Turkish Journal of Medical Sciences

Volume 28 | Number 5 Article 14

1-1-1998

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Tr. J. of Medical Sciences
28 (1998) 537-540

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The Role of Ultrafiltration Therapy on Blood Pressure of Hypertensive Chronic Hemodialysis Children

Received: March 20, 1997

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Abstract: Hypervolemia is supposed to be the principal factor in hypertension in chronic hemodialysis adults. In this study, the role of intensive ultrafiltration (UF) treatment to reduce hypertension due to hypervolemia in hemodialysis children was investigated. The inferior vena cava (IVC) was also evaluated as an index of UF therapy. Twenty-three hemodialysis children with the mean age 10.6±3.1 years were classified due to their blood pressure status. IVC measurements were performed with 2-D echocardiography and inferior vena cava index (IVCI) was calculated as diameter of inferior vena cava (mm)/ body surface area (m^2). UF therapy was applied to each hypervolemic patient for four successive days and all of the patients were followed up for 4 weeks. Plasma levels of atrial natriuretic peptide (RIA), noradrenalin (high performance liquid chromotography) and plasma renin activity (RIA) of three patients having persistent hypertension were investigated. IVCI and plasma atrial natriuretic peptide levels of 12 healthy children were studied as a control group.

At the begining of the study, 11 patients had hypertension and 14 patients had high IVCI. 14 hypervolemic children had UF therapy. Eleven patients responded to UF therapy and had normal blood pressures. After 4 weeks of follow up period 12, patients were again found to have hypertension. Following UF, hypertension was persisted in 3 of them. Since IVCI and ANP levels of these three patients were high, hypervolemia or some other factors was thought to be responsible for hypertension. Volume overload was found to be the most important factor in the pathogenesis of HT in hemodialysis children. UF was effective in reducing hypertension. IVCI might be a reliable parameter to control ultrafiltration therapy in the management of hypervolemic hemodialysis children.

Key Words: Children; hemodialysis; hypertension; hypervolemia; ultrafiltration.

Introduction

Hypertension (HT) is very commonly associated with chronic renal failure and blood pressure has a tendency to increase as renal function is lost (1, 2, 3). HT in chronic renal failure is supposed due to several factors as activated circulating and local renin angiotensin system, increased sympathetic activity, decreased sensitivity of the baroreceptors and increased the loss of vasodepressors produced by the kidneys such as PGE_{II}, bradykinin and to the abnormalities of renal medullolipin, L-arginine-derived agmatin, endothelin and nitric oxide (1, 3). However, the most important factor in HT in chronic renal failure is accepted as the volume overload (1, 3, 4, 5).

The fluid volume is assumed to be the principal factor in determining hypertension in most adult patients with chronic renal failure. Blood pressure can be corrected by removal of excess fluid and sodium through ultrafiltration (UF), especially in uremic adults (4, 5). To our knowledge the literature contains no controlled study pointing the ratio of the volume factor in HT in dialysed children.

The aim of this study was to investigate the role of intensive UF treatment to reduce hypertension due to hypervolemia in children on chronic hemodialysis (HD) and to evaluate inferior vena cava (IVC) as an index of UF treatment.

Materials and Methods

Twenty-three patients, 10 girls and 13 boys, on chronic hemodialysis program were admitted to the study. Their ages ranged from 5 to 15 years with the mean age 10.6±3.1 years. Eighteen of the patients had HD 3 times a week and the remaining 5, twice a week

Table 1. Evaluation of the patients throughout the 4 weeks follow-up period.

