

Original Research Article

Quality and Superiority of Anticoagulation therapy in neurological patients in a tertiary care hospital

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Abstract

Background: Oral anticoagulation (OAC) is used in neurology practice for primary and secondary stroke prevention in atrial fibrillation (AF). Since, there are lacunae of literature on the quality of anticoagulation in neurological patients this study was planned.

Objective: To Evaluate the quality of oral anticoagulation therapy in neurology patients.

Materials and methods: A prospective study was conducted on patients attending tertiary care neurology OPD who were prescribed oral anticoagulant (OAC). Consecutive sampling technique was used. Their international normalized ratio (INR) values were prospectively observed and the earlier INR values of the patients who were already on OAC were retrospectively scrutinized. The level of anticoagulation, factors intrusive with OAC and complications were noted.

Results: The results were based on 70 patients with median age 45 year. Fifty patients received OAC for secondary stroke prevention, 16 for cerebral venous sinus thrombosis (CVST) and four for deep vein thrombosis (DVT). Of the 1280 INR reports, 500 (39.5%) reports were in the therapeutic range, 496 (38.5%) were below and 280 (21.9%) were above the therapeutic level. Stable INR was obtained in 30 (42.86%) patients only. The overall complication rate was 16.4 per 100 person-years.

Conclusions: In the present study, it was concluded that stable therapeutic INR is tough to maintain in neurological patients. Optimal modification of diet, drug and dose of oral anticoagulant may support in stabilization of INR.

Key words

Anticoagulant therapy, INR, Stroke, Deep vein thrombosis.

Introduction

Oral anticoagulation (OAC) is used in neurology exercise for primary and secondary stroke prevention in atrial fibrillation (AF), prosthetic mechanical valve; dilated cardiomyopathy (DCMP) and cerebral venous sinus thrombosis (CVST) [1, 2, 3]. In many of these indications OACs are used lifetime. Oral anticoagulants have a narrow therapeutic range with danger of bleeding or thromboembolism. Efficiency of OAC therapy is observed by measurement of prothrombin time, expressed as international normalized ratio (INR). The frequency of nursing depends on the stability of INR and may differ from daily to three monthly [4]. Despite regular monitoring, good INR control is tough to attain. In a meta-analysis including 95 studies done mostly prospectively or in anticoagulation clinic on patients with AF on OAC, median percentage of INR in therapeutic range was 56 per cent (range 34.2-70.7%), below in 26 per cent (range 8.7-51%) and above in 13 per cent (range 6-38.5%) [5]. Continuing the INR in the therapeutic range is difficult as the effect of OAC is predisposed by food, drug, age, gender and genetic polymorphism [6]. Since there is lacunae of literature for evaluating the status of anticoagulation in neurology patients so the present study was planned to evaluate the quality and stability of INR in the neurology patients receiving OAC.

Materials and methods

Study Design: Prospective Observational study

Study Settings: Patients attending the Neurology OPD of tertiary care hospital.

Study Duration: May 2016 to April 2018 (2 years)

Sampling Technique: Consecutive Sampling Technique

Sample Size: A total of 90 patients were enrolled in which, 20 patients were lost to follow up so the study was done in 70 patients which was the sample size of the study.

Inclusion Criteria: Patients attending Neurology OPD were included.

Exclusion Criteria: Those with patients with pregnancy, hepatic and renal failure, multi-organ dysfunction and those less than 18 years of age or unwilling to participate in the study were excluded.

Methodology

A detailed history and clinical examination were done. The demographic details of the patients including age, gender, diet, ethnicity and religion were noted. Presence of anemia, edema, petechial hemorrhage, epistaxis, hematemesis and melena were enquired. Neurological examination included level of consciousness, mental status, muscle power, tone, tendon reflexes, sensations and co-ordination. Electrocardiography, Doppler, echocardiography and MR venography were done as per clinical indication. The patients were categorized into rheumatic heart disease (RHD), prosthetic valve, dilated cardiomyopathy (DCMP), cerebral venous sinus thrombosis (CVST), deep vein thrombosis (DVT) and miscellaneous disorders. Adequacy of anticoagulation was defined by the INR value based on recommended therapeutic range for different conditions [7, 8]. The starting dose of nicoumalone was 2 mg/day and the dose were adjusted based on INR value. The INR was measured every three days until two consecutive INR values were in the therapeutic range. Thereafter, INR was repeated after one week; if INR was in therapeutic range then repeated monthly. The patient with suboptimal INR was enquired about diet and OAC dose and compliance. Any of these factors if found abnormal, was corrected and INR was repeated after 1-2 wk. If INR was suboptimal even after correcting these factors, the dose of OAC was increased by 10-20 per cent.

Nicoumalone was the preferred OAC but those already on OAC other than this drug was advised to continue the prescribed drug. The anticoagulation status was categorized into three groups based on the recommended INR value for the respective disease- optimal (in the therapeutic range), suboptimal (below the therapeutic range) and above the therapeutic range. Stable INR was

defined by three consecutive INR values in therapeutic range at least one month apart without changing dose of oral anticoagulant. During the follow up period, complications were noted, and corresponding INR values were recorded.

