة الأذينين في محافظة بابل كما ان المرضى الذين يستعملون العلاج لايحققون النسب العالمية الضرورية لحمايتهم من الخثر الهاجرة وبخاصة الطارئة الوعائية الدماغية.

Abstract

Background: Atrial fibrillation (AF) is a common cardiac arrhythmia and is a major independent risk factor for peripheral thromboembolism mainly strokes. Anticoagulation with vitamin K antagonists is the most effective therapy for stroke prophylaxis in AF.

Methods : In this study; 236 patients were included complaining of sustained or paroxysmal AF.

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They were admitted to medical ward or attended outpatient clinic in Al-Hilla Teaching Hospital in Babylon governorate during the period from 1st Jan. 2008 to 1st Jan. 2010.

At the time of enrollment; INR was done for all patients and previous INR results were requested and reported. Stable therapeutic anticoagulation was defined as two INR values (measured at least two weeks apart) were within or above therapeutic range.

Then patients were classified into different stroke risk groups. Based on these categories; treatment modalities, it's effectiveness and compliance were calculated.

The antithrombotic therapies were considered consistent with guidelines when OAC was prescribed for high and intermediate (subtype A) risk groups and acetyl salicylic acid-aspirin (ASA) was prescribed for intermediate (subtype B) and low risk groups.

The patients on OAC were considered "within target INR range" if INR was within recommended target range in 50% or more of occasions.

Results : A total of 236 patients with AF were studied; age range was 18-86 years, 58.5 % (138/236) of them were males.

38.6% (91/236) of our patients were on recommended treatment according to guidelines recommendations. 55.1% (130/236) of our patients were ideally indicated for OAC therapy and only 43.1% (56/130) of them were on OAC therapy. 35.2% (83/236) of our patients were in high risk group and only 44.6% (37/83) of them were on OAC therapy

Conclusion : There is a clear under-treatment of AF in Babylon even in patients with high stroke risk, and the patients on OAC therapy weren't achieving target INR.

Introduction

Atrial fibrillation (AF) is a common cardiac arrhythmia accounting for about one-third of hospitalization for arrhythmias[1]. AF is a major independent risk factor for peripheral thromboembolism mainly strokes as rate increases by six times[2]; in addition to transient ischemic attacks (TIAs) and non-cerebral emboli[2,3]. This is mediated by embolism of stasis-precipitated thrombi originating in the left atrial appendage[4]. AF with rapid ventricular response may cause a tachycardia-related cardiomyopathy[5].

It has been found that risk of stroke is identical in both paroxysmal and sustained AF[3,5,6,7].

This indicates that AF isn't a benign condition; rather, it is associated with an increased mortality and morbidity[8].

Anticoagulation with vitamin K antagonists is the most effective therapy for stroke prophylaxis in AF[9,10]. The narrow therapeutic index of warfarin (the representative drug of oral anticoagulant therapy-OAC) require that the intensity of anticoagulation be closely and frequently monitored and maintained with International Normalized Ratio (INR) within the guidelines recommendation to optimize efficacy while minimizing bleeding risk[11]. The pharmacokinetics of warfarin are subject to variability due to interactions with multiple drugs and foods, making maintenance of INR within target difficult to achieve in clinical practice without close coagulation monitoring and frequent dose adjustments[11]. In most cases of AF, target INR is between 2.0 and 3.0 except in mitral mechanical prosthetic valve where the target is between 2.5 and 3.5[1,11,12,13,14,15].

It has been found that OAC therapy can reduce relative risk of stroke by an average of 58-68% of high risk patients with optimal treatment (annual risk reduction is 4.9% per year[6,16,17]. Currie et al found that survival in AF patients on OAC was 52 months while it was 38.2 months in patients on no treatment[15].

