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The effect of hypertonic glucose infusion on dialysis adequacy in non-diabetic hemodialysis patients

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ABSTRACT

Aims: Hemodialysis Patients suffer from many problems and complications during disease and their treatment. One of the most important and common problems is hypotension and dialysis adequacy. This study has been designed and implemented to determine the effect of hypertonic glucose on dialysis adequacy and blood pressure in non-diabetic dialysis patients.
Methods: The present study was a quasi-experimental and single group study that 45 none-diabetic hemodialysis patients from the chosen hospitals were selected and hypertonic glucose infused patients for two weeks and three times a week, after two weeks durability, patients were assessed without manipulation for two weeks. In addition blood pressure and dialysis adequacy of the patients were measured in manipulation phase before and after each infusion of hypertonic glucose .Data collection tools included demographic information and dialysis adequacy was calculated by Daugirdas formula at the end of every stage in two study environments. Then the data were analyzed by using SPSS 17 software and descriptive statistical tests (abundance- mean), inferential tests (paired t test, mane Whitney, Friedman, Kruskal-wallis and wilcoxon)
Results: The results showed that dialysis adequacy and also blood pressure of the patients had been increased significantly in manipulation phase (p=0.001). And analysis of data between the gender (p=0.001) and vascular access (p=0.001) showed significant differences (p=0.001),but in other cases, there was no significant difference.
Conclusion: results of this study showed that injection of hypertonic glucose increased dialysis adequacy in hemodialysis patients significantly and prevented hypotension.

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1. Introduction

Hemodialysis is one of the important ways of treatment in patients with acute and chronic renal failure. The purposes of dialysis are removing excess material and stabilize the internal environment of the body and it is also a

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method for removing toxins and poisons that can cause injury and permanent or fatal damages [1]. Today, more than 200 thousand people in the U.S. are suffering from chronic renal failure and more than a million people are living in the world through hemodialysis [2]. Dialysis patients according to specific physical and psychological illness experience many difficulties. They are in the hospital three times a week for 4 hours each time and this means that they are away from home that this problem can leave remarkable effect on their job program, employment status, economic status, self-esteem and high levels of dependency[3]. Now if the adequacy of dialysis performed is not sufficient, blood toxins level and patient's clinical symptoms are not well controlled and therefore increases the patients' mortality and morbidity rates. On the other hand the limitations of hemodialysis units such as; number of devices, time, number of patients and etc. do not allow unlimited hemodialysis. Therefore, patients should be dialyzed so that the patient's general condition improve and be affordable in terms of both economic and social. Dialysis adequacy is an important and also effective factor in reducing these problems [4]. Considering that the better dialysis process means better quality of life and living status and less side effects, therefore, identifying effective factors for improving dialysis adequacy and its increase way is important [5]. Several known factors effect on dialysis adequacy such as; diet, filter type, speed of machine, dialysis time, teaching to the patient, underlying disease(especially diabetes) [5].

In the dialysis clearance of urea by the clearance formula or dialysis clearance (KOA) which is a constant value for each filter and blood flow of filter depends on T(time)- V (Volume of distribution of urea in body fluids which depends on the height, sex and weight) are calculated by the normal level of the ½. According to reliable sources, level of less than 0.8 is indication of inadequacy. Also, percentage of urea after to before is another indicator with the normal level less than 0.42, that reaching to the level of 0.5 and more is indication of inadequacy of dialysis. Percent reduction of urea (PRU) has a linear relation with KT/V and it is very important. But in researches there is another index as urea reduction ratio (URR) that is also considered which the acceptable level for it is more than 65%.[6,2] If removing the urea is insufficient, it will be inadequate dialysis, regardless of plasma urea. However, only low levels of plasma urea is not necessarily indicative of adequate dialysis and its plasma level is not only dependent on removing the urea but it is also dependent on production rate of it and the amount of urea production depends on protein intake and Pre-dialysis plasma urea low level is may be because of low intake of protein. So what's important in assessing the adequacy is the removing amount of urea in a 4 hours session of dialysis and the plasma urea level is not the only thing that matters[5] .

