Nephro-Urol Mon. 2018 May; 10(3):e66060. doi: 10.5812/numonthly.66060.

Published online 2018 March 26. **Research Article**

Sertraline Prevents Hypotension During Hemodialysis: A Randomized Clinical Trial

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Received 2018 January 14; **Accepted** 2018 March 07.

Abstract

Background: Hemodialysis-induced hypotension is one of the most common problems in patients, who undergo hemodialysis. Evidence suggests the positive impacts of Selective Serotonin Reuptake Inhibitors (SSRIs) on preventing hypotension during dialysis. The current study investigated the hypothesis that sertraline could effectively prevent hypotension during hemodialysis.
Methods: In a clinical trial, 30 patients on hemodialysis with hypotension during hemodialysis, who were referred to Tabriz University of Medical Sciences were enrolled. Patients were treated with sertraline at a dose of 50 mg daily for 2 weeks. Systolic blood pressure, diastolic blood pressure, mean arterial pressure, and heart rate of patients before and after the intervention were measured and compared. Adverse events due to the administration of sertraline were also evaluated in the patients.
Results: Of the 30 studied patients, 17 (56.7%) were male and 13 (43.3%) were female. Systolic blood pressure, diastolic blood pressure, and mean arterial pressure increased significantly after sertraline administration (P = 0.001). Also, the mean heart rate of patients significantly decreased (P = 0.001). However, headache was seen in 7 (23.3%), dizziness in 3 (10.0%), and gastrointestinal complications in 2 (6.7%) patients.
Conclusions: Based on the results of this study, sertraline effectively and safely prevents hypotension during dialysis without causing serious side effects.

Keywords: Sertraline, Hypotension, Hemodialysis

1. Background

Hypotension is one of the most common complications of hemodialysis, and reduces the effectiveness or efficacy of dialysis (1). It has been defined by current kidney disease outcomes quality initiative guidelines as "$\geq$ 20 mmHg fall in systolic blood pressure (BP) from pre-dialysis to nadir intradialytic levels plus $\geq$ 2 responsive measures" (2). Hypotension may also lead to the collapse of the arterial and venous fistula (AVF) and substantially reduce the quality of life of these patients (3).

The main cause of hypotension during dialysis is incorrect calculation of ideal weight for the patients (4). In many cases, the cause of hypotension is autonomic neuropathy, especially in elderly and patients with diabetes. Despite efforts to improve the function of this system in these individuals, no satisfactory and effective treatment has yet been provided (5).

Some medications, such as ephedrine and non-steroidal anti-inflammatory drugs (NSAIDs), have been suggested to reduce vasodilatation during hemodialysis, yet have been associated with many side effects (6, 7). Also, it has been shown that the use of midodrine, a selective alpha-adrenergic agonist, results in several complications, such as urinary retention and increased blood pressure, which can be very dangerous to the patient (8, 9). Paresthesia and itching are other side effects of this drug. Therefore, its use is not recommended (10).

Some evidence suggests that sertraline, as a selective serotonin reuptake inhibitor (SSRIs), can be effective in the treatment of dialysis-induced hypotension. Regarding the fact that sertraline is also an antidepressant, it may also be helpful in this regard. It has been found that treat-

ment with sertraline meaningfully increases blood pressure before and after dialysis leading to a substantial decrease in the hypotension episodes and need for interventions in these patients (11). In another study, it was revealed that sertraline administration remarkably reduced dialysis-induced hypotension episodes without causing significant side effects (12). It has also been shown that sertraline plays a vital role in lowering uremic pruritus and improving postural tachycardia syndrome (POTS) (13-16). On the other hand, another study showed that addition of sertraline to other therapies had no additive impact on improving blood pressure in patients, who were under hemodialysis (17).

The current study aimed at investigating the effect of sertraline on dialysis-induced hypotension at Tabriz University of Medical Sciences. Accordingly, sertraline could be used as a safe and low-cost method for the treatment of hypotension during dialysis.

2. Methods

2.1. Study Design and Patients

This study was a randomized clinical trial (RCT) conducted on 30 patients with persistent dialysis-induced hypotension at Imam Reza, Sina and Artesh hospitals of Tabriz University of Medical Sciences (TUOMS) between April 2016 and 2017. This study was registered at the Iranian clinical trial site under IRCT201604273742N4 code and the regional ethics committee of TUOMS, Iran, approved it's protocol under the code of TBZMED.REC.1394.855.

