



Effect of Anticoagulant and Antiplatelet Drugs on Outcome of Arterio-Venous Fistula Created for Hemodialysis Access

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Abstract

Background: Arteriovenous fistula (AVF) creation is the primary mode of achieving vascular access for hemodialysis in chronic renal failure (CRF). Because of high complication rates like thrombosis, maintenance of the fistula is a major challenge. Although antiplatelet and anticoagulant drugs are emerging rapidly for improving the outcome of AVF but fear of bleeding, hematoma, subsequent compression of AV fistula and blockade restrict their use in many dialysis centers.

Objective: To see the effect of anticoagulant & antiplatelet drugs in improving primary patency rate and reducing early thrombus formation of AVF.

Methods: This clinical trial was conducted in the Department of Urology Bangabandhu Sheikh Mujib Medical University, Dhaka from November, 2018 to October, 2019. Ninety six ESRD patients who underwent AV fistula with immediate postoperative had thrill and murmur were included as study population as per selection criteria. Informed written consent was taken from all the patients. Patients were divided into two groups using computer generated random number (group I and group II). In group I, patients anticoagulation and antiplatelet drugs were used and in group II, patients anticoagulation and antiplatelet drugs were not used after creation of AVF. Patients were followed up on 3rd POD, at 2 weeks and at 4 weeks after the operation and re-evaluated with clinical examinations and investigations. The outcome were evaluated and compared between two groups.

Results: In this study maximum patients were more than 40 years old in both groups. Mean age was 47.89 ± 12.54 years in group I and 46.29 ± 14.78 in group II. Males were predominant in both groups. Male to female ratio was 3.36:1 and 5.8:1 in group I and group II respectively in this study. In this study 35.4% in Group I and 45.8% in Group II patients had hypertension. 47.9% in Group I and 60.4% in Group II patients had DM. Thrombosis was significantly lower in study group (group I) than control group (group II). Primary patency was significantly higher at 4th week after treatment in group I than group II. Bleeding was observed in one (2.1%) patients at 1st POD in group I who came with emergency & managed conservatively. Haematoma was observed in 1 (2.1%) patients at 3rd POD in group I.

Conclusion: Use of antiplatelet and anticoagulant agents prevented the loss of AV patency. But it still needs to be determined whether the potential benefits of anticoagulant & antiplatelet therapy outweighs the risk of adverse events.

Keywords: Arteriovenous fistula, antiplatelet, anticoagulant, hemodialysis.

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Introduction:

Patients with a glomerular filtration rate (GFR) less than 30 mL/min/1.73m² (CKD stage 4) should be educated on all modalities of renal replacement therapy (RRT) options, including transplantation, so timely referral can be made for the appropriate modality and placement of a permanent dialysis access if necessary (KDOQI guideline, 2006). Vascular access is “the life line” for patients with end stage renal disease (ESRD) and haemodialysis (HD) is the commonest form of renal replacement therapy (RRT). An ideal vascular access provide safe and effective therapy by enabling the removal and return of blood via an extracorporeal circuit (Hoggard, 2008). Good quality, well functioning and stable vascular access is a major factor in determining survival of ESRD patients. Autogenous arteriovenous fistula (AVF), prosthetic vascular graft and central venous catheter (CVC) are the modalities of vascular access for HD. An autogenous arteriovenous fistula (AVF) is recommended as the optimal technique (Fluck and Kumwendab, 2011). External arteriovenous fistula (AVF) is the primary mode of achieving vascular access for hemodialysis in patients with chronic renal failure and was first introduced in 1960 by Quinton-Scribner. Because of high complication rates like thrombosis, (Quinton et al., 1960) maintenance of vascular access for hemodialysis is a major challenge in care of hemodialysis patients. Autologous AVF introduced by Brescia and Cimino in 1966, overcame many of the problems of external dialysis shunts, but thrombosis and blockage of fistula still remain an annoying problem in day to day practice for each vascular surgeon (Brescia et al., 1966). Many of the predictors of fistula failure such as older age, female sex, black race, diabetes mellitus, obesity, and low blood pressure are controversial and not readily amenable to modification (Prischl et al., 1995). An increased thrombotic tendency is an important cause of complications in chronic haemodialysis patients leading not only to possibly fatal complications like ischaemic heart disease or stroke, but also to thrombosis of the vascular access (Lindner et al., 1974). This latter complication remains the main problem in vascular access for haemodialysis. Moreover, vascular access complication mainly consisting of thrombotic events is responsible for 17–25% of hospitalizations in dialysis patients (Feldman et al., 1996). In most cases, thrombosis is associated with low blood flow (Bosman et al., 1998) The most important reason a decreasing blood flow is intimal hyperplasia formation at the

venous anastomosis or in the the outflow tract of the graft (Bassiouny et al., 1992). Hypotension, hypovolaemia, or external compression may be involved in these non-stenotic thrombotic event (Windus et al., 1995). Also, there has been a growing appreciation of the role of hypercoagulability states found in these patients. Hypercoagulability in patients on chronic haemodialysis can be caused by a variety of factors, mainly consisting of platelet abnormalities and plasma factor abnormalities.

