Effect of aspirin in preventing thrombosis of tunneled dialysis catheters and increasing catheter survival in dialysis patients; controlled clinical trial study

Amin Rezazadeh1, Sousan Mohammadi Kebar1*, Khatereh Isazadehfar1, Saeed Hoseininia1, Mohammadbagher Didar-Shetaban1, Mohammad Bahadoram4

1Department of Internal Medicine, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran
2Department of Community Medicine, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran
3Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran
4Chronic Renal Failure Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

*Corresponding author: Sousan Mohammadi Kebar, Email: s.mohammadi@arums.ac.ir

ABSTRACT

Introduction: Central catheters that are inserted for dialysis, often fail due to clots in the lumen or veins with a 63% prevalence. Recent studies have shown that aspirin not only acts as an antiplatelet, but also causes diminishing oxidative stress and inflammation.

Objectives: The purpose of the study was to investigate the effectiveness of aspirin in preventing thrombosis in tunneled dialysis catheters in the internal jugular vein and increasing catheter survival in dialysis patients.

Patients and Methods: This randomized clinical trial was conducted on 114 dialysis patients who were divided randomly into two matched groups in terms of age and gender. One group was treated with 80 mg daily aspirin regimen while other group was treated with placebo. Additionally necessary information such as age, gender, cause of renal failure, concomitant diseases like diabetes and hypertension, history of cardiovascular disease and stroke, peripheral vascular diseases, history of statin use and history of anti-thrombotic drugs were obtained of patients by checklists.

Results: The incidence of venous thrombosis in the aspirin group was 3.5% and in the control group was 14%. The difference was statistically significant ($P = 0.001$).

Conclusion: Results showed that administration of aspirin can be effective in increasing catheter survival in dialysis patients and preventing thrombosis of catheters especially in diabetics and male patients.

Trial Registration: The trial was approved by the Iranian registry of clinical trials (identifier: IRCT20181128041785N1; https://www.irct.ir/trial/35610, ethical code; IR.ARUMS.REC.1397.190).

Implication for health policy/practice/research/medical education: This clinical trial study aimed to find the effect of aspirin in preventing thrombosis of tunneled dialysis catheters and increasing catheter survival in dialysis patients. The results of this study showed that the administration of aspirin can be effective in increasing catheter survival in dialysis patients and preventing thrombosis of catheters especially in diabetics and male patients.

Please cite this paper as: Rezazadeh A, Mohammadi Kebar S, Isazadehfar K, Hoseininia S, Didar-Shetaban MB, Bahadoram M. Effect of aspirin in preventing thrombosis of tunneled dialysis catheters and increasing catheter survival in dialysis patients; controlled clinical trial study. J Nephropharmacol. 2022;11(2):e10464. DOI: 10.34172/npj.2021.10464.

Introduction:

Complications of vascular access are the most important causes of morbidity and hospitalization in dialysis patients. A successful dialysis in these patients depends on the good function of the vascular access way (1,2). The most common complication of vascular access is clot formation in their lumens, which is also true about central venous catheters that are inserted for dialysis (3). Despite various efforts to prevent clots formation in catheters such as heparin, this complication still occurs in some cases. Prevention of clot formation in the catheters lumen is very important and it should start from the time of catheter implantation. In previous studies, an increase in intravenous catheter's patency with warfarin has been reported (4,5). A pervious study found administration of aspirin was effective to prevent clot formation in dialysis patients (6). Central catheters that are inserted for dialysis, often fail due to clots in the lumen or veins with a 63% prevalence (7). Catheter dysfunction is defined as an insufficient blood flow to perform dialysis. Enough blood
flow is defined as 300 cc/min (8). Clotting in the catheter’s lumen is a common complication. The average survival in dialysis catheters is 73 to 84 days. The most important reason for their failure is the formation of clots, while its cause is not well-known (9). Recent studies have shown that aspirin not only acts as an antiplatelet, but also causes diminishing oxidative stress and inflammation (10,11).

