Original Article

Comparison between long-acting and short-acting loop diuretics in patients with chronic kidney disease: evaluation of efficacy and safety

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Abstract

Patients with chronic kidney disease（CKD）were treated with a long-acting loop diuretic, Azosemide and a short-acting loop diuretic, Furosemide in a crossover fashion. The two drugs were compared after crossover switch using a multicenter study design focusing on evaluation of diuretic effects and symptoms associated with quality of life. There was no significant difference between Azosemide and Furosemide treatment after crossover switch in alleviation of edema, blood pressure, and body weight, or change in daily urinary volume or sodium excretion. On the other hand, change in urinary protein excretion from start to end of treatment was less in Azosemide treatment（−0.239g/day）than in Furosemide treatment（0.353g/day）after crossover switch（p=0.0556）. In a questionnaire survey of symptoms after treatment, the percentage of patients complaining of "hand cramp" was higher after Azosemide than after Furosemide treatment; however this difference was not statistically significant（p=0.0935）. When asked "Which drug do you wish to continue?", 30% selected Furosemide, 35% selected Azosemide and 35% gave a neutral answer. In conclusion, Azosemide was similar to Furosemide in efficacy and tolerability.

（Keywords: CKD, Chronic Renal Failure, Diuretics, Furosemide, Azosemide）

Introduction

In patients with advanced chronic kidney disease（CKD）, the volume of body fluid is excessive because of deficient renal function or disorders of the renal parenchyma, and clinical symptoms such as hypertension[1] and edema occur. The 7th report of the Joint National Committee（JNC VII）recommends the use of loop diuretics in combination with ACEIs or ARBs in advanced CKD[2]. Diuretics are thus used frequently to prevent excessive volume status, and the type of diuretics used in CKD is just about the loop diuretic. Furosemide is a short-acting loop diuretic that has been in frequent use for many years. In our experience, the quality of life of patients is reduced by the use of this drug because of its rapid diuretic action and short duration of efficacy. Among the loop diuretics that are available, Azosemide has a long duration of action produced by Sanwa Kagaku Co, Japan. However, this drug is seldom used in patients with CKD. We recently encountered a patient in whom Azosemide exerted efficacy and safety

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comparable with those of Furosemide while causing fewer unidentified complaints compared with Furosemide. Following this experience, we undertook the present crossover study, designed to compare the efficacy and safety of Azosemide and Furosemide in patients with CKD.

Subjects and methods

Subjects

The study involved 34 CKD patients. Inclusion criteria were: age between 20 and 75 years; no limitation on gender; outpatients receiving loop diuretics; and serum potassium level between 3.5 and 5.0 mEq/L. Exclusion criteria were: patients receiving steroids for treatment of nephrotic syndrome; patients with malignant hypertension (diastolic pressure ≥130 mmHg); patients with hepatic coma; patients with markedly low serum sodium or potassium level; patients with anuria; and other patients judged inappropriate for the study by the attending physician. The background variables of these patients are summarized in Table 1. 14 of objects were diabetic nephropathy, 8 were nephritic syndrome, 5 were nephrosclerosis, 1 was vasculitis, and the remaining 5 were unknown etiology. The mean estimated glomerular filtration rate (eGFR) at the start of this study was 34.9 ± 4.7ml/min.

Methods

In a study comparing the efficacy of Azosemide with Furosemide in healthy volunteers[3] and an early clinical study in patients with various edematous disease[5,8], 60 mg Azosemide was considered to be equivalent to 40 mg Furosemide. Therefore, in the present study the equivalent ratio of Furosemide 40 mg and Azosemide 60 mg was used for initial and second drugs. However, since this study was not intended to determine the amount of Azosemide equivalent to Furosemide, increasing or reducing the Azosemide dose level after switching was permitted in cases where such increase/reduction was needed (Table 1). The drug for initial administration, Azosemide (30–120 mg/day) or Furosemide (20–80 mg/day), was selected at random by the envelope method. One or two months later, the initial drug (Azosemide or Furosemide) was switched to the other drug (Furosemide or Azosemide) and the second drug was administered for another 1–2 months (crossover study). Hematological tests, urinalysis, and a questionnaire survey on unidentified complaints after medication were carried out at the start and at the end after 1–2 months of treatment with each drug.