	Initial findings (pre-UF)		Findings after 4 weeks follow up period (post-UF)			
BLOOD PRESSURE	≤90p n:12	>90p n:11	≤90p n:11		>90p n:12	
			Initial normotensive n:3	Initial hypertensive n:8	Initial normotensive n:9	Initial hypertensive n:3
SYSTOLIC	105.5±13.8	145.±20.7	93±58	114±11	152±16	163±25
DIASTOLIC mmHg	67.9±14.8	94.1±15.3	63±15 (n:3)	75±8 (n:8)	98±19 (n:9)	93±12 (n:3)
CLINICALLY OVERLOAD	0	11	0	0	9	3
IVCI mm/m2	8.2±1.2	10.4±1.0	8.9±2.0		9.9±2.8	
	9.5±0.7 n:3		7.5±1.0	8.6±0.4	9.7±2.0	12.9±4.0
	7.7±1.2 n:9		n:3	n:8	n:9	n:3
UF THERAPY (n)	3	11	0	0	9	3
Response to UF (n)	3	8	0	0	9	0

Table 2. The parameters investigated in three patients having persistent hypertension.

	Patients (n:3) with persisiting hypertension after therapy	Normal values
IVCI mm/m2	12.9±4.0	7.0±0.9 (12 healthy controls)
ANP pg/ml	143±25	102±39 (12 healthy controls)
PRA ng/ml/hr	0.8	0.8±0.4 (Normal range)
Noradrenalin (pg/ml)	128.1	104-548 (Normal range)
Adrenalin (pg/ml)	86.6	88 (Normal range)

with cuprophane dialysers. The dialysate was biarbonate buffered and contained 133 mmol/l of sodium.

Clinical signs (dispne-ortopne, juguler venous pulsation, hepatomegaly and gallop rhytym) and IVC indices (IVCI) were investigated for detecting overhydration in each patient. Hypertension was accepted as the sistolic and diastolic blood pressure values over 90 percentile according to height and weight (6). Patients were callisified into two groups due to their blood pressure status as ≤90 percentile and >90 percentile. IVC measurements were performed with 2-D color flow doppler echocardiography (HP sonos 1000) by the same cardiologist and IVCI was calculated as diameter of IVC(mm) / body surface area (m^2). IVC indices, found higher than the values of the healthy control group, in this study were accepted as overhydrated. We used 95% confidence limits (mean±2 standard deviation) of the control group to define overhydration in each patient with or without hypertension. During the dialysis, UF therapy was applied to each hypervolemic patient for four successive days. For each patient the amount of ultrafiltrated fluid was kept as 15% of the body weight. All of the patients were followed up for 4 weeks. During this period all of the patients were urged to restrict water and salt intake. Plasma levels of atrial natriuretic peptide (ANP), noradrenalin, adrenalin and plasma renin activity (PRA) of the three patients having persistent HT were also investigated. Radio immun assay (RIA) (Amersham-ANP Biodata renin MAIA KIT) was used to determine plasma concentration of ANP and PRA. Noradrenalin and adrenalin were investigated by high performance liquid chromotgraphy with electrochemical detector. IVCI and plasma ANP levels of 12 age equivalent healthy children were studied as a control group.

Results

At the beginning of HD program, 11 of the 23 patients were found hypertensive. All of these hypertensive children were also clinically fluid overloaded. None of the other 12 normotensive patients showed any signs of fluid overload. IVCI values were high in all 11 patients of hypertensive group. However 3 of 12 normotensive children presented a high IVCI without any clinical signs of fluid overload. Thus, 14 of 23 patients were accepted as fluid overloaded due to IVCI and were commenced on UF treatment besides regular hemodialysis. The mean ± SD values of IVCI were found as 7.0±0.9 mm/m^2 in healthy control group.

At the end of the 4 weeks follow-up period, it was

observed that 11 patients had blood pressures below 90 percentilve while 12 patients had blood pressures above 90 percentile. When the patients were evaluated due to their initial blood pressure values, it was found that nine out of the 12 initially normotensive patients showed HT during the follow-up period and the remaining 3 were still normotensive. Although eight of the intially hypertensive 11 patients, showed normal blood pressures after the UF therapy, HT persisted in 3 of them. All of the hypertensive patients in both groups were clinically overloaded and showed high IVCI compared to the other patients with normal blood pressure. Nine patients who developed HT during the follow up period were treated with UF and showed normal blood pressure measurements after UF treatment. Only 3 patients from the initially hypertensive group persisted to show high blood pressure despite the UF treatment. The evaluation of hemodialysis children at the beginning of the study and at the end of follow-up period was given at table I. ANP, PRA, adrenalin and noradrenalin values of the three persisited hypertensive children were found in normal ranges (Table 2).