As noted above, one of the factors in hemodialysis patients is circulating blood volume and blood pressure, considering that the urea is distributed in all body fluids easily and also according to the law of osmosis if two solutions with different concentrations are separated by a semi-permeable membrane, more dilute solution of molecules through a semi-permeable membrane pores are moving toward a more concentrated solution. Therefore, a change in osmolality caused by hypertonic glucose infusion, has a direct effect on the volume and free up the flow of interstitial fluid into the vascular fluid and will lead to increased blood pressure. Therefore, hypertonic glucose can be effective on dialysis adequacy [7].

Injection of hypertonic glucose is one of the common treatments in hemodialysis units in order to treat common complications during dialysis. These complications include; low blood pressure, muscle tension, nausea and vomiting and ataxia syndrome. Most of these complications are due to changes in osmolality or extracellular fluid volume [8,9]and hypertonic glucose can correct these conditions

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and mitigate these side effects and on the other hand increased blood pressure and glucose can lead to increased endurance in dialysis patients to continue to the end of 4 hours of process.
On the other hand sugar is the fuel of cells and in case of remaining in the circulatory system it will be used for energy generation and like hypertonic saline and normal saline there are no side effects in dialysis patients who have problems with disposal of waste and minerals. unlike normal saline (0.9%) and sodium chloride (5%) which are used to correct the low blood pressure (which is a very common complication of dialysis) afterwards no trace of it remains [7]. Due to the importance of dialysis adequacy and lack of researching in this field, this study aims to determine the effect of hypertonic glucose injection on non-diabetic patients undergoing hemodialysis and their dialysis adequacy.

2. Methods

A total of 50 patients were evaluated in this study with the method of crossover in two hospitals, selected hospital number 1 (21 people) and selected hospital number two (24 people), 5 patients (four of them due to lack of interest and one due to the risk of acute complications during dialysis and the need to administer hypertonic sodium chloride) were excluded from the study and the final analysis was performed on 45 patients.
This research is an interventional study. At first we went to the HD section of the selected hospitals for sampling and samples were selected purposively and it was based on input and output parameters. Then subjects were randomly divided into two groups.
Inclusion criteria: Patients were older than 18
They had at least six months of permanent hemodialysis. No other chronic diseases that lead to disability and a direct effect on dialysis adequacy (Such as diabetes, severe heart disease, respiratory, motor–mental neurological disorders, malignant disease, liver failure).
Exclusion criteria: The incidence of acute complications and problems during the study period (Such as cardiopulmonary resuscitation or hospitalization). Patients who require hypertonic Nacl infusion due to complications of dialysis. Lack of interest or ability to participate in any of the samples during the study.
The first group was manipulated with intervention in the form of injection of hypertonic glucose for two weeks .According to the lack of accebility to the same study, after formation of specialized working group that was formed from five people of nephrologist faculty members of the study society in 2011 we get to this result that study time for every group is two weeks. Intervention has been started at each session of dialysis during the 3rd hour of the process with the amount of 50ml of hypertonic glucose 50 %. Because most of the problems and complications happen in the last hour of dialysis when the patient has lost a high volume. The urea before and after dialysis were examined. Then we started wash out period for two weeks and then two weeks without the intervention it was evaluated. The process was different for the second group, there was no intervention for two weeks but they were evaluated during this time and after that intervention took place. After testing at every stage, the urea was measured to determine the dialysis adequacy before and after dialysis then data were collected.
To determine the adequacy of dialysis, the information form related to dialysis adequacy including specifications relating to the patient's weight, ultrafiltration of device, Dialysis duration, filter clearance rate, dialysis liquid flow speed was completed by project executer. Pre-dialysis urea level and weight were also measured.
After the end of dialysis and before separating the patient from device, there is a resampling of the arterial blood before dialysis. Two minutes before sampling the machine was adjusted to 50 ml per minute pump. At the end of dialysis patient's weigh was also measured and finally,