Statistical analysis

Recorded observations were stored in Microsoft Excel sheet and data were expressed as percentages. Total duration of follow up was calculated by totalling follow up of all the patients and complication was calculated in per 100 person-years. Chi square test for categorical and independent t-test or Mann-Whitney U test for continuous variables was done. The factors inducing the stability of INR were assessed by univariate followed by multivariate analysis. SPSS Version 22 was used (trial version). P-

value <0.05 was considered statistically significant.

Results

As per **Table – 1**, during the study period, 90 patients on OAC were enrolled. Twenty patients were excluded because of lost to follow up. The median age of the remaining 70 patients was 45 (range 21-69) years and 47 were males (67%). The study was male preponderance. Forty (51.9%) patients belonged to the rural area. Among the 70 patients taking OAC, 50 (71%) were receiving OAC for stroke, 23% for cerebral venous sinus thrombosis. Among the 1280 INR reports, 39% are within therapeutic range, 38% were below and 23% were above therapeutic range.

Table – 1: Demographic details and Clinical Parameters of the study participants.

Parameters	Number	%
Age (years)		
Median	45 years (21-69)	
Males	47	67
Females	23	33
OAC Stroke	50	71
CVST	16	23
DVT	4	6
INR Reports		
Within Therapeutic range	500	39
Below therapeutic range	496	38
Above therapeutic range	284	23

Table – 2: Interpreters of stable anticoagulation in the patients getting oral anticoagulant (n=70).

Interpreters	Stable INR (30)	Unstable INR (40)	P-VALUE
Age (years)	44.6±15.4	42.3±16.4	0.21
Stroke	30	20	0.01*
CVST	10	6	0.11
DVT	3	1	0.20
Serum Protein (g/dl)	7.2±0.5	7.1±0.6	0.001*
Serum Albumin (g/dl)	4.2±0.1	3.8±0.8	0.03*
Nicoumalone dose (mg/day)	2.6±1.2	2.8±1.2	0.01*
Complications	14	10	0.32

*p<0.05 was statistically significant

Table – 3: Comparison of Quality of anticoagulation between stroke and Thrombosis (n=77).

Parameter	Stroke	Thrombosis	P-VALUE
Age (years)	44.5±13.4	38.3±11.4	0.01*
Duration between 2 INR in months	1.52	1.57	0.21
INR Number			
Therapeutic range (TR)	350	150	0.20
Below TR	300	196	0.001
Above TR	200	80	0.03
Stability of INR			
Stable INR	30	13	0.001*
Unstable INR	20	7	0.11
Complications	20	2	0.01*

*p<0.05 was statistically significant

As per **Table – 2**, stable INR was noted in 30 of 70 (42.6%) patients only. There was variable response of oral anticoagulants requiring variable doses to maintain INR in therapeutic range. Stroke, CVST, DVT among them only stroke was significant predictor for stable anticoagulation (p<0.05), while serum protein and Albumin were also significant predictor. Nicoumalone dose was required >2 mg for both stable INR and Unstable INR and was significant predictor. Out of 70 patients, 24 had complication in which 14 were in stable INR and 10 in unstable INR, but it was not significant.

As per **Table – 3**, the patients with stroke had higher stability but had more complications. Age has been a significant in stroke. While in 24 patients belonged to stroke and 2 belonged to thrombosis which was significant. These complications were at a rate of 9.5 and 7.1 per 100 person-years, respectively with an overall complication rate 16.4 per 100 person- years.

Discussion

In the present study, 39 per cent INR reports were in the therapeutic range. This was lower than the reported frequency of 43-72 per cent [9, 10]. Retrospective studies reported 51 per cent INR in therapeutic range in US, 58 per cent in Canadian 15 and 17.8 per cent in Indian patients [11]. In Stroke Prevention in Atrial Fibrillation II (SPAF II) study, 72 per cent INR values were in the therapeutic range [12]. The inferior quality of

OAC in our study compared to that reported in prospective studies may be due to less frequent INR testing. The optimal INR can be achieved in 90 per cent on alternate day monitoring compared to 50 per cent when monitored monthly [13]. In the literature, the retrospective studies have shown inferior results compared to prospective studies and randomized controlled trials, and this was attributed to regular and frequent follow up. Therapeutic INR is difficult to achieve in the first six months [14]. Stable INR was obtained in 42.6 per cent patients which was higher than a previous study [15]. Diet plays an important role in maintaining stability of anticoagulation. There is great variation in Indian diet with respect to consumption of non-vegetarian diet and green vegetables in vegetarian diet. The overall complication rate in our study was 16.4 per 100 patient-years. In an earlier study, median rate of major hemorrhage was 2.2 per 100 patients' years and that of thromboembolism was 2.5 per 100 patient years 1 which were much lower compared to our results. There are studies showing complications rate similar and/or higher than ours [16, 17]. The high incidence of complications may be due to low quality of oral anticoagulation.

Conclusion

Our study was a hospital-based study on a small sample. A large well plan study is needed on stability of INR in Indian patients and the features responsible for inconsistency. In

neurological patients' achievement and maintenance of optimal INR is often tough. Various modifiable factors including diet, choice of drugs and their dosage are significant predictors of stability hence should be carefully adjusted.

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