Preoperative vein mapping, use upper arm rather than forearm, intraoperative heparin administration, surgical ligation of vein branches, and transposition of deep fistulas to more superficial locations, are approaches that might increase the likelihood of attaining a successful fistula and have been recommended by several investigators (Silva et al., 1998). Although antiplatelets and anticoagulants are emerging rapidly for improving the outcome of AVF but fear of bleeding, hematoma, subsequent compression of AVF and blockade restrict their use in many dialysis centers. This study analyses the effect of anticoagulant & antiplatelets drugs given postoperatively on AVF created for hemodialysis access in patient with chronic renal failure .

Materials and Method:

This present Randomized clinical comparative study was carried out in the department of urology ,Bangabandhu Sheikh Mujib Medical University between the periods of November, 2018 to October, 2019. Total ninety six patients were randomly divided into two groups according to computer generated number (Group I, total patients 48 who received anticoagulant & antiplatelet drugs and group II, total patient 48 who not received anticoagulant & antiplatelet drugs). In this study inclusion criteria, patients undergoing AV fistula with immediate postoperative presence of palpable thrill and machinery murmur and exclusion criteria. Patients with, known coagulopathy, acute ulcer disease, systolic blood pressure higher than 200 mm Hg or diastolic blood pressure higher than 115 mmHg & lower limit of Blood pressure <120/80, advanced liver disease, inability to discontinue antiplatelet or anticoagulant therapy including clopedegral drug during the study, pregnancy, history of myocardial infarction or cerebrovascular accident within the previous 12 months. Study variables are comparison of Primary patency rate, comparison of AV fistula blockade due to thrombosis, complication- Bleeding and Haematoma.

Selection criteria:**Inclusion criteria:**

- Patients undergoing AV fistula with immediate postoperative presence of palpable thrill and machinery murmur.

Exclusion criteria:

Patients with

- Known coagulopathy
- Known acute ulcer disease
- systolic blood pressure higher than 200 mm Hg or diastolic blood pressure higher than 115 mmHg & lower limit of Blood pressure <120/80
- advanced liver disease,
- Inability to discontinue antiplatelet or anticoagulant therapy including clopedegral drug during the study.
- pregnancy
- History of myocardial infarction or cerebrovascular accident within the previous 12 months.

Variables:

The following variables were included.

Independent variables:

- Age
- Sex
- Cause of primary renal disease- Diabetes, Hypertention, Glomerulonephritis
- Comorbidities- DM, HTN

Study variables:

- Comparison of Primary patency rate
- Comparison of AV fistula blockade due to thrombosis
- Complication- Bleeding and Haematoma

Observation and result:

This randomized clinical study was carried out on 96 ESRD patients who underwent AV fistula in the Department of Urology, Bangabandhu Sheikh Mujib Medical University, from November 2018 to October 2019 to see the effect of anticoagulant and antiplatelet drugs on the primary patency of Arterio-Venous Fistula created for hemodialysis access.

Table I: Distribution of the study subjects according to age (N=96)

Age (years)	Group I (n=48) n (%)	Group II (n=48) n (%)	p-value
≤30	6 (12.5)	10 (20.8)	
31 - 40	9 (18.8)	6 (12.5)	
41 - 50	13 (27.1)	10 (20.8)	
51 - 60	14 (29.2)	16 (33.3)	
>60	6 (12.5)	6 (12.5)	
Mean ± SD	47.89 ± 12.54	46.29 ± 14.78	0.568

Unpaired t test was done to measure the level of significance

Table I shows distribution of the study subjects according to age. Most of the patients were in age group 41 – 60 years. Mean age of the study subjects was 47.89 ± 12.54 years and 46.29 ± 14.78 years in Group I and Group II respectively.

Table II: Distribution of the study subjects according to gender (N=96)

Gender	Group I (n=48) n (%)	Group II (n=48) n (%)	p-value
Male	37 (77.1)	41 (85.4)	0.296
Female	11 (22.9)	7 (14.6)	

Chi-Square test was done to measure the level of significance

Table II shows distribution of the study subjects according to gender. Males were predominant in both groups. Male to female ratio was 3.36:1 and 5.8:1 in Group Is and Group II respectively.

Table III: Distribution of the study subjects according to co-morbidity (N=96)

Co-morbidity	Group I (n=48) n (%)	Group II (n=48) n (%)	p-value
DM	23 (47.9)	29 (60.4)	0.219
HTN	17 (35.4)	22 (45.8)	0.299
Glomerulonephritis	21 (43.8)	19 (39.6)	0.678

Chi-Square test was done to measure the level of significance

Table III shows distribution of the study subjects according to co-morbidity. DM and HTN was lower in Group Is than Group IIs, GN was higher in Group Is than Group II but there was no significant differences in DM, HTN and GN between Group I and Group IIs.

