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Original Article

Hemodialysis associated dysautonomia; Effect of optimization of dialysis and nutrition: A prospective study

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Abstract

Background: Autonomic neuropathy is common among hemodialysis patients, even if they are asymptomatic. The aim of this study is to assess the effect of optimization of patients` dialysis and nutrition on the presence of autonomic dysfunction in these patients guided by sympathetic skin response (SSR) test.

Methods: Fifteen patients on maintenance hemodialysis (12 males and 3 females) their age ranged from 24 to 67 years, most of them were on bicarbonate dialysis were included in our study. Initially, the patients were assessed clinically and by laboratory investigations and their dialysis was assessed by studying their urea kinetic modeling. Their nutrition was assessed by laboratory parameters and by calculating the normalized protein catabolic rate (nPCR). Their autonomic functions were assessed by clinical examination, hand grip and SSR test. Dialysis dose was readjusted to achieve a target kt/v value of 1.3/session thrice weekly. Also, their nutrition was reviewed to achieve nPCR of 1.2 gm/kg/day and caloric intake of 30-40 KCal/kg/day through diet manipulation and support. They were reassessed after 3 months.

Results: Analysis of the data showed a statistically significant improvement of the observed subclinical autonomic neuropathy evidenced by a significant change in the hand grip ($p = 0.044$), and a high statistically significant improvement in the sympathetic skin response test parameters (both amplitude and latency) ($p=0.001$) after optimization of both hemodialysis and nutrition status.

Conclusion: Improving dialysis and patients nutrition by using urea kinetic modeling is valuable in improving their autonomic functions as assessed by SSR test.

Key words: Autonomic neuropathy; hemodialysis; SSR

Introduction

Inadequate hemodialysis and nutrition have been reported to be major causes of patient morbidity and mortality [1]. Inadequate hemodialysis may be overlooked and may remain unrecognized when therapeutic decisions are exclusively based on clinical parameters [2]. Study of urea kinetic modeling has emerged as a tool to assess the quality of dialysis delivered [3] and by changing different dialysis session variables, dialysis could be optimized.

Correlation between kt/v values and patient morbidity and mortality has been reported [4]. A urea reduction ratio of 55-50% (corresponding to a kt/v of 1.0) was associated with a 1.28 higher mortality rate compared to those receiving higher reduction ratio [5]. Furthermore, the importance of an adequate caloric and protein nutrition has been emphasized by several groups [6-9].

Autonomic dysfunction occurs in 50% of patients on maintenance hemodialysis and may be reflected clinically with hypotension during the dialysis session [10].

In this work, we tried to find out if optimization of dialysis and patients nutrition can induce an improvement of autonomic neuropathy. For better assessment of autonomic neuropathy, we opted to use the sympathetic skin response test which carries the advantages of being sensitive, specific and objective [11-12].

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Material and methods

In this work fifteen patients with end stage renal failure under maintenance hemodialysis were included. They were 12 males and 3 females with an age range 24-67 years. All patients were non diabetic, clinically stable with suitable vascular access.

At the beginning of the study, patients were assessed clinically and biochemically. The amount of dialysis delivered and nutrition provided were evaluated mathematically through urea kinetic modeling [13]. Dialysis prescription was adjusted thereafter where all patients were scheduled to three sessions weekly and the duration of each session differed according to the patients weight, to achieve a target kt/v of 1.3/session. Furthermore, patients nutrition was manipulated so as to achieve a normalized protein catabolic rate (nPCR) of 1.2 gm/kg/day. This was achieved through encouragement of the patients to improve their diet by taking a diet containing protein of 1.2 gm/kg/day, and calories of 35 Kcal/kg/day.

This dialysis and nutrition standard was kept stable for 3 months at the end of which patients were re-evaluated.

Clinical evaluation: was performed and included general, local, and neurological examination as well as hand grip test at the start and 3 months after the optimization of dialysis and nutrition.