This study was authorized in advance by Jichi Medical University Ethics Committee.

Measurements

The following parameters were measured before and after treatment with each drug: body weight, blood pressure (systolic and diastolic), edema, laboratory data (serum total protein, albumin, Na, K, Cl, Ca, P, urea nitrogen, creatinine, uric acid, white blood cell count, red blood cell count, hemoglobin, hematocrit, and platelet count) and urinalysis (24 hours urinary volume, urinary protein, Na, K, Cl, Ca, P, urea nitrogen, creatinine, uric acid). Several parameters were calculated, such as glomerular filtration rate, calculated blood and urinary osmolalities, transtubular potassium gradient (TTKG), urinary Na/K ratio, urinary anion gap, urinary Ca/P ratio, tubular reabsorption of phosphate, fractional excretion of sodium, fractional excretion of potassium, fractional excretion of chloride.

Changes in each parameter after treatment from the pretreatment level were tested for statistical

Table 1 Background variables

	AZ+FU group	FU+AZ group	Test
No. of subjects	18	16	
Sex	13 males, 5 females	9 males, 7 females	NS (chi-squared test)
Age	64.9±2.6	69.2±2.1	NS (*t*-test)
eGFR	34.9±7.0 ml/min/1.73m^2	38.0±6.4 ml/min/1.73m^2	NS (*t*-test)
Etiologies of CKD	DM 9, NS 3, Nephrosclerosis 3, Unknown 3	DM 4,NS 5, Nephrosclerosis 3, AAV 1, Unknown 3	NS (chi-squared test)
Dosage	AZ, FU	FU, AZ	
	30 mg (2), 20 mg	20 mg (3), 30 mg	
	60 mg (12), 40 mg	20 mg (4), 60 mg	
	120 mg (4), 80 mg	40 mg (6), 60 mg	
		60 mg (1), 120 mg	
		80 mg (2), 120 mg	
AZ-treated group	67.1 ± 7.9 mg	65.6 ± 7.1 mg	NS (*t*-test)
FU-treated group	37.5 ± 5.1 mg	45.8 ± 5.1 mg	NS (*t*-test)

AZ azosemide, *FU* furosemide
eGFR estimated glomerular filtration rate, *DM* diabetes mellitus,*NS* nephrotic syndrome
AAV anti-neutrophil antibody associated vasculitis

significance using the paired Student's *t*-test. The unpaired Student's *t*-test was used for intergroup comparison of drugs. Unidentified complaints associated with each drug were investigated by questionnaire survey at the end of treatment with each drug, and symptoms were graded and analyzed using the paired Wilcoxon rank sum test. Drug efficacy against edema was evaluated at the end of treatment with each drug, using the criteria shown below. Data on efficacy were analyzed with the Wilcoxon rank sum test. Edema was graded on a four-grade scale: IV (evidently severe), III (moderate, with visible pitting), II (mild, only slightly visible), or I (absent).

Results

No significant change in systolic blood pressure, diastolic blood pressure, or body weight was noted after treatment with Azosemide or Furosemide compared with the pretreatment level. The number of patients showing alleviation of edema was greater after treatment with Azosemide than after treatment with Furosemide, but the difference was not statistically significant (P= 0.2754; Fig. 1: The severity of edema wasn't evaluated completely in 7 patients.).

No significant change in total protein, albumin, serum electrolytes (Na, K, Cl, Ca, P), blood urea nitrogen, or uric acid was noted after treatment with Azosemide. Hematological parameters (white blood cell count, red blood cell count, hemoglobin, hematocrit, platelet count) showed no significant change after treatment with Azosemide. However, serum creatinine rose significantly after treatment with Azosemide (P= 0.0418). No biochemical or hematological parameter showed a significant change after treatment with Furosemide. When the two drugs after crossover switch were compared, no significant difference was noted in any biochemical or hematological parameters (Table 2).