Objectives
It may be helpful to administer antiplatelet drugs to prevent thrombosis. Due to the relatively high prevalence of catheter dysfunction related to thrombosis and the cost of catheter replacement on the health system, we decided to study the effectiveness of aspirin on the prevention of thrombosis of the jugular vein’s tunneled catheter and increase the shelf life of the catheter.

Patients and Methods
Study design
This randomized clinical trial was conducted on 114 patients who were implanted with a tunneled catheter in jugular vein for dialysis. Patients were randomly divided into two matched groups in terms of age and gender-each of them included 57 cases (Figure 1). One group received aspirin and another group received placebo which was made by Razi Company, Iran while the placebo pills were similar to aspirin in form and shape. The average age of patients in aspirin group was 68.8 ± 9.8 years and in placebo group it was 64.2 ± 11.8 years and the difference between the two groups was not significant. In the placebo and intervention groups, 34 (45.9%) and 40 (54.1%) patients had hypertension, respectively (P=0.634). Around 58 (50.8%) had a history of diabetes mellitus (DM), 46 (40.4%) had congestive heart failure (CHF) and 3 (2.6%) patients had a history of deep vein thrombosis (DVT). We employed randomize blocking method in order to randomize patients. All of the patients completed the consent form before the study and the patients’ background information including age, gender, cause of kidney failure, concomitant disease such as diabetes or hypertension, history of cardiovascular disease and stroke, peripheral vascular disease, history of statins or anticoagulants use were taken from patients to determine their probable effect over time on the duration of the catheter's survival in both intervention and control groups.

Dialysis patients with new permanent catheters were included in this study and patients with bleeding leading to blood transfusions in the last three months, severe proliferative diabetic retinopathy, uncontrolled systolic blood pressure above 200 mm Hg and diastolic above 110 mm Hg, platelet count less than 100000/µL, INR >1.3 and patients treated with dipyridamole, ticlopidine, sulfipyrazone, clopidogrel or nonsteroidal anti-inflammatory drugs were excluded. Catheter dysfunction from the beginning, catheter infection and previous coagulation disorders in patients were contraindications to aspirin administration. A catheter was inserted in all patients by the same surgeon and the inserted catheter size was 14 in all patients. Around 57 patients were treated with aspirin regimen which was 80 mg/daily and another 57 patients were in the placebo group. Patients and medical

![Figure 1. CONSORT flow diagram.](http://www.jnephropharmacology.com)
personnel did not know the type of medication prescribed in both groups. The number of days of proper function of the catheter in both intervention and control groups was compared. All patients were observed for six months.

Data analysis
The data obtained in the study were processed by using the IBM, SPSS statistics version 24.0 for Windows statistical software package. To determine statistical significance of rate of values in two groups, we applied the chi-square test. The differences were considered statistically significant at significance level of $P<0.05$.

Results
The incidence rate of thrombosis in the aspirin and placebo groups was 3.5% and 14%, respectively. Also, the difference between two groups was significant ($P=0.034$; Table 1).

Of the total patients, 10 (8.8%) had thrombosis that seven patients were male, two in the intervention group and five in the placebo group and three patients were females, three women in the control group. There was a significant relationship between thrombosis and gender of patients ($P=0.021$).

The average hemodialysis sessions among the patients with thrombosis in the placebo and intervention group were the same and three sessions per week. There was no significant association between the effect of aspirin in preventing venous thrombosis of the jugular vein and increasing the catheter survival by the number of hemodialysis sessions per week. Of two patients with thrombosis in the intervention group, all had hypertension and of the eight patients in the placebo group, six patients had hypertension. There was no significant association between the effect of aspirin in preventing venous thrombosis of the jugular vein and increasing the duration of catheter survival in terms of presence or absence of hypertension. Among patients with diabetes and the individuals who received aspirin, one patient (2%) and among patients with diabetes that do not take aspirin, one patient (2%) and among non-diabetic patients that do not take aspirin, one patient (2%) developed thrombosis, therefore the difference between the two groups was not statistically significant.

