Intra Arterial Tirofiban in The Peri Operative Priming for Intracranial Stent Deployment in Aneurysms – A cross Sectional Study

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Abstract

Introduction: Tirofiban is a glycoprotein IIb/IIIa receptor antagonist that inhibits platelet aggregation. Primary and secondary objectives of this study were to determine the efficacy and to determine the safety profile of intra arterial tirofiban in the peri operative priming for intracranial stent deployment in aneurysms respectively.

Materials and Methods: This was a cross sectional study in a tertiary care centre in Kerala. Patient admitted with sub arachnoid haemorrhage/aneurysm posted for endovascular stent associated procedures and willing for the study were selected. The pre procedure assessment of neurological status was done. Patient underwent the procedure where peri operative priming with intraarterial tirofiban was given. The development of any neurological deficits within 24 hours was assessed using Glasgow coma scale and National Institute Health Stroke Scale. Laboratory blood parameters before and after procedure were also reviewed.

Results: Study involved 58 patients with aneurysm who were given intraarterial tirofiban. No significant difference (p value 0.521) in Glasgow coma scale on admission (14.89 ± 0.462) and on discharge (14.74 ±1.650). Analysis was done using SPSS version 20.00. Paired samples t test and Wilcoxon signed rank test were used.

Conclusion: Results showed that intra arterial tirofiban is effective and the procedure was uneventful with no complications. Patients recovered well and the hospital stay was of minimum duration.

Keywords: Tirofiban, Aneurysm, Stent, Glasgow Coma Scale, Cross Sectional Studies

Introduction

An abnormal dilation of blood vessel is known as aneurysm. Intracranial aneurysm is common with a prevalence of 4 %[1]. Rupture of intracranial aneurysm can lead to sub arachnoid haemorrhage. In a previous study, the world-wide incidence of aneurysmal sub arachnoid haemorrhage across all study periods was 7.9 per 100,000 person-years[2]. Surgical clipping and endovascular procedures remain the mainstay of treatment. Endovascular procedures are less invasive which involves stents and coils. Vasospasm and platelet aggregation leads to the development of secondary ischemia in patients with aneurysmal subarachnoid haemorrhage. Anti platelet therapy can aid in prevention of secondary ischemia. Pharmacological modalities involve use of abciximab, eptifibatide and tirofiban. However, the prospective data of abciximab and eptifibatide efficacy is limited[3,4]. The cost effectiveness of these drugs is also significant. Tirofiban has the advantage of shorter plasma half-life and is reversible. It is a non-peptide antagonist of the platelet glycoprotein (GP) IIb/IIIa receptor which inhibits platelet aggregation. Tirofiban has been found to be effective as pre medication in stent assisted coiling of aneurysms when given intravenously[5]. Tirofiban has been recommended by Food and Drug Administration to reduce the rate of thrombotic cardiovascular events in patients with non-ST elevation acute coronary syndrome. This study can provide insight regarding its use in peri operative priming for intracranial stent deployment in aneurysms in preventing thromboembolic episodes. Figure 1 shows the mechanism of action of tirofiban.

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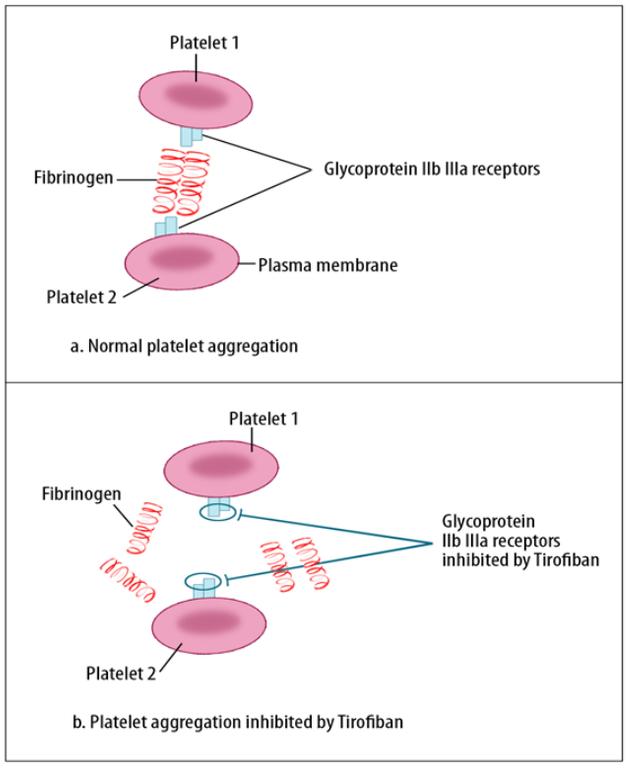

Figure 1: Schematic representation of mechanism of action of tirofiban

Patients and methods

Primary objective

To determine the efficacy of intra arterial tirofiban in the peri operative priming for intracranial stent deployment in aneurysms in preventing thromboembolic episodes

Secondary objective

To determine the safety profile of intra arterial tirofiban in the peri operative priming for intracranial stent deployment in aneurysms

Sample size calculation

(Based on the mean and standard deviation of National Institute Health Stroke Scale before (13.88±2.36) and after (9.52±2.74) the procedure was observed in an earlier publication[6] and with 95 % confidence and 80% power, the minimum sample size was calculated to be 5.