Discussion

Hypervolemia and renin angiotensin system have been accepted to be the most important two factors in the pathophysiology of hypertension in chronic renal disease. It was reported that at a glomerular filtration of 10 to 20% of normal, 95% of patients were hypertensive (3). In this study, before and after the four weeks follow-up period, 20 hypertensive patients (86.9 %) were totally detected. As the renal function is impaired and hemodialysis is necessary, the volume factor becomes more important (1, 4, 5). Excess salt and water can only be disposed by ultrafiltration (1). It was shown that 80-85% of hypertensions in adult hemodialysis patients could be controlled by UF therapy (1).

Initially 11 patients were found to have high blood pressures while 9 patients had hypertension after the following period. Although UF therapy was performed to all of the patients having high blood pressures (n:20), 17 of them responded to the therapy. It was suggested that HT of these patients who had normal blood pressures following UF therapy was related to hypervolemia (Table 1). As a result 85% (n:17) of our pediatric hemodialysis patients had hypertension due to volume factor as mentioned in adults in the literature (1).

Echocardiography of IVC appairs to be available tool in the assessment of postdialytic dry weight in adults (4, 7, 8, 9) and in children (10). In this study IVC index was found to be correlated with HT, too. Initial hypertensive group (n=11) were found to have high mean IVC indices (10.1±1 mm/m^2) at the beginning. Following the UF therapy, 8 of these patients were found to have normal blood pressures with lower IVC indices (8.6±0.4 mm/m^2) and 3 with persistent hypertension had higher IVC indices (12.9±4.0 mm/m^2). However, 3 patients having initial normal blood pressures also showed high mean IVC indices (9.5±0.7 mm/m^2). The same 3 patients had normal blood pressures and IVC indices (7.5±10 mm/m^2) after the following period. Since 21.4% of our overload patients with high IVC indices did not show high blood pressures, it was thought that IVCI was more valuable tool in estimating the fluid status in hemodialysis children than the clinical criteria including HT.

Inappropriate PRA, which may be caused by the ectopic synthesis of renin, renal ischemia and activation of the intrarenal baroreceptors, was found to be responsible from HT in end stage renal failure (1, 2). During 4 weeks of follow up, 3 patients (15%) had persistent HT. In these patients who did not response to UF, PRA as a cause of hypertension was investigated and was found normal. None of the patients were supposed to have HT due to excessive renin activity.

Role of sympathetic overactivity in end stage renal failure was mentioned by some authors in the past and with more solid evidence recently (1, 2). However, persistent hypertensive patients did not show elevated adrenalin and noradrenaline levels in this study.

Many studies have showed a correlation between ANP and overhydration (5, 8, 10, 11). ANP concentrations of 3 patients having persistent HT were found higher (143±25 p/ml) than normal (102±39). In addition these 3 patients had also high IVC indices as 12.9±4.0 mm/m^2 at the end of UF therapy. All of these findings showed that the remaining three patients might also have volume overload despite the standard UF therapy. The standard UF therapy might be inadequate to dispose excess salt and water in these 3 patients. Other factors such as abnormalities of renal medullopilin, L-arginine-derived agmatin, endothelin or nitric oxide might also be responsible for the hypertension.

In conclusion, hypervolemia was found to be the most important factor in the pathogenesis of HT in hemodialysis children. UF was observed to be effective in reducing HT, and IVCI looks like a reliable parameter to estimate hypervolemia and the response to ultrafiltration therapy.

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