Among non-diabetic patients and the individuals who received aspirin, one patient (2%) and among non-diabetic patients that do not take aspirin, one patient (2%) developed thrombosis, therefore the difference between the two groups was not statistically significant.

There was no significant relationship between thrombosis formation with age or gender ($P>0.05$). The incidence of thrombosis was not related to the number of hemodialyses. Likewise, the incidence of thrombosis was not associated with the incidence rate of hypertension in all groups.

Discussion
The prevention of the formation of venous thrombosis and reduction of incidence of venous thrombosis after anti-platelet aggregative drug therapy such as aspirin can be played an important role in the patient’s condition and quality of life. In this study, the average age of all patients was $66.5 \pm 11.04$ years and the difference between the two groups was not significant. In a study which was conducted by Mozafar et al, on the efficiency of aspirin on double lumen permanent catheter efficacy in end-stage kidney failure on 180 patients with end-stage renal disease who were divided into two groups-control and intervention, the mean of catheter survival in two groups were compared. The average age of patients in this study was 71.1 which was almost equal to the present study (11). In the treatment group with aspirin, the mean survival time in the group was significantly higher than the control group ($5.3 \pm 4.7$ years versus $3.9 \pm 2.7$ years; $P=0.012$), which could be related to the significant positive effect of aspirin in our study as well. Abdul-Rahman and Al-Howaish compared warfarin versus aspirin in preventing catheter dialysis thrombosis on 58 patients with 20 patients in the warfarin intervention group, 19 patients in the aspirin intervention group and 19 patients in the control group. In this study, the average age of the patients was 62.3 years, which is similar to the results of the present study. Malfunction-free catheter survival in 12 months was 75% in the warfarin group, 68.4% in the aspirin group and 36.8% in the control group. There was no statistically significant difference between the warfarin and aspirin groups, while the difference between these groups and the control subjects was statistically significant ($P=0.001$) (8). Our study shows the positive effect of aspirin on catheter survival too. The study by Obialo et al, in the United States regarding the comparison of warfarin with aspirin in dialysis catheter function included 64 patients totally with eleven patients in the warfarin intervention group, 21 patients in the aspirin intervention group and 31 patients who were in the control group. The durability of the catheter in the group of interventions with aspirin, warfarin and control were 91%, 73% and 29%, respectively. The age of the patients in this study was 74.6 years, which may be due to the higher average of patient’s age in this study (12). This study is consistent with our

### Table 1. The demographic and clinical characteristics of patients in two groups

| Variables         | Aspirin | Placebo | $P$ value |
|-------------------|---------|---------|-----------|
|                   | No.     | %       | No.       | %       |           |
| Incidence rate of thrombosis | 2       | 3.5     | 8         | 14      | 0.001     |
| History of DVT    | 2       | 3.5     | 1         | 1.8     | 0.546     |

http://www.jnephropharmacology.com
study and shows the positive effect of aspirin therapy on catheter survival too. Likewise Couban et al compared the effects of warfarin versus aspirin to prevent catheter vein thrombosis in cancer patients. Around 255 patients were included in their study who were randomly divided into two groups which were matched regarding age and gender. The first group was treated with prophylactic treatment with 1 mg of warfarin daily and the second group was treated with 80 mg of aspirin daily. Patients were followed for 90 days and they were considered positive if the catheter did not function for the reason of thrombosis. After completing the study and analyzing the results, no significant difference was found between the results of the two groups. The average age of the patients was 67.9 years, which was approximately equal to the present study (13). In some studies, gender distribution was almost proportional and equal and gender did not appear to affect the risk of dialysis catheter thrombosis in patients (11, 13).