Sample size obtained in this study was 58.

Inclusion criteria

Patient aged > 18 years with
diagnosis of subarachnoid haemorrhage

Exclusion criteria

Patient with bleeding / clotting disorders

Patient with subarachnoid haemorrhage with no aneurysm rupture and prior stent placement for any intracranial vascular lesion

This is an observational cross-sectional study done in a tertiary care centre in Kerala (May 2018 – June 2023). Patient admitted under Department of Neurosurgery with a diagnosis of sub arachnoid haemorrhage posted for endovascular stent and stent associated procedures and willing for the study are selected. Diagnosis was confirmed by clinical examination and radio imaging. The pre procedure assessment of neurological status is done. The study tools used were Glasgow coma scale and National Institute Health Stroke Scale. The patients were not on antiplatelets before the procedure due to the relative contraindication in ruptured aneurysms. Patient undergoes the procedure where peri operative priming with intraarterial tirofiban is given. Braided stent (leo baby and leo plus) which is mixed type and has property of low profile flow diversion was used.

Intra arterial tirofiban was used perioperatively immediately on opening of the stent (5 miligram /100 mililitre solution 1miligram stat) and the remaining 4 miligram was continued for 12 hours intravenously. The antiplatelet drugs were loaded orally once the tirofiban injection was over and continued for 6 months with dual antiplatelet drugs and 1-2 years on single antiplatelet drugs (as recommended by the manufacturer).

The development of any neurological deficits within 24 hours is assessed to ascertain the efficacy of intra arterial tirofiban. Laboratory blood parameters were also reviewed.

Paired samples t test and Wilcoxon signed rank test were used for analysis.

Data was analysed using SPSS version 20.00. Approval from Institutional ethics committee approval was received for this study. Informed consent from all individual participants were taken.

Results

Our study involved 58 patients with aneurysm who were given intra arterial tirofiban.

Table 1 provides the demographic details of the study participants. There was a female preponderance (70.7%) in this study.

Sample size obtained	58
Duration of hospital stay (days)	10 (7,15)
Males (%)	29.3
Females (%)	70.7
Age (mean ± standard deviation) in years	58.07 ± 12.792

Table 1: Demographic details

The most common comorbidities in patients with aneurysmal sub arachnoid haemorrhage in this study were hypertension (46.55%), diabetes mellitus (22.41%), dyslipidaemia (17.24%) and coronary artery disease (10.34%).

The most common location of aneurysm in this study were right internal carotid artery (24.10%), anterior communicating artery (13.8%) and left internal carotid artery (13.8%) followed by left middle cerebral artery (12.10%).

Table 2 describes the analysis of Glasgow coma scale score during admission and discharge of patients of this study. The p value was significant in analysis of Glasgow coma scale score during admission and discharge.

Table 2: Glasgow coma scale score analysis

Glasgow coma scale on admission	14.89 ± 0.462	p value 0.521* (significant)
Glasgow coma scale on discharge	14.74 ± 1.650	

Table 3 depicts the detailed analysis of National Institute Health Stroke Scale score on admission and 24 hours after endovascular stent and stent associated procedures. The analysis was done using paired samples t test and Wilcoxon signed rank test. p value was significant in analysis of National Institute Health Stroke Scale score on admission and 24 hours after procedure.

Table 3: National Institute Health Stroke Scale score analysis

	Percentiles			Wilcoxon Signed Rank Test
	25th	50th (median)	75th	Asymp. Sig. (2-tailed)
National Institute Health Stroke Scale on admission	0.00	0.00	0.00	1.000* (significant)
National Institute Health Stroke Scale 24 hours after procedure	0.00	0.00	0.00	

The laboratory blood parameters considered in this study were activated partial thromboplastin time, prothrombin time, platelet count and international normalized ratio.

Activated partial thromboplastin time was 30.785 ± 9.124 seconds in this study.

Table 4 depicts the detailed analysis of laboratory blood parameters before and after endovascular stent and stent associated procedures (mean ± standard deviation). The analysis was done using paired samples t test and Wilcoxon signed rank test. p values were significant in all the three parameters.