In urinalysis, no significant change was noted in daily urinary volume, glomerular filtration rate, protein excretion, creatinine, urinary electrolyte levels (Na, K, Cl, Ca, P), urinary urea nitrogen or urinary uric acid level following treatment with Azosemide. Also after treatment with Furosemide, no significant

Fig. 1. Severity of edema

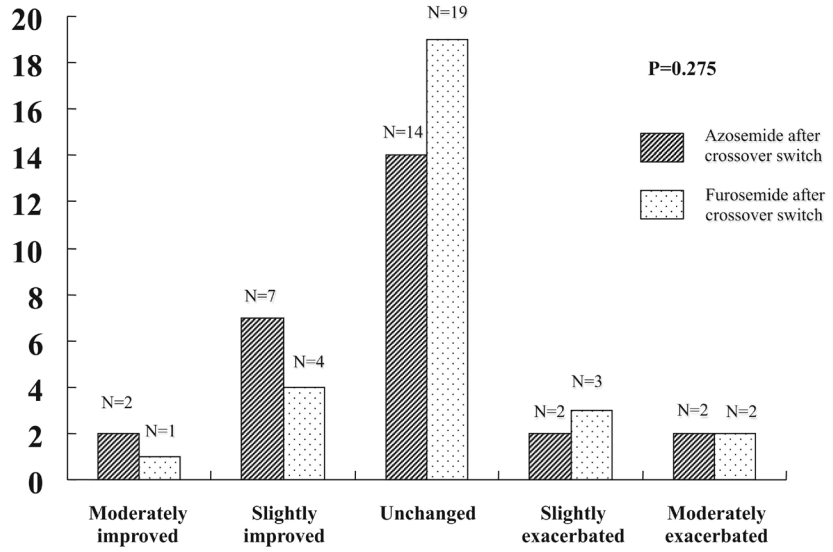


Table 2 Results of biochemical tests

	Azosemide after crossover switch				Furosemide after crossover switch				Intergroup difference
	Start of AZ	End of AZ	Change	*P* value	Start of FU	End of FU	Change	*P* value	*P* value
TP (g/dL)	6.9 ± 0.1	6.9 ± 0.1	0.07 ± 0.05	0.169	7.0 ± 0.1	7.0 ± 0.1	-0.04 ± 0.06	0.481	0.145
Ab (g/dL)	3.6 ± 0.1	3.7 ± 0.1	0.06 ± 0.04	0.178	3.7 ± 0.1	3.7 ± 0.1	-0.04 ± 0.04	0.349	0.103
Na (mEq/L)	141.0 ± 0.6	140.9 ± 0.4	-0.1 ± 0.4	0.795	141.2 ± 0.4	140.6 ± 0.6	-0.6 ± 0.6	0.332	0.496
K (mEq/L	4.5 ± 0.1	4.5 ± 0.1	0.03 ± 0.08	0.729	4.5 ± 0.1	4.5 ± 0.1	0.1 ± 0.1	0.94	0.603
Cl (mEq/L)	107.1 ± 0.9	107.4 ± 0.9	0.2 ± 0.6	0.682	107.8 ± 0.9	107.3 ± 0.8	-0.5 ± 0.7	0.494	0.431
Ca (mEq/L)	8.8 ± 0.1	8.8 ± 0.1	-0.01 ± 0.06	0.813	8.9 ± 0.1	8.8 ± 0.1	-0.08 ± 0.06	0.223	0.447
P (mEq/L)	4.1 ± 0.2	4.0 ± 0.2	-0.10 ± 0.13	0.443	3.9 ± 0.1	3.9 ± 0.2	-0.01 ± 0.10	0.919	0.571
BUN (mg/dL)	38.1 ± 4.0	38.7 ± 3.8	0.5 ± 1.8	0.779	37.3 ± 3.7	38.6 ± 3.5	1.3 ± 1.4	0.356	0.733
Cr (mg/dL)	2.3 ± 0.3	2.4 ± 0.3	0.13 ± 0.06	0.042*	2.5 ± 0.3	2.6 ± 0.3	0.07 ± 0.05	0.054	0.439
eGFR (ml/min/1.73m^2)	31.2 ± 4.5	33.7 ± 4.2	7.1 ± 0.42	0.218	33.3 ± 4.2	31.1 ± 4.5	7.2 ± 0.4	0.989	0.545
Uric acid (mg/dL)	6.8 ± 0.3	7.0 ± 0.3	0.30 ± 0.2	0.17	6.7 ± 0.3	6.9 ± 0.3	0.20 ± 0.1	0.188	0.724
WBC (/mL)	7.3 ± 0.4	7.2 ± 0.4	-0.07 ± 0.3	0.789	7.2 ± 0.4	7.2 ± 0.4	-0.07 ± 0.2	0.745	0.996
RBC (×10^4/mL)	350.9 ± 12.4	355.3 ± 12.0	4.4 ± 3.5	0.218	357.8 ± 12.3	359.2 ± 13.6	1.4 ± 5.2	0.784	0.635
Hb (g/dL)	11.0 ± 0.4	11.1 ± 0.4	0.05 ± 0.11	0.635	11.2 ± 0.4	11.2 ± 0.4	0.007 ± 0.14	0.962	0.798
Ht (%)	32.5 ± 1.1	32.8 ± 1.0	0.26 ± 0.4	0.475	33.0 ± 1.0	33.0 ± 1.2	0.02 ± 0.4	0.964	0.679
Plt (×10^4/mL)	**24.6 ± 1.7**	24.3 ± 1.5	-0.26 ± 0.6	0.665	24.4 ± 1.4	24.1 ± 1.5	0.31 ± 0.6	0.612	0.955