It has been found that OAC is superior to ASA and/or clopidogril for prevention of vascular events in high risk patients[3,4,17,18,19]; however, poor anticoagulant follow up with variable INR makes benefits of OAC therapy little (if any) over ASA[20]. No role for combined OAC and ASA except in mechanical prosthetic valve as it increase risk of major bleeding without additional protective benefits[21].

The increased risk of hemorrhage remain the major drawback to OAC therapy and is associated with the intensity of anticoagulation[17,22]; however, the benefits of preventing emboli outweigh the risk of bleeding[23].

Despite overwhelming evidence of the benefits of controlled OAC therapy on stroke reduction in AF, there is still considerable under-treatment[23]. The annual rate of major bleeding was 1 % for both controls and patients on ASA while it was 1.3 % in patients on OAC with good INR monitoring[24].

Management of OAC therapy by specialized centers, such as anticoagulation clinics or by patients self-management may improve the use of anticoagulation and it's quality, thereby facilitates optimal management in patients with AF[25,26,27,28,29].

In France and Germany; they found that shift from conventional to patient self management (PSM) of OAC resulted in 30% reduction in complication rates[30,31]. The oral direct thrombin inhibitor (Ximelagatran) is a potentially promising anticoagulant as it is administered without coagulation monitoring and less bleeding[11].

According to American College of Chest Physicians Evidence Based Clinical Practice Guidelines[16,32,33,34,35]; the risk of stroke in AF is classified into:

1. High risk group (annual risk of stroke is about 10.8%); includes patients with rheumatic mitral valve disease, prosthetic mechanical valve, history of stroke, TIA or non-cerebral emboli. For this group OAC therapy is indicated.
2. Intermediate risk group (annual risk of stroke is about 5.3%); includes:

   A : Patients older than 75 years or patients with two or more of the following risk factors; hypertension, diabetes mellitus, thyrotoxicosis, impaired left ventricular function, dilated heart chambers and ischemic coronary artery disease. For them OAC therapy is indicated.

   B : Patients with one of the above risk factors. For them OAC or aspirin (ASA) is indicated.
3. Low risk group (annual risk of stroke is about 0.5-1.4%); includes patients younger than 75 years and have non of the above mentioned risk factors. For them ASA is indicated.

Objective

To evaluate how well patients with AF were maintained on the recommended anticoagulant therapy and within the recommended INR target in Babylon.

Methods

In this study; 236 patients were included complaining of sustained or paroxysmal AF. They were admitted to medical ward or attended outpatient clinic in Al-Hilla Teaching Hospital in Babylon governorate during the period from 1st Jan. 2008 to 1st Jan. 2010.

For all patients; full medical history were taken, thorough clinical examination were done and sent for electrocardiography (ECG) and chest X ray (CXR). All patients had echocardiography either a previous valid report or a recent one.

At the time of enrollment; INR was done for all patients and previous INR results were requested and reported. Stable therapeutic anticoagulation was defined as two INR values (measured at least two weeks apart) were within or above therapeutic range. If the patient had a previous INR reading, we did a recent one for him, and if no previous reading found, then another INR reading was taken 2 weeks later (this occurred in 11 patients).

The patients with sustained AF were only enrolled in this study if their AF was present for more than 1 month for better assessment of effective OAC therapy.

The patients with paroxysmal AF were only enrolled in this study if their attack is 3rd one i.e. patients with 1st or 2nd attacks were excluded.

Then patients were classified into different stroke risk groups depending on American College of Chest Physicians Evidence Based Clinical Practice Guidelines.

Based on these categories; treatment modalities, it's effectiveness and compliance were calculated.

The antithrombotic therapies were considered consistent with guidelines when OAC was prescribed for high and intermediate (subtype A) risk groups and ASA was prescribed for intermediate (subtype B) and low risk groups.

The patients on OAC were considered "within target INR range" if INR was within recommended target range in 50% or more of occasions.

To do INR; a venous blood sample was taken and collected in tubes using sodium citrate as anticoagulant.

Results

A total of 236 patients with AF were studied; age range was 18-86 years, 58.5 % (138/236) of them were males.