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Table 1: Demographic information

index		number	Percentage
gender	female	18	40
	male	27	60
age	18-30	2	4.4
	30-40	3	6.7
	40-50	8	17.8
	50 and more	32	71.1
Hospital	Selected No1.	21	46.7
	Selected No2.	24	53.3
Blood type	A	20	44.4
	B	10	22.2
	O	13	29
	AB	2	4.4
Vascular access	fistula	39	62.2
	cortex	6	13.3
Pump rpm	200-250	28	62.2
	250-300	17	47.8
Duration of dialysis	Less than 5yrs	36	80%
	More than 5yrs	9	20%
Systolic blood pressure	70-90	5	11.1
	100-120	28	62.2
	120 and more	12	26.7
Diastolic blood pressure	40-60	21	46.7
	60-80	14	31.1
	80 and more	10	22.2

the samples were sent to laboratory to be tested with one kit. (It should be noted that because of long distant between hospitals in both of the hospitals, necessary coordination had been done with the elated technicians)

Ultrafiltration rate is obtained by subtracting the weight before and after hemodialysis. after receiving the sample results, blood urea nitrogen was calculated by Daugirdas 2 formula that is one of the global acceptable formulas to determine the adequacy of hemodialysis and then the data were analyzed by using SPSS17 software and descriptive statistical tests (abundance- mean), inferential tests (paired t test, mane Whitney, Friedman, Kruskal-Wallis and wilcoxon)

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Table 2: Absolute and relative frequency distribution of the population in terms of adequacy of dialysis (Basic)

Dialysis adequacy / Hospital	At least	At most	Mean and standard deviation
Selected No.1	0.92	1.88	1.46 (0.4)
Selected No.2	0.79	1.50	1.11 (0.17)

Table 3: Index of the KT/V in interventional procedures

stages	KT/V amount (Standard deviation ±) mean	Friedman statistical test
basic	1.28 (0.3)	45= number
intervention	1.40 (0.3)	71.897 = K2
2 weeks after intervention	1.277 (0.3)	5 = f
4 weeks after intervention	1.28 (0.3)	= Level of significance (p=0.0001)

Table 4: Comparison of KT / V level in steps of intervention with each other

Statistic → / ↓stages	Wilcoxon statistical test Level of significance	Z amount
Basics with intervention	P=0.000	5.681
Basics with 2 weeks after intervention	P=0.850	-0.180
Basics with 4 weeks after intervention	P=0.655	-٠0.446
Intervention with 2 weeks after intervention	P=0.000	-5.826
Intervention with 4 weeks after intervention	P=0.000	-5.782
2 weeks after with 4 weeks after	P=0.647	٠0.458

3. Results

In this study, 27 patients (60%) were male and there is a significant relation between gender and dialysis adequacy in the stages of this research by Kruskal-Wallis test (p-0.046) and also KT/V index in different stages of the study had significant difference in gender by freedman test (Table 1)(p=0.001).

The mean age of the first group of subjects was (15.77) 57.81 with the lowest of 25 and highest of 83 and the values for the second group was respectively (15.10) 60.75–30 and 88. Using the Kruskal-Wallis test showed no significant difference between age groups (p=0.292) and also this study shows that the KT/V index has significant difference in the different age

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groups at the different stages of research by Friedman test(p=0.001) .

In this study the initial dialysis adequacy for patients was measured one month before the intervention and also for evaluating the initial dialysis adequacy with intervention stages and washout stages and to determine whether the effects of hypertonic glucose were remained on patients or not, one month after the intervention, dialysis adequacy were measured and indicators in KT/V and URR were compared which indices of dialysis adequacy show significant differences in intervention (Table 2)(p=0.001).

