



Use of fludrocortisone for intradialytic hypotension

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Intradialytic hypotension during dialysis adversely affects a patient's prognosis and increases mortality. We report a case in which intradialytic hypotension that persisted after the administration of midodrine was relieved after the use of fludrocortisone. Administration of 0.2 mg of fludrocortisone occurred 30 minutes before dialysis. We compared 45 sessions of dialysis without fludrocortisone administration and 45 sessions of dialysis with fludrocortisone administration in one patient. The number of times in which systolic blood pressure became lower than 80 mmHg and the number of early terminations of dialysis due to a decrease in systolic blood pressure were higher in the sessions without fludrocortisone administration than in the sessions with fludrocortisone administration ($P < 0.05$). Fludrocortisone may be helpful for the treatment of intradialytic hypotension that does not respond to midodrine administration.

Keywords: Fludrocortisone, Hypotension, Midodrine, Renal dialysis

Introduction

Hypotension during dialysis has a detrimental effect on the prognosis of the patient and increases the mortality rate [1,2]. It is therefore important to prevent and treat hypotension during dialysis. Dialysis-related components, such as high-calcium dialysis solutions, low-temperature dialysis solutions, and ultrafiltration (UF) modeling, are used for the prevention and treatment of intradialytic hypotension (IDH) [3]. However, few medications other than midodrine can be clinically applied in the treatment of IDH.

There have been many reports of relief of orthostatic hypotension using fludrocortisone (Florinef; Samil Phar-

maceutical, Seoul, Korea). Fludrocortisone may be helpful in the treatment of IDH, but there is insufficient data to substantiate its effect [4]. In 2005, there were two case reports in which fludrocortisone administration led to decreases in body-weight gain and blood pressure (BP) during dialysis [5]. We report a case in which midodrine-resistant IDH was relieved by administering fludrocortisone.

Case report

A 66-year-old woman with diabetic nephropathy began dialysis in 2004 and received regular hemodialysis (HD) three times a week. The patient was anuric for years, and her BP intermittently decreased during HD beginning in June 2013, therefore 10 mg of midodrine was administered. The patient's IDH became more frequent and stopped responding to midodrine administration beginning in October 2015. There was no specific cause of the IDH, such as heart failure, myocardial infarction, or a brain injury, identifiable in either echocardiography or brain magnetic resonance imaging. The serum thyroid hormone levels were within the normal range (thyroid-

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stimulating hormone, 1.9 mU/mL; free thyroxine, 1.3 ng/dL), and a dexamethasone suppression test to screen for Cushing's syndrome showed a normal response. The patient had been taking 20 mg of amitriptyline, which was not considered the cause of the IDH due to the clinical course. The patient was not taking any narcotics or antidepressant that might have affected the IDH.

The patient had a high systolic blood pressure (SBP, mean: 189 mmHg) before dialysis, but the average drop in BP during dialysis was 89 mmHg. Midodrine was not initially administered due to high BP and was only administered during HD when the SBP decreased to between 130 and 140 mmHg. However, BP continued to decrease after the administration of midodrine, and the average low for the SBP was 100 mmHg. UF modeling, low-temperature dialysis, and increasing the dry body weight from 62.4 kg to 63.5 kg were applied in the dialysis prescription, but IDH continued to occur.

The BP drop during HD in this patient was midodrine resistant. Comparing the data from the 20 dialysis sessions just before midodrine administration (May 2013 to June 2013) with the data from 45 dialysis sessions after midodrine administration (January 2017 to April 2017), there were no changes in the number of early terminations of dialysis (6/45 vs. 3/20, $P = 0.568$), the number of the lowest SBPs that were < 80 mmHg (6/45 vs. 5/20, $P = 0.209$), the and average value of the lowest SBP (100.8 ± 17.9 vs. 90.3 ± 19.6 mmHg, $P = 0.051$). Although the interdialytic weight gain (2.9 ± 4.7 vs. 2.7 ± 0.4 kg, $P = 0.044$) and average difference between the starting and lowest SBPs (89.0 ± 23.3 vs. 70.3 ± 17.6 mmHg, $P = 0.001$) were statistically different before and after midodrine treat-

ment, we think these differences were not due to midodrine but rather the four-year gap between the data sets.

Administration of 0.2 mg of fludrocortisone (3 times per week, 30 minutes before dialysis) began on April 12, 2017. Midodrine was administered continuously and in the same manner both before and after fludrocortisone administration. We studied the number of early terminations of dialysis, the number of times in which the lowest SBP was less than 80 mmHg, SBP before dialysis, the lowest SBP, the difference between the starting and lowest SBPs, and interdialytic weight gain throughout 90 consecutive dialysis sessions, 45 before and 45 after fludrocortisone administration, from January 2017 to August 2017.

Table 1 shows BP, body weight, and the levels of electrolytes and hemoglobin before and after fludrocortisone administration. The levels of electrolytes and hemoglobin were measured before each dialysis session. For the statistical analysis, Fisher's exact test was used for the number of early terminations of dialysis and the number of lowest SBPs < 80 mmHg, and the Mann-Whitney test was used for the levels of electrolytes and hemoglobin, interdialytic weight gain, and SBP. The mean SBP before dialysis and fludrocortisone administration was significantly higher (189 mmHg) than that after fludrocortisone administration (147 mmHg, $P < 0.05$). An additional 7.5 mg of amlodipine was administered on days without dialysis sessions.