Table 4: Analysis of laboratory blood parameters

Parameters	Mean	Standard Deviation	Sig. (2-tailed) (Significant)
Platelet count before procedure	271.6724	74.48617	0.049*
Platelet count after procedure	260.2759	67.99375	
Prothrombin time before procedure	13.8333	2.66427	0.050*
Prothrombin time after procedure	14.1754	2.83997	
International normalized ratio before procedure	0.9970	0.22233	0.059*
International normalized ratio after procedure	1.0251	0.23899	

Discussion

Investigators analysed the data from case record form to excel spread sheet beginning to light various trends. Mean age was 58.07 ± 12.792 years in this study. Our study had a female preponderance (70.7%). A study by Chang Hyo Yoon et al had male: female ratio as 8:20[7] and the mean age was 57.3 ± 10.5 years in another study[5]. The duration of hospital stay showed a median of 10 days in our study. Another study by Brinjikji W et al found that the mean length of hospital stay was 3.6 ± 5 in glycoprotein IIb/ IIIa group[8]. The length of stay in patients without infection in hospital in another study by Feng S et al was an average of 11.25 ± 7.33 days ($P < 0.001$)[9]. The most common comorbidity was found to be hypertension (46.55%), diabetes mellitus (22.41%), dyslipidaemia (17.24%) in this study. A study conducted in 2021 by Yun Ho Noh et al, showed the most common comorbidity in the tirofiban group to be hypertension (54.5%) followed by diabetes mellitus (27.3%)[10]. Common locations of aneurysm in our study were right internal carotid artery (24.1%), followed by anterior communicating artery (13.8%) and left internal carotid artery (13.8%) and left middle cerebral artery (12.1%). In a study by Chang Hyo Yoon et al, the most common sit of aneurysm was in anterior communicating artery (25.8%)[7]. Glasgow coma scale score in our study during admission was 14.89 ±0.462 and during discharge was 14.74 ± 1.650. A study by In-Suk Bae et al, found the Glasgow coma scale score in patients with sub arachnoid haemorrhage during admission to be 12.1±3.7[11]. The Glasgow outcome score at discharge in tirofiban group was an average of 4.5 in a study by Kim S et al[5]. National Institute Health Stroke Scale on admission and discharge in our study was same with a median score of 0. In a study by Zhao et al, the National Institute Health Stroke Scale on admission was 15 (12,21)[12]. The median National Institute Health Stroke Scale on discharge or day 7 was 2 in a study by Lin L et al[13]. The platelet count (10^3/mocrolitre) was 271.67 ± 74.48 before procedure and 260.27 ± 67.99 in our study. The median platelet count on admission was 192 (147.2–236.7) in tirofiban group by Zhao et al[12]. A decrease in platelet count after treatment with tirofiban by 10,000 (135,000–165,000) per microlitre was found in a study by Brockmann C et al[14]. The platelet count (in 10^3/ microlitre) on admission was 241.0 (194.5

– 278.0) in another study conducted by Michael Veldeman et al[15]. The activated partial thromboplastin time was 30.785 ± 9.124 seconds in our study. A 2019 study by Chang Eui Hong et al, had activated partial thromboplastin time to be 27.46 ± 2.94 seconds in the ruptured aneurysm group[16]. Activated partial thromboplastin time and prothrombin time are mainly used as tests of anticoagulation monitoring[17]. In our study, prothrombin time was 13.8 ± 2.6 seconds before procedure and 14.1 ± 2.83 seconds after procedure. The baseline prothrombin time in another study by Karen Matevosyan et al, was 13.8 (12.8–17.6) seconds[18]. Our study found international normalized ratio to be 0.9 ± 0.2 before procedure and 1.02 ± 0.2 after procedure. The International Normalized Ratio on admission was 1.03 (0.95–1.11) by Zhao L et al[12]. The International Normalized Ratio on admission was 1.1 (1.0–1.2) in another study by Michael Veldeman et al[15]. No adverse drug reactions were reported in this study. Adverse effects were noted in 6 patients in a study by Siebler M et al in tirofiban group[19].

Limitation:

The study was done in the absence of a comparison group. This could be a possible limitation of the study.

Conclusion

Intra arterial Tirofiban is found to have effective antiplatelet activity in patients undergoing endovascular stenting procedures with aneurysmal sub arachnoid haemorrhage. It showed good tolerability and effectiveness to prevent further thrombotic or haemorrhagic complications in the dosage used in this study. Results of this study also showed positive outcomes in these group of patients. The antiplatelet activity of tirofiban sufficient enough to reducing the propensity for thromboembolic episodes within 24 hours in patients with sub arachnoid haemorrhage who underwent endovascular stent associated procedures. Patients recovered well and the hospital stay was of minimum duration. Intra arterial Tirofiban could be recommended as the drug of choice for intracranial stenting in sub arachnoid haemorrhage due to better tolerability, better action and safety profile as the international normalized ratio effectiveness is maintained.

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