In general; 38.6% (91/236) of our patients were on recommended treatment according to guidelines recommendations.

25.4% (60/236) of our patients were on OAC therapy.

55.1% (130/236) of our patients were ideally indicated for OAC therapy according to above mentioned recommendations, only 43.1% (56/130) of them were on OAC therapy.

35.2% (83/236) of our patients were in high risk group, 44.6% (37/83) of them were on OAC therapy, and of those; only 45.9% (17/37) were achieving target INR. This means that only 20.5%

(17/83) of high risk group patients were compliant with guidelines recommendations.

41.1% (97/236) of our patients were in intermediate risk group, 47 of them were eligible for OAC and only 40.4% (19/47) were on treatment. While the remaining 50 patients were eligible for either OAC or ASA and 8% (4/50) were on OAC. Of the treated patients; only 36.8% (7/19) were achieving target INR. This means that only 14.9% (7/47) OAC eligible intermediate risk group patients were compliant with guidelines recommendations.29.2% (31/106) of patients eligible for ASA therapy were on treatment; 93.5% (29/31) of them were taking their ASA daily.

Table (1) The use and effectiveness of OAC according to risk group.

Risk group	No.	%	On RT		Within T	
			No.	%%	No.	%%
High	83	35.2	37	44.6	17	45.9
MVD	30	12.7	15	50	7	46.7
PMV	4	1.7	3	75	2	66.7
CVA	41	17.4	17	41.5	6	53.3
TIA	2	0.8	0	0	---	---
PTE	6	2.5	2	33.3	1	50
Intermediate	97	41.1	46	47.4	8	34.8
Elderly (for OAC)	21	8.9	6	28.6	1	16.7
2 RF (for OAC)	26	11	13	50	6	46.2
1 RF (OAC or ASA)	50	21.2	4 (OAC) 23 (ASA)	54	1 ---	25 ---
Low	56	23.7	8 (ASA)	14.3	---	---

No.: number. On RT: on recommended treatment. Within T: within target INR. %: percentage. %%: percentage of the subgroup. MVD: mitral valve disease. PMV: prosthetic mitral valve. CVA: cerebrovascular accident. TIA: transient ischemic attack. PTE: peripheral thromboembolism. RF: risk factor. OAC: oral anticoagulants. ASA: aspirin.

76.7 % (181/236) of patients had sustained AF and 53.4% (126/236)of patients were from urban areas.

34.1% (47/138) of male patients were on OAC therapy and 46.8%(22/47) of them were within target INR; whereas, only 13.3%

(13/98) of female patients were on OAC and 23.1% (3/13) of them were within target INR.

30.9% (39/126) of urban patients were on OAC and 48.7% (19/39) of them were within target INR, while only 19.1% (21/110) of rural patients were on OAC and 28.6% (6/21) of them were within target INR.29.8% (54/181) of patients with sustained AF were on OAC and 44.4% (24/54) of them were within target INR; whereas only 10.9% (6/55) of patients with paroxysmal AF were on OAC and 16.7% (1/6) of them were within target INR. Patients with long term disease (sustained AF) had better compliance with treatment (both OAC and ASA). No significant difference in ASA compliance between males and females or urban and rural patients.

Table (2) The use and effectiveness of OAC according to sex, geographical area and type of AF.

The factor		No.	%	On RT		Within T		P. value
				No.	%%	No.	%%	
Gender	Male	138	58.5	47 (OAC) 17 (ASA)	34.1 12.3	22 15	46.8 88.2	<0.0001 (OAC) >0.05 (ASA)
	Female	98	41.5	13 (OAC) 14 (ASA)	13.3 14.3	3 11	23.1 78.6	
G. Area	Urban	126	53.4	39 (OAC) 19 (ASA)	30.9 15.1	19 18	48.7 94.7	<0.05 (OAC) >0.05 (ASA)
	Rural	110	46.6	21 (OAC) 12 (ASA)	19.1 10.9	6 10	28.6 83.3	
AF Type	Sustained	181	76.7	54 (OAC) 21 (ASA)	29.8 11.6	24 18	44.4 85.7	<0.0001 (OAC) <0.05 (ASA)
	paroxysmal	55	23.3	6 (OAC) 10 (ASA)	10.9 18.2	1 8	16.7 80	