Neurophysiologic study: was performed and included the SSR test, by using HITACHI CM 1587M. All patients were studied while supine in a semi darkened room, so as to avoid external stimuli which could interfere with the results. Recordings were made from both the palm and the dorsum of the hand. The area just above the wrist was cleaned with alcohol twice, then the cutaneous electrodes were applied, then electrical stimuli of 20-40 mv was applied to the median nerve at the wrist. Each stimulus was delivered at irregular intervals (> 50-60 S) to avoid habituation. SSR amplitude and latency were recorded before achieving targeted kt/v and nPCR, and compared with amplitude and latency obtained 3 months of dialysis and nutrition optimization.

Statistical analysis of the data

All data were expressed as frequencies or mean and standard deviation. Comparison of quantitative data were done using T-test. Chi-square test was used for comparison of qualitative data. P value less than 0.05 was considered as statistically significant.

Results

The clinical and laboratory characteristics of our patients at the start of this study are summarized in table (1). Their dialysis was insufficient as the mean Kt/v was less than 1. One third of them was indulged in a twice hemodialysis schedule. Moreover, a low serum albumin (mean = 3.04 g/dl) and inadequate protein intake (mean nPCR = 0.94 g/kg/day) confirmed their poor nutritional status (table1).

Table 1. Demographic characteristics of the patients at the start of the study[1]

1- Age (Year)	40 ± 10
2- Sex: Male: Female	12 : 3
3- Marital condition: Married: Single	12 : 3
4- Dauration of dialysis (in months)	50 ± 25
5- Lean body weight (in kilogram)	65.4 ± 16.4
6- Hypertension (Hypertensive : Normotensive)	9 : 6
7- Predialysis creatinine(mg/dl)	13.3 ± 2.5
8- Predialysis BUN (mg/dl)	85.2 ± 5.4
9- Hemoglobin (g/dl)	9.23 ± 0.52
10- Kt/v	0.980 ± 0.237
11- nPCR (g/kg/day)	0.943 ± 0.181
12- Predialysis serum bicarbonate (mmol/L)	18 ± 0.50
13- Total protein (g/dl)	6.5 ± 0.14
14- Albumin (g/dl)	3.040 ± 0.168
15- Twice dialysis session: Thrice session/ week	5 : 10

[1]Categorical variables are presented as sum number of patients and continuous variables as mean ± SD.

Manipulation of dialysis and nutritional status resulted in a significant improvement of urea kinetic modeling parameters as reflected by a significant rise of Kt/v and a significant increase of serum albumin and nPCR to the target value that was reassessed at the end of the third month of the study (table 2).

Our patients were anemic, their mean hemoglobin at the end of the study was (9.3 ± 1.8 g/dl) was nearly identical to its value at the start of the study (9.2 ± 2 g/dl) (p = 0.380). The patients did not receive erythropoietin therapy due to its unavailability.

Clinical examination to test the presence of autonomic neuropathy by the use of hand grip testing revealed a significant improvement of autonomic neuropathy, where the percentage of patients who had positive test was 80 % (12 patients) before the study that decreased to 60 % (9 patients) at the end of the study (p = 0.044).

Table 2. Assessment of the dialysis efficiency and nutritional status, before and after 3 months of dialysis optimization[1]

	Before the study	*After 3 months*	*P*
Kt/v	0.89 ± 0.23	1.27 ± 0.09	0.001
Pre-dialysis serum bicarbonate (mmol/ L)	18.1 ± 2.2	20.5 ± 2.1	0.004
nPCR (g/kg/day)	0.94 ± 0.18	1.12 ± 0.11	0.003
Total proteins (g/dl)	6.58 ± 0.55	7 ± 0.44	0.036
Serum albumin (g/dl)	3.04 ± 0.17	4 ± 0.41	0.002

[1]The values are presented as mean ± SD

The use of SSR test parameters showed a highly statistical significant improvement in both the amplitude and latency (table 3).