Table IV: Distribution of the study subjects according to thrombosis. Thrombosis is evaluated by physical examination and Doppler study (N=96)

Thrombosis	Group I (n=48) n (%)	Group II (n=48) n (%)	p-value
Yes	7 (14.6)	16 (33.3)	0.031
No	41 (85.4)	32 (66.7)	

Chi-Square test was done to measure the level of significance

Thrombosis was observed significantly smaller in number in Group I than Group II.

Table V: Distribution of the study subjects according to primary patency (N=96)

Primary patency	Group I (n=48) n (%)	Group II (n=48) n (%)	p-value
3 rd POD	47 (97.9)	45 (93.7)	0.217
At 2 nd week	43 (89.6)	39 (81.2)	0.247
At 4 th week	41 (85.4)	32 (66.7)	0.031

Chi-Square test was done to measure the level of significance

Primary patency rate was found significantly higher at 4th and non significantly higher at 2nd week after treatment in Group I than Group II.

Table VI: Bleeding and Haematoma at different post operative day in Group I (N=48)

	At	Frequency (n)	Percentage (%)
Bleeding	1 rd POD	1	2.1
Haematoma	3 rd POD	1	2.1

Bleeding was observed in one (2.1%) patients at 1st POD and Haematoma was observed in 1 (2.1%) patients at 3rd POD.

Discussion:

Failure of AVF is a major problem in hemodialysis patients. The major causes of failure of fistula other than the technical causes are older age, female sex, black race, diabetes mellitus, obesity, and low blood pressure

(Feldman et al., 2003; Miller et al., 2003). Proper selection of the vein as determined by size of the vessel (more than 2.5 mm), preoperative vein mapping to exclude thrombosed vessel, surgical ligation of vein branches, and transposition of deep fistulas to more superficial locations are approaches that might increase the likelihood of attaining a successful fistula (Robbin et al., 2000; Allon et al., 2001). Nowadays, antiplatelet and anticoagulants are widely used for improving AVF outcome. There has been a divided opinion on the use of these agents and a lot of studies can be found on various databases which are done to look for the role of these agents in outcome of AVF (Yogi et al., 2012).

The main reason against the use of these agents is fear of bleeding. A randomized controlled trial that examined the efficacy of combination therapy of aspirin and clopidogrel for prevention of arteriovenous graft failure was stopped before completion because the prevalence of hemorrhagic complication was significantly higher in the intervention group (Kaufman et al., 2003).

Since both the drugs were used together in the study of Livio et al. (1986), they could not conclude which one is more associated with bleeding. Aspirin is well known to increase the risk of gastrointestinal bleeding in the uremic population (Livio et al., 1986), but there have been no studies of the effects of clopidogrel on bleeding in this population. Bleeding in our study was seen very least notice even with use of anticoagulant and antiplatelet agent. In our study we had encountered only one case with bleeding amongst which one had been given anticoagulant/ antiplatelet agent.

Few studies were done before have shown similar results as ours suggesting a benefit of use of antiplatelet agents in making of an AVF. These agents were started 2-7 days prior to surgical creation of the fistula in their cases (Janicki et al, 1994) whereas we usually used LMWH intra operatively and extend it for 2-3 days according to the thrill felt postoperatively and continue with aspirin or warfarin for 2-3 weeks postoperatively (Crowther et al., 2002; Zellweger et al., 2005).

In this study maximum patients were more than 40 years old in both groups. Mean age was 47.89 ± 12.54 years in group I and 46.29 ± 14.78 in group II. There was no statistical significant difference between these two groups. The age of the patients corresponds with the study of Yogi et al., (2012). Mean age 46.3 years and 42.5 years in group I and group II respectively in their study.

Males were predominant in both groups. Male to female ratio was 3.36:1 and 5.8:1 in group I and group II respectively in this study. Male predominance was in the study of Yogi et al. (2012).

In this study 35.4% in Group I and 45.8% in Group II patients had hypertension. 47.9% in Group I and 60.4% in Group II patients had DM. In the study of Yogi et al. (2012), 70.4% and 43.8% had hypertension in group I and group II respectively; 33.3% and 35.4% had DM in group I and group II respectively. Dember et al. (2008) found DM in 49.2% and 47.0% cases in group I and group II respectively.

In this study, thrombosis was significantly lower in study group (group I) than group II. Primary patency was significantly higher at 4th week after treatment in group I than group II. Bleeding was observed in one (2.1%) patients at 1st POD in group I. Haematoma was observed in 1 (2.1%) patients at 3rd POD in group I. Bleeding and Haematoma cases were managed with conservative treatment. Bleeding was observed in 1 case in both groups in the study of Yogi et al., (2012). Dember et al. (2008) concluded that Clopidogrel reduced the frequency of early thrombosis of new arteriovenous fistulas.

Conclusion:

Judicial use of antiplatelet/anticoagulant agents in cases of AVF for hemodialysis access may be beneficial in preventing the chances of occlusion of AVF and maintain primary patency without significantly increasing the risk of bleeding.

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