4. Discussion

In the present study, the average level of dialysis adequacy of patients at normal conditions in intervention and control groups showed lower dialysis adequacy. In this study, the mean KT/V in selected hospital No.1 (0.43) was 1.46 and in selected hospital No.2 (o.17) was 1.11 and the average level of URR was 65.13%. The results showed that only half of patients (50%) had the optimal level of KT/V which is more the ½ and only 46% of patients had URR level more than 65%. In this study subjects were equal in terms of demographic and disease features because of their study type. The results showed only between gender and vascular access and systolic blood pressure was a significant correlation and in other cases, the difference was not statistically significant, which in terms of gender had a similar result with the study of Ebrahimi et.al and Borzu et.al and the study of Hojat[15.14.2] and also in survey for difference vascular access difference based on dialysis adequacy, significant difference was observed which represents a more efficient use of fistula in dialysis patients for higher adequacy in dialysis and to avoid recirculation of blood phenomenon. Various studies show the inadequacy of the various centers in Iran. For example, Borzu et.al in their study in Hamedan had reported the average KT/V more than 1.2(16.66%)[15] or in the study of Delavari et.al they had a similar result on dialysis adequacy, which was 78.9%of patients who had dialysis adequacy of less than 1.2 [16]. In the study of Hojat in 2010 in Jahrom this level in 64.17% of the samples had acceptable adequacy that showed dialysis quality in this study in compare with the same studies has more appropriate level that probably because of the centers are training centers and the studies are various that cause constant training and awareness raising of the personnel and patients. This study shows the effects of hypertonic glucose on dialysis adequacy during the intervention period and indicates a significant difference by Friedman test.(p=0.000) and also comparison of the rate changes of KT/V in stages of intervention shows that infusion level of hypertonic glucose causes a significant change (P=0.001), that null hypothesis is confirmed. Due to the importance of increasing dialysis adequacy in patients, according to USRDS (United State Renal Data System)it can be noted that by increasing every 0.1 in KT/V up to 1/2, mortality risk decreases by 7 percent.[15,12]

NCD (National Cooperative Dialysis Study) also proved if the dialysis adequacy is better, uremic complications on different body systems and mortality of patients will reduce.[12.8]

In this study The mean dialysis adequacy in the intervention group had significantly increased after injection of hypertonic glucose, because hypertonic glucose with reducing complications and increasing glucose and blood pressure in dialysis patients causes increase of patient's endurance in continuing dialysis process for 4 hours and because of that urea solution is available in the interstitial fluid of patients which can help to remove more urea and in the result it causes to increase dialysis adequacy in HD patients. Robert the Nth et.al studied the effects of infusion of glucose on blood volume during hemodialysis; hypertonic glucose infusion caused a significantly greater increase in blood volume in hemodialysis patients, which is in similarity with our study [17].

Borzou et.al studied the effect of an increase in blood flow rate on dialysis adequacy in HD

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patients; results showed 25% increase in the rate of dialysis adequacy in HD patients due to increased blood flow that is in consistent with the hypothesis of the study. [15]

Neil Cheryl et.al had a study with the aim of treatment of muscle cramps during dialysis with using hypertonic glucose, which showed that hypertonic glucose is effective as muscle cramps treatment during dialysis and by removing these complications we can improve the quality of dialysis and increase the tolerance of patients for 4 hours of dialysis, which is consistent to this study [18].

According to sex ratio of patients significant point is that men subjects were more than women, in other studies this point was also notable. Including study of Ebrahimi et.al in which the ratio was 55/6% to 44/4% [5]. And for Borzu and Associates study in 1385, this ratio has been 66% to 34%[10] and Hojat study stated the ratio 64/7% to 35/3%[2] and in study of Norouzi et.al in Ahvaz,the stated ratio was 61% to 38%[11]. In this regard, further study is needed to investigate the cause of renal failure in men. The average age for the study of Hojat et.al was 58/18 and for Babahaji et.al it was 54/74 and for study of Raisifar et.al it was 52.9 and Borzu et.al reported 55, that are similar to this study [14-12,10,8].

5. Conclusion

The results showed that one of the contributing factors to improve dialysis adequacy in HD patients is infusion of hypertonic glucose. Hypertonic glucose reduces complications and increases glucose and blood pressure in dialysis patients in order to continue dialysis process for 4 hours and because hypotension is a common complication of dialysis and in 25 to 55 percent of cases it occurs in patients, so it is important. There are many reasons for hypotension such as increased uptake of liquid, ultrafiltration during dialysis, reduced Plasma osmolality due to the rapid reduction of blood urea and water displacement into the cells and decreased effective circulating volume and etc. which by using hypertonic glucose these problems will be corrected and also because urea solution is available in the interstitial fluid of patients which could help to remove more urea and to increase dialysis adequacy in HD patients.

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