In the study by Couban et al, of 255 patients, symptomatic central venous catheter-associated thrombosis was seen in 11 (4.3%) of patients while the difference between two groups was not statistically significant (4.6% versus 4%, $P=0.34$) (13). Our patients were dialyzed three times a week for four hours. This definition has been conducted in other studies like the study of Abdul Rahman et al and the study of Obialo et al (8, 12). We do not find any significant relationship between the effect of aspirin on the prevention of thrombosis of the jugular vein catheters and increasing the shelf life of the catheters. However in some studies, hypertension was more pronounced in men and the response to anticoagulant therapy was higher in those with hypertension (1, 12). Whether aspirin really had an effect on high blood pressure is debatable; however, in this study we also see that the effect of aspirin in hypertensive and non-hypertensive patients was similar (2, 13). Of 114 patients, 46 had CHF history, 20 of them were in the intervention group and 26 patients were in the control group but the difference in catheter survival between two groups was not statistically significant. The relationship between the effect of the aspirin drug and the presence of CHF similar to this study wasn't found in any of the similar studies. This statistic was 55% in the study of Muzafar et al (11), 48% in the study of Obialo et al (12), and 45% in the study of Abdul-Rahman and Al-Howaish (8). The reason for this difference is probably due to the fact that the average age in our study was lower and the cardiac output below 40% was considered as the definition of heart failure. There was no mention of DVT in other studies and it was not possible to compare the results. In the study by Abdul-Rahman and Al-Howaish, no statistically significant difference between the group under intervention with aspirin and warfarin was detected (8). In a study by Obialo et al the durability of the catheter in the group of interventions with aspirin, warfarin and control were respectively 91%, 73%, and 29%. The rate of gastrointestinal bleeding in the intervention group with aspirin, warfarin and control was respectively 24%, 18% and zero percent confirming the effect of aspirin (12).

In a study by Couban et al, a difference between aspirin and Plavix as a suitable drug to prevent catheter thrombosis was demonstrated; however this study did not have a control group (14). In intervention group, the effect of aspirin on diabetic patients in our study is clear that there was a significant relationship between gender and thrombosis formation, the effect of aspirin on the prevention of venous catheter thrombosis and increased catheter survival due to the presence or absence of diabetes. The incidence rate of thrombosis in the aspirin group with 3.5% was significantly lower than the placebo group with 14% and the results showed that the aspirin was effective in reducing the rate of catheter thrombosis in dialysis patients. In a study, Zhang et al, showed that oral aspirin can effectively reduce the incidence rate of venous thrombosis in breast cancer patients with postoperative chemotherapy after peripherally inserted central catheter insertion which was in line with our study results.

**Conclusion**

The effect of aspirin in preventing venous thrombosis of the jugular vein and increasing the shelf life of the catheter was greater in diabetic patients than others. Finally, use of aspirin can be effective in increasing catheter’s survival in dialysis patients and prevention thrombosis of tunneled catheters of the internal jugular vein. It is recommended that another study should be conducted with Plavix and placebo in the future with large samples.

**Limitation of study**

There was no formal limitation in this study but only two patients were excluded from the study due to their own satisfaction.

**Authors’ contribution**

AR and MB in study design, clinical examination, data collection, assisted with statistical analysis, author of the manuscript. SMK assisted with clinical examination and sampling. KI treated patients, assisted with editing the manuscript. SH assisted with project design, assisted with editing the manuscript. MDS assisted in data collection, follow-up patients and complete the checklist and write the final reports.

**Conflicts of interest**

The authors declare no conflicts of interest relevant to the submitted materials and did not receive funding for the completion of this research.

**Ethical issues**

The research was conducted in accordance with the tenets
of the Declaration of Helsinki. The Ethics Committee of Ardabil university of medical sciences approved this study (IR.ARUMS.REC.1397.190). Accordingly, written informed consent was taken from all participants before any intervention. This clinical trial protocol was also approved by the Iranian Registry of Clinical Trials (identifier: IRCT20181128041785N1; https://www.irct.ir/trial/35610). Additionally, this study was a part of M.D., thesis of Mohammadbagher Didar-Shetaban at this university.