2.2. Inclusion and Exclusion Criteria

This research included every patient, who 1, was over 18 years of age under hemodialysis; 2, had persistent hypotension during dialysis; 3, did not have other causes of hypotension, such as heart failure, tamponade, and recent cardiac infarction; 4, did not have a specific cause for hypotension, such as being overweight over 3 kg before dialysis; and 5, had written informed consent to participate in the study.

On the other hand, the study excluded patient, who 1, had intake of any type of SSRIs; 2, had use of other monoamine-oxidase drugs; 3, had a history of liver disease or seizure; 5, showed intolerable side effects, such as a severe headache and dizziness; and 6, did not provide consent to participate in the study.

2.3. Study Method

Thirty patients were randomly selected using convenient sampling and assigned to the study after confirmation of the trial by the ethics committee of TUOMS, considering the inclusion and exclusion criteria of the study. The purpose of the study was explained to all participants as well as the possible benefits and complications of sertraline, and informed written consent was obtained. All patients were initially subjected to psychiatric examination for assessment of suicidal behavior and the absence of contraindication for receiving SSRI and were then included in the study if outcomes were confirmed by a relevant psychiatrist.

Duration of dialysis in all patients before and after the intervention was the same and for 4 hours. During the study, a psychiatrist and a clinical pharmacist also supervised the process of the study. The systolic and diastolic blood pressure, heart rate, and mean arterial pressure (MAP) of the patients were measured and recorded before the intervention. The mean of all 4 studied parameters was calculated and recorded. Accordingly, all patients were treated with 50 mg of sertraline daily, and after 2 weeks of administration (to reach an acceptable blood level of medication), systolic blood pressure, diastolic blood pressure, heart rate, and MAP of these patients were recorded every 15 minutes during dialysis, and then the mean of these parameters was calculated and recorded again. During the study, all possible drug adverse effects were recorded (complications from sertraline use are rare and if there are complications, such as headache, gastrointestinal disorders, etc., patients would be visited by the relevant psychiatrist, and the needed measures would be taken).

2.4. Ethics

This study was in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki declaration of 1975, as revised in 2008 (18).

Patients received a complete explanation of the possible benefits and potential complications of sertraline (based on previous studies, a serious side effect was unlikely) and were told that all their information would be kept confidential, and their personal information would not be mentioned anywhere. Also, written informed consent was obtained from the patients and the study was confirmed by the ethics committee of TUOMS. There was no additional intervention except the administration of 50 mg of sertraline, daily. Also, the cost of sertraline used in the study was provided by the project manager and supported by the vice chancellor of TUOMS, and no additional costs were received from patients and their families.

2.5. Statistical Analysis

The SPSS™ Version 20 software was used for all statistical analyses. The obtained data were expressed as mean $\pm$ standard deviation (SD), frequency, and percentages.

Paired t-test was used to compare quantitative variables before and after the intervention.

The number of available patients with dialysis-induced hypotension and Cochran formula (online at http://www.parsmodir.com/db/research/cochran.php) were used to determine the sample size. The power (1-β) and α were considered as 80% and 0.05, respectively.

3. Results

Of the 30 studied patients, 17 (56.7%) were male and 13 (43.3%) were female with a mean age of 46.10 $\pm$ 13.89 years. Table 1 and Figure 1 show the comparison of systolic and diastolic blood pressure, MAP, and heart rate during dialysis in patients before and after the intervention. According to this Table, the mean systolic and diastolic blood pressures and MAP after the intervention was significantly higher than that before the intervention during dialysis (P = 0.001). Also, results revealed that mean heart rate of the patients during dialysis was considerably lower after the intervention compared with that before the intervention (P = 0.001).

During the entire study, no significant side effect of sertraline was reported to result in drug discontinuation. Table 2 represents the frequency of side effects associated with sertraline consumption observed during the study.

4. Discussion

Chronic kidney disease (CKD) is defined as irreversible and progressive loss of renal function. Most patients with CKD will eventually require permanent hemodialysis (19). Replacement therapy, such as hemodialysis in patients with CKD imposes a significant and growing burden on the healthcare system in many countries, especially in developing countries (4).

Dialysis-induced hypotension (DH) is a cardiovascular problem, which can occur in both acute and chronic forms during hemodialysis (20). Dialysis-induced hypotension occurs on average in about 30% of hemodialysis patients, and its pathophysiology is mainly multifactorial. Furthermore, DH has been shown to be associated with both host-related factors, such as cardiovascular disease, systolic and diastolic blood pressure dysfunction, and hemodialysis factors, such as the velocity and volume of the ultrafiltration fluid (20, 21).