The number of dialysis sessions during which the lowest SBP was less than 80 mmHg was higher before fludrocortisone administration than after fludrocortisone administration. The difference between the SBP before dialysis

Table 1. Changes in systolic blood pressure (SBP), body weight, and electrolytes before and after fludrocortisone administration

Variable	Before administration	After administration	P value
Dialysis sessions	45	45	—
Early terminations of dialysis	6	0	0.026
Lowest SBPs, < 80 mmHg	6	0	0.026
SBP before dialysis (mmHg)	189.8 (15.8)	147.8 (17.7)	< 0.001
Difference between initial and lowest SBPs (mmHg)	89.0 (23.3)	45.9 (20.5)	< 0.001
Lowest SBP (mmHg)	100.8 (17.9)	101.8 (12.3)	0.605
Interdialytic weight gain (kg)	2.9 (4.7)	2.0 (0.6)	0.034
Plasma sodium*	134.0 (3.2)	135.3 (2.2)	0.686
Plasma potassium*	6.3 (0.2)	5.4 (0.4)	0.029
Hemoglobin*	10.6 (1.0)	9.6 (0.5)	0.200

Data are presented as number only or mean (standard deviation).

*n = 4.

and the lowest SBP during dialysis was significantly lower after fludrocortisone administration. The patient experienced a temporary loss of consciousness (once) or sleepiness (3 times) when her BP dropped before fludrocortisone administration. The mean (standard deviation) interdialytic weight gain significantly decreased from 2.9 (4.7) kg before fludrocortisone administration to 2.0 (0.6) kg after fludrocortisone administration. The serum potassium level decreased from 6.3 (0.2) mmol/L to 5.4 (0.4) mmol/L ($P = 0.019$); however, there were no statistically significant changes in the serum sodium ($P = 0.686$) or hemoglobin ($P = 0.200$) levels (Table 1).

Discussion

The current case report is the second study in which fludrocortisone administration relieved IDH. When fludrocortisone is used to treat orthostatic hypotension, it enhances the sensitivity of blood vessels to circulating catechol amines [6], increases peripheral vascular resistance [7] and blood volume, and enhances norepinephrine release from sympathetic neurons [8]. Fludrocortisone may have a similar effect on IDH as on orthostatic hypotension. In this patient, autonomic dysfunction was a possibility considering the accompanying severe constipation and the long duration of diabetes. Because of fludrocortisone's effects on the sympathetic nervous system, it could be that the presence of autonomic dysfunction in this patient positively influenced the action of fludrocortisone.

For orthostatic hypotension, fludrocortisone administration is initiated with 0.1-mg tablets and can be increased to a dosage of 0.3 to 0.5 mg/day [8]. The only previous case report in which fludrocortisone was used for IDH treatment administered 0.05 mg/day [5]. In the current case, daily administration was initially planned but could not be implemented because patient adherence was low. Instead, 0.2 mg of fludrocortisone was given 3 times per week, 30 minutes before dialysis. Because peak plasma concentration is reached in 2 hours [9], administering the medication 30 minutes before dialysis seemed to be effective for the current patient, whose BP typically dropped in the second half of the dialysis session.

An adverse effect of fludrocortisone is edema due to increased fluid volume, supine hypertension, and hypokalemia [4,10,11]. After fludrocortisone administration,

the patient's BP was measured and recorded at home to manage supine hypertension. The average SBP before dialysis was lower after fludrocortisone treatment than that before fludrocortisone treatment in this study. We believe the reason for this was the addition of 7.5 mg of amlodipine after fludrocortisone administration on non-dialysis days to control hypertension. The SBP on non-dialysis days was lowered from 180–200 mmHg to 140–160 mmHg after adding amlodipine. Before fludrocortisone administration, we could not prescribe proper antihypertensive medications because the patient's BP dropped during dialysis.

The patient's average interdialytic weight gain was reduced from 2.9 to 2.0 kg after fludrocortisone administration. The decrease in interdialytic weight gain may have had an effect on IDH. A decrease in interdialytic weight gain can be induced by downregulation of the renin-angiotensin-aldosterone system at the end of the dialysis session because of better-maintained arterial pressure [5].

In previous studies on changes in potassium levels and BP when fludrocortisone was administered in patients undergoing dialysis, fludrocortisone (0.05–0.3 mg) decreased the potassium level but did not affect predialysis BP [11,12]. However, in another study, administration of 0.3 mg of fludrocortisone twice a day resulted in a decrease in the potassium level and an increase in supine BP [13]. Increased colonic excretion of potassium by stimulating Na^+/K^+ transport by ATPase (*ATP1*) [11,14], as well as intracellular shifting of potassium [11], may play an important role in the potassium-lowering effects of fludrocortisone for chronic kidney disease patients.

This paper is limited in scope because it is based on the observation of 1 patient. It may be helpful to administer mineralocorticoids in a greater number of patients who experience midodrine-resistant hypotension during dialysis. The second limitation was that we did not perform tests to confirm autonomic dysfunction. Based on the fact that the patient had a history of long duration diabetes and the presence of diabetic retinopathy and neuropathy, there is a high probability that she may have had autonomic dysfunction. The presence of diabetic autonomic dysfunction may be the reason the patient responded to fludrocortisone therapy so effectively.

This case report shows that fludrocortisone may be helpful for the treatment of IDH that does not respond to

midodrine administration without serious side effects.

Conflicts of interest

All authors have no conflicts of interest to declare.

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