TP total protein, *Ab* albumin, *BUN* blood urea nitrogen, *Cr* creatinine, *WBC* white blood cells, *RBC* red blood cells, *Hb* hemoglobin, *Ht* hematocrit, *Plt* platelets

change was noted in any parameter of urinalysis. There was no significant difference in any parameter of urinalysis between the two groups (Table 3).

There was no significant difference in calculated plasma and urinary osmolalities, transtubular potassium gradient, urinary protein, urinary Na/K ratio, urinary anion gap, urinary Ca/P ratio, tubular reabsorption of phosphate, fractional excretion of uric acid, fractional excretion of sodium, fractional excretion

Table3 Urinary excretion parameters

	Azosemide after crossover switch				Furosemide after crossover switch				Intergroup difference
	Start of AZ	End of AZ	Change	*P* value	Start of FU	End of FU	Change	*P* value	*P* value
Protein excreted (mg/day)	1951.7 ± 488.8	1893.3 ± 543.7	-58.4 ± 137.6	0.675	2265.6 ± 607.6	1880.7 ± 428.4	-384.9 ± 429.7	0.381	0.476
Cr excreted (g/day)	0.8 ± 0.06	0.9 ± 0.05	0.05 ± 0.03	0.153	0.9 ± 0.06	0.8 ± 0.06	-0.08 ± 0.06	0.19	0.065+
Na excreted (mmol/day)	149.1 ± 12.1	139.0 ± 12.0	-10.1 ± 7.8	0.207	136.4 ± 11.7	131.6 ± 13.3	-4.7 ± 13.1	0.722	0.727
K excreted (mmol/day)	34.6 ± 2.7	34.8 ± 2.9	0.9 ± 2.6	0.921	34.9 ± 4.4	30.7 ± 3.3	-4.2 ± 2.6	0.129	0.179
Cl excreted (mmol/day)	149.0 ± 11.1	136.6 ± 11.6	-12.4 ± 8.1	0.137	136.9 ± 12.2	128.0 ± 12.6	-9.0 ± 13.0	0.497	0.816
Ca excreted (mg/day)	47.6 ± 10.2	53.1 ± 12.8	5.5 ± 3.9	0.17	55.9 ± 20.7	44.1 ± 12.1	-11.9 ± 9.6	0.229	0.105
P excreted (g/day)	0.5 ± 0.03	0.5 ± 0.04	0.01 ± 0.03	0.511	0.5 ± 0.05	0.5 ± 0.05	-0.03 ± 0.03	0.409	0.370
BUN excreted (g/day)	5.5 ± 0.4	5.3 ± 0.4	-0.18 ± 0.2	0.463	5.1 ± 0.4	5.2 ± 0.5	0.06 ± 0.3	0.854	0.538
Uric acid excreted (g/day)	0.3 ± 0.03	0.3 ± 0.03	0.011 ± 0.01	0.348	0.3 ± 0.04	0.2 ± 0.03	-0.04 ± 0.03	0.267	0.174
Daily urine volume (mL/day)	1593.4 ± 88.5	1540.6 ± 100.3	-52.8 ± 60.7	0.393	1628.5 ± 121.0	1668.8 ± 122.0	40.4 ± 80.5	0.621	0.354
GFR (mL/min)	30.2 ± 5.7	31.4 ± 5.4	1.1 ± 2.1	0.603	24.9 ± 6.7	24.8 ± 5.9	-0.14 ± 2.3	0.952	0.688

Cr creatinine, *BUN* blood urea nitrogen, *GFR* glomerular filtration rate

of potassium or fractional excretion of chloride after treatment with Azosemide. No significant difference was noted in any of these parameters after treatment with Furosemide. However, urinary protein excretion/creatinine rose significantly after treatment with Furosemide (P= 0.0360; Fig. 2).