Funding/Support
No funding.

References
1. Hakim R, Himmelfarb J. Hemodialysis access failure: a call to action. Kidney Int. 1998;54:1029-40. doi: 10.1046/j.1523-1755.1998.00122.x.
2. Smits JH, van der Linden J, Blankestijn PJ, Rabelink TJ. Coagulation and haemodialysis access thrombosis. Nephrol Dial Transplant. 2000;15:1755-60. doi: 10.1093/ndt/15.11.1755.
3. Boraks P, Seale J, Price J, Bass G, Ethell M, Keeling D, et al. Prevention of central venous catheter associated thrombosis using minidose warfarin in patients with haematological malignancies. Br J Haematol. 1998;101:483-6. doi: 10.1046/j.1365-2141.1998.00732.x.
4. Haire WD, Lieberman RP, Lund GB, Edney JA, Kessinger A, Armitage JO. Thrombotic complications of silicone rubber catheters during autologous marrow and peripheral stem cell transplantation: prospective comparison of Hickman and Groshong catheters. Bone Marrow Transplant. 1991;7:57-9.
5. Vascular Access 2006 Work Group. Clinical practice guidelines for vascular access. Am J Kidney Dis. 2006;48 Suppl 1:S176-247. doi: 10.1053/ajkd.2006.04.029.
6. Suhocki PV, Conlon PJ, Jr, Knell MH, Harland R, Schwab SJ. Silastic cuffed catheters for hemodialysis vascular access: thrombolytic and mechanical correction of malfunction. Am J Kidney Dis. 1996;28:379-86. doi: 10.1016/s0272-6386(96)90495-3.
7. Rysz J, Banach M, Cialkowska-Rysz A, Stolarek R, Barylski M, Drozdz J, et al. Blood serum levels of IL-2, IL-6, IL-8, TNF-alpha and IL-1beta in patients on maintenance hemodialysis. Cell Mol Immunol. 2006;3:151-4.
8. Abdul-Rahman IS, Al-Howash AK. Warfarin versus aspirin in preventing tunneled hemodialysis catheter thrombosis: a prospective randomized study. Hong Kong J Nephrol. 2007;9:23-30. doi: 10.1016/s1561-5413(07)60005-2.
9. Weiss MF, Scivittaro V, Anderson JM. Oxidative stress and increased expression of growth factors in lesions of failed hemodialysis access. Am J Kidney Dis. 2001;37:970-80. doi: 10.1016/s0272-6386(05)80013-7.
10. Viener A, Aviram M, Better OS, Brook JG. Enhanced in vitro platelet aggregation in hemodialysis patients. Nephron. 1986;43:139-43. doi: 10.1159/000183813.
11. Mozafar M, Samsami M, Sobhiyeh MR, Jabbehdari S, Fallah Zavareh M. Effectiveness of aspirin on double lumen permanent catheter efficacy in ESRD. Nephrohol Mon. 2013;5:762-5. doi: 10.5812/nuresearch.8733.
12. Obialo CI, Conner AC, Lebon IF. Maintaining patency of tunneled hemodialysis catheters--efficacy of aspirin compared to warfarin. Scand J Urol Nephrol. 2003;37:172-6. doi: 10.1080/00365590310008983.
13. Couban S, Goodyear M, Burnell M, Dolan S, Wasi P, Barnes D, et al. Randomized placebo-controlled study of low-dose warfarin for the prevention of central venous catheter-associated thrombosis in patients with cancer. J Clin Oncol. 2005;23:4063-9. doi: 10.1200/jco.2005.10.192.
14. Zhang C, Xiong X, Deng S, Wang F. Clinical study of aspirin in the prevention of thrombosis in breast cancer patients with postoperative chemotherapy after PICC insertion. Yangtze Med. 2018;2:255-61. doi: 10.4236/ym.2018.24027.