Table 3. Skin sympathetic response test, before and after 3 months of dialysis optimization[1]

	Before the study	*After 3 months*	*P*
Amplitude (mv)	0.295 ± 0.029	0.50 ± 0.12	0.001
Latency (seconds)	1.24 ± 0.22	1.47 ± 0.11	0.001

[1]The values are presented as mean ± SD

Discussion

During the last decade, study of urea kinetic modeling has attracted increasing interest as a way to evaluate and improve the amount of dialysis delivered to uremic patients. Many reports showed improvement of patient nutrition and survival as a result of achieving the target kt/v [1,4,14].

Autonomic dysfunction occurs in 50% of patients on maintenance hemodialysis and may be reflected clinically with hypotension during the dialysis session [10]. It was reported that a higher proportion of patients on hemodialysis showed an impaired SSR, suggesting that subclinical neuropathy may be more common in hemodialysis than in peritoneal dialysis patients [15].

Uremic neuropathy is primarily an axonal degeneration and while some demyelination is observed, it is relatively a minor feature. All fiber sizes both myelinated and unmyelinated, are affected, although the largest fibers are selectively vulnerable, and the distribution is distal [16].

Sympathetic skin activity mediates sudomotor function and the SSR has been used to evaluate autonomic function in patients with suspected dysautonomia. It specifically tests skin sympathetic fibers and not the parasympathetic or the motor sympathetic fibers that mediate many of the clinical symptoms of dysautonomia. Hence SSR is a useful method to evaluate a part of the peripheral nervous system – small unmyelinated C fibers that can not be assessed by current clinical electromyographic laboratory techniques [17].

Clinical diagnostic tests of autonomic neuropathy, valsalva maneuver, blood pressure and heart rate changes are difficult to be performed, necessitating a high degree of patients cooperation. Moreover these clinical tests depend on a well trained non biased operator. Review of literature shows a great variability in definition of normal valsalva and postural (30:15 R-R interval) ratios [18].

So, we opted to use the easiest clinical test which is the hand grip test, and to depend completely on the objective sympathetic skin response test in evaluating our patients. SSR is a simple, non invasive reliable indicator of sympathetic sudomotor outflow in central and peripheral nervous system disorders and has been shown to be useful in assessing autonomic dysfunction [11,12].

Delivering adequate dialysis and provision of sufficient proteins and calories intake guided by urea kinetic studies was reported to improve the neurophysiological parameters especially the electromyography, and fatigue test but not nerve conduction velocity [9]. Although, the use of SSR in renal failure patients was limited to a few studies [17-22], non of these studies correlated the change of SSR with the manipulation of both dialysis and nutrition. Our study is unique in this aspect, testing the effect of optimization of both dialysis and nutrition upon SSR parameters in a prospective fashion.

We found a beneficial effect of dialysis and nutrition optimization on autonomic neuropathy as evidenced by an improvement in hand grip and SRR testing. One study [17], reported a positive correlation between abnormalities of nerve conduction studies and SSR but

it did not find a correlation between duration of dialysis, kt/v and SSR parameters. However, the design of this study did not include any manipulation of dialysis variables so its result regarding the absence of correlation between kt/v and SRR should be taken with some caution. Moreover, a statistically significant correlation was found between the mean amplitude of the foot SSR and sensorimotor nerve conduction velocities and weekly frequency of hemodialysis in one study [22]. We thought that the correlation of SSR test with urea kinetic modeling and dialysis optimization was a virgin area that was not thoroughly studied in the literature.

From this study we may conclude that:

1. In uremic patients under maintenance hemodialysis, even when asymptomatic and clinically stable, autonomic neuropathy does exist.
2. Use of urea kinetic modeling for optimization of dialysis and achievement of the target kt/v together with improvement of the patients nutrition are associated with significant improvement in autonomic neuropathy as assessed by a significant improvement in SSR. However, a larger number of patients and a longer-term follow up are warranted.

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