Analysis of responses to the questionnaire on unidentified complaints associated with diuretics showed no significant difference between the two groups (Fig. 3).

Furosemide was selected as the preferred drug by 6 (30%) of the 20 patients and Azosemide by 7 patients (35%), and 7 patients (35%) expressed no preference.

Fig.2. Urinary protein excretion

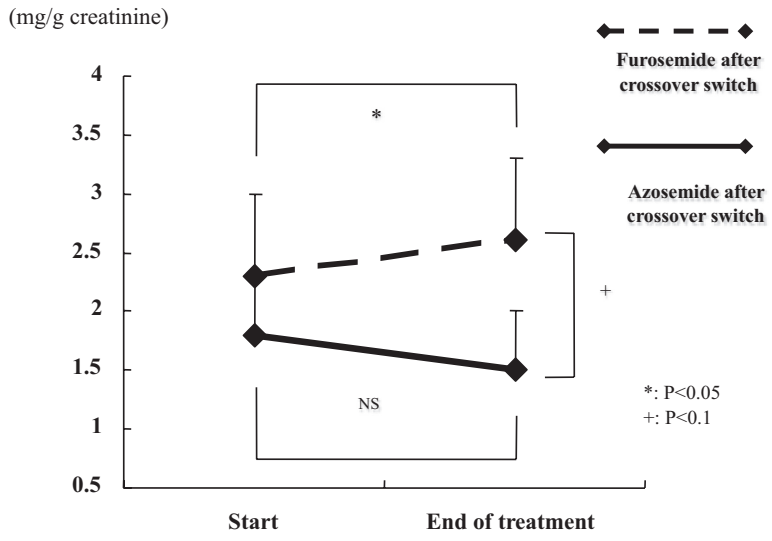
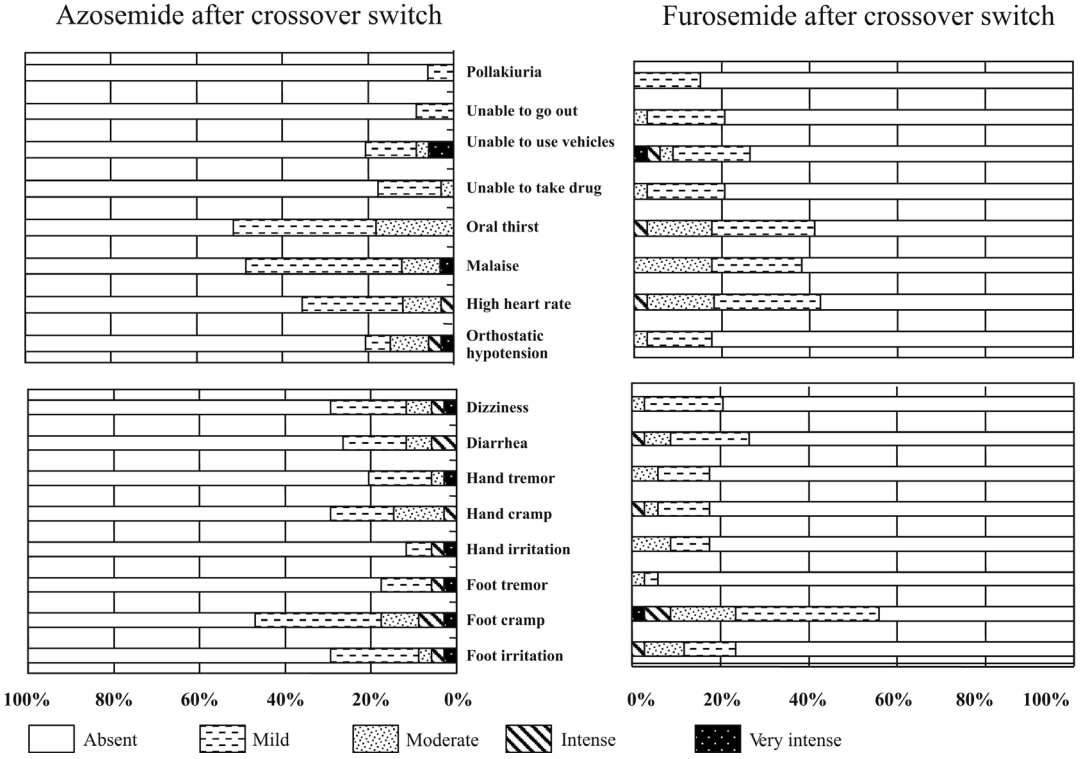