No.: number. On RT: on recommended treatment. Within T: within target INR. %: percentage. %%: percentage of the subgroup. Geog.: geographical. OAC: oral anticoagulant. ASA: aspirin. Sig.: Significant P-value (if less than 0.05).

Discussion

The benefits of OAC therapy in AF had been proved and emphasized but the side effects and burden of treatment with reduced doctor's interest and patient's ignorance may contribute to

poor compliance and consequently to treatment failure or even no treatment taken.

In this study; we found that there is a significant under-treatment and non-compliance to guidelines recommendations in patients with AF in Babylon.Similar results (although to a lesser extent) were found in Switzerland by Zehnder et al as only 52% of AF patients with recommended OAC therapy were on treatment.

From the 48% untreated patients; 18% took no treatment because of presence of a contraindication to OAC and 30% has no obvious cause[6].

In USA; McCormick et al had found that 42% of AF patients were on OAC therapy with therapeutic range of INR value maintained in only 51% of the time[35].

Another similar result was stated by Baker et al as they found that AF patients in USA spend only about one-half the time within therapeutic INR[36].

Boulanger et al also found that 47.1% of USA patients were on OAC and they spend only half the study time within therapeutic INR[37].

Lin et al found that 24.7% of AF patients were receiving appropriate antithrombotic therapy in Taiwan[38].They found the lowest treatment rates in patients with high bleeding risk (previous hemorrhage, liver or renal disease, peptic or psychiatric disease or malignancy), hypertension, coronary heart disease and age ≥ 60 years[38].

In UK; Jones et al found that 68% of their patients were within target INR range[39].In our study; The under-treatment and non-compliance included both sustained and paroxysmal AF, however; it is more in paroxysmal AF, and included both genders, although more in females, and included both urban and rural patients, however; more in rural patients.

About one 3rd of patients in high risk group were compliant to recommended INR target, however; better compliance was seen in all patients taking ASA reaching 84% and 80% in intermediate and low risk patients subsequently.

Best drug compliance was seen in patients with prosthetic mechanical valve (50% on OAC; all of them were achieving target INR); this may be because of continuous patients education doctors concerns about possible serious complications.

Worse drug compliance was seen in elderly patients (only 4,8% on OAC; none of them was achieving target INR); this may be

because of doctors fears of possible bleeding complications and non-compliance of elderly.

We found under-treatment of patients with low stroke risk as only 17.9% of them were on ASA and this may be because of under-estimation of possible (even little) risks.

More under-treatment was seen in paroxysmal than sustained AF as arrhythmia comes in attacks reducing doctor's interests and patient's compliance.

Again; more under-treatment was seen in female than male patients and this may be due to low educational state and neglection of females in Iraqi society.

Rural patients were further under-treated than urban patients which may be because of ignorance, poverty and far distance from cities where hospitals and doctor's clinics and laboratories are available.

A comparable compliance to ASA was seen in both sustained and paroxysmal AFs, female and male patients and urban and rural patients, and this may be because of simplicity of ASA dosage and no frequent follow up is needed.

Conclusion

There is a clear under-treatment of AF in Babylon even in patients with high stroke risk, and the patients on OAC therapy weren't achieving target INR. The possible causes may includes: old age, female gender, living in rural areas, low educational state, non-compliance to treatment, lab. errors, doctors under-estimation and long term disease.

Patient's education has an important role in improving OAC use in AF and with a good follow up, risks will be acceptably law. This will encourage doctors to prescribe OAC to recommended patients. Educational courses to doctors to intensify the role of OAC in AF may also help.

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