Some measures have been introduced to prevent DH, including accurate assessment of dry weight of patients, prevention of excess salt and fluid intake, proper temperature of dialysis fluid, prevention of food intake during dialysis, use of bicarbonate as buffer instead of acetate, no use of low-sodium and low-calcium dialysis fluid, dose adjustment of antihypertensive medications, and increase in the duration or frequency of hemodialysis (22, 23). Until now, there has been no definitive treatment for DH, and despite the use of the aforementioned strategies, the occurrence of hypotension during dialysis is still inevitable in some patients. On the other hand, some studies have shown that SSRIs are effective in preventing hypotension during dialysis (15, 24).

Based on the results of this study, the mean systolic as well as diastolic pressure, and MAP significantly increased after sertraline administration. Also, sertraline intake significantly decreased the mean heart rate in patients. The results of this study indicated that the use of sertraline in patients on hemodialysis could effectively prevent the occurrence of DH without causing significant side effects.

In line with this, Dheenan et al. conducted a study to investigate the effect of sertraline on DH. During this study, the patients were treated with sertraline (50 or 100 mg daily) due to depression and hypotension during dialysis for 6 weeks. The results of this study showed that sertraline administration meaningfully increased MAP and decreased hypotension episodes developed during hemodialysis sessions. Also, this study found that the number of therapeutic interventions for hypotension in the post-sertraline period was significantly lower (15).

In another study, Yalcin et al. examined the effect of sertraline (100 mg/daily for four weeks) on DH. The results of this study showed that weight after hemodialysis and volume of ultrafiltration were similar before and after the intervention. Also, no change in albumin and hematocrit levels were observed in the patients. However, post-dialysis systolic and diastolic blood pressures were remarkably increased and the need for therapeutic interventions was significantly decreased after the intervention (12).

Razaghi et al. also studied the impact of sertraline (50 to 100 mg/daily for 12 weeks) on DH in a placebo-controlled trial. Twelve patients completed all phases of the study. The results of this study showed that sertraline resulted in a 3.8 mmHg and 4.9 mmHg increase in systolic and diastolic blood pressures at the end of the intervention, respectively. Treatment with sertraline also resulted in a 43% reduction in hypotension incidence (11).

On the other hand, in a study by Brewster et al., the authors showed that daily administration of sertraline at 50 mg dose did not affect systolic, diastolic, and mean arterial pressure in the studied subjects (17).

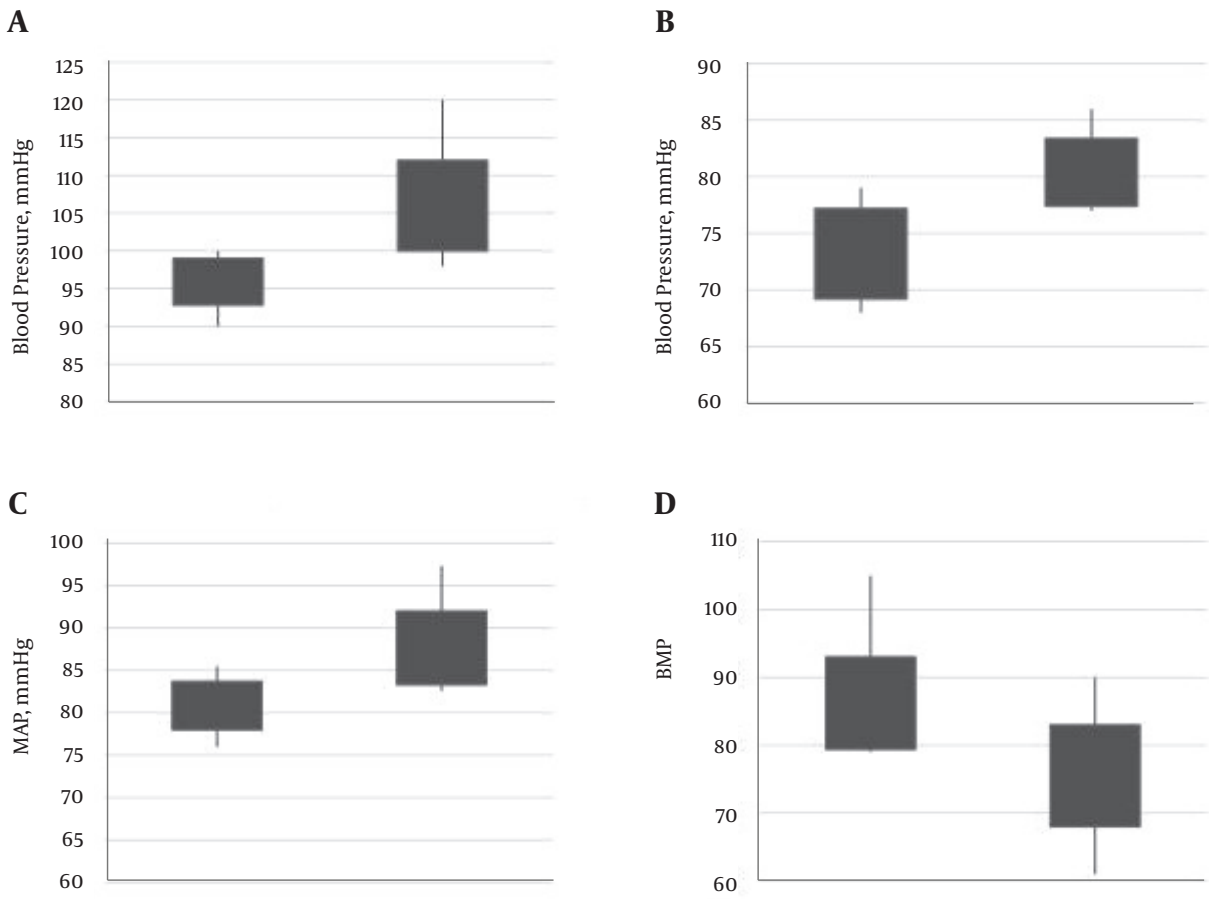
In conclusion, based on the results of this study and a few studies performed in this field, it appears that sertraline is an efficient, safe, and economically reasonable therapeutic alternative for preventing DH. The researchers also showed that its adverse effects were negligible in this set of

Table 1. The Comparison of Systolic and Diastolic Blood Pressures, MAP and Heart Rate During Dialysis in Patients, Before and After the Intervention

Variables	Mean ± SD	Min., mmHg	Max., mmHg	P Value
Systolic BP				P = 0.001
Before intervention	96.10 ± 3.36	90	100	
After intervention	104.16 ± 8.52	98	120	
Diastolic BP				P = 0.001
Before intervention	73.43 ± 3.89	68	79	
After intervention	80.40 ± 3.05	77	86	
MAP				P = 0.001
Before intervention	80.97 ± 2.84	76	85.33	
After intervention	87.63 ± 4.34	82.66	97.30	
Heart rate				P = 0.001
Before intervention	86.33 ± 6.78	75	105	
After intervention	75.33 ± 7.12	61	90	

Abbreviations: BP, Blood Pressure; MAP, Mean Arterial Pressure; SD, Standard Deviation.

Figure 1. The Comparison of A, Systolic; B, Diastolic Blood Pressures; C, MAP and D, Heart Rate During Dialysis in Patients Before and After the Intervention



BPM, beat per minute; MAP, mean arterial pressure. The bars on the left and right represent before and after the intervention, respectively.

Table 2. The Frequency of Side Effects Associated with Sertraline Use Observed During the Study GI, Gastrointestinal[a]

Side Effect	Frequency
Headache	7 (23.3)
Dizziness	3 (10)
GI complications (vomiting, nausea)	2 (6.7)
No complication	18 (60.0)

[a]Values are expressed as No. (%).

patients.

Acknowledgments

The authors are grateful of all the patients for their patience and contribution to this study.

Footnotes

Authors' Contribution: Study concept and design, Hamid Noshad and Sepideh Herizchi; acquisition of data, Reza Ghorbani and Farid Karkon Shayan; analysis and interpretation of data, Farid Karkon Shayan and Behnaz Ghamari; drafting of the manuscript, Reza Ghorbani, Farid Karkon Shayan and Sepideh Karkon Shayan; critical revision of the manuscript for important intellectual content, Hamid Noshad and Sepideh Herizchi; statistical analysis, Farid Karkon Shayan, Behnaz Ghamari and Sepideh Karkon Shayan; administrative, technical, and material support, Hamid Noshad, Reza Ghorbani and Sepideh Herizchi; study supervision, Hamid Noshad.

Financial Disclosure: There were no competing interests for this article.

Funding/Support: This paper was based on Reza Ghorbani's speciality dissertation submitted to the chronic kidney disease research centre, Tabriz University of Medical Sciences, Tabriz, Iran.

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