Fig. 3. Questionnaire survey of patients about complaints specific to diuretics



Discussion

In patients with chronic kidney disease, the reduction in renal function is often complicated by conditions such as hypertension, edema, and heart failure.

Many of the frequently used loop diuretics (furosemide, etc.) increase the likelihood of loss of electrolyte balance and entail a risk for thrombosis and embolism due to dehydration and blood concentration due to the diuretic activity of loop diureteics. Furthermore, it has been suggested that Furosemide reduces patients' quality of life. The class of loop diuretics includes the long-acting agent Azosemide. It has been reported that Azosemide exerts diuretic activity for 10–12 h, in contrast to only 4–6 h for Furosemide[3,6,7]. Although the diuretic potency of Azosemide differs little from that of Furosemide, Azosemide exerts its diuretic action more slowly and is unlikely to cause loss of electrolyte balance, elevation of serum uric acid level and reduction in quality of life through induction of pollakiuria, etc.[4,8]. Because of these features, long-acting Azosemide has been often used for outpatients managed at our facility. Before the present study, our impression was that the incidence of leg cramp, one of the unidentified complaints associated with diuretic therapy, is lower after treatment with Azosemide. However, no direct comparison between Azosemide and Furosemide had been carried out, and no report was available concerning long-term observations of patients with renal disease treated with these drugs. We therefore performed the present crossover study, directly comparing the two drugs in patients with CKD. This study revealed no significant difference between the two drugs in any of the efficacy indicators we studied. Furthermore,

analysis of individual indicators revealed no significant difference in the effect on serum electrolytes (particularly K), serum uric acid level between the two drugs. Blood urea nitrogen and serum creatinine increased slightly more after treatment with Azosemide than after Furosemide, although the difference was not statistically significant. There was little difference between the two drugs in urinary excretion of electrolytes, uric acid, creatinine, blood urea nitrogen, etc. However, total urinary protein excretion corrected for creatinine rose significantly after treatment with Furosemide, and the magnitude of change in this parameter tended to be larger after treatment with Furosemide than after treatment with Azosemide. The patients' quality of life revealed no significant difference between responses after treatment with Azosemide and those after treatment with Furosemide. When patients were asked which was their preferred drug, 35% said it was Azosemide 30% said it was Furosemide, and 35% gave a neutral answer.

The effect in alleviating edema did not differ significantly between the two drugs, but seemed to be slightly better with Azosemide than with Furosemide. However, there was no significant difference in daily urinary volume or change in body weight between the two drugs. This discrepancy in clinical results seems to be attributable to a difference in transfer of water from interstitial space to intravascular space. In a double-blind study in patients with various edematous diseases, Oshima et al.[8] showed that the effect in alleviating edema was significantly greater with Azosemide than with Furosemide. Oshima et al. suggest the following reason for this difference between the two drugs: unlike long-acting drugs, which slowly guide fluid from the edematous space into blood vessels, short-acting drugs cannot guide adequate volume of water out of the edematous region because their diuretic action is short-lasting.

The first problem we encounter when using loop diuretics is diuretics-induced hypokalemia. Previous work found no significant difference between Furosemide and Azosemide in the incidence of hypokalemia in patients with various edematous diseases[8,9]. However, some investigators reported that Azosemide is less likely to cause rapid onset of hypokalemia because urinary excretion of K is less rapid after treatment with Azosemide[3,6]. In the present study of patients with compromised renal function, no significant difference was noted between the serum K level after treatment with Azosemide and that after treatment with Furosemide. Urinary K excretion tended to be higher with Azosemide than with Furosemide, although the difference was not statistically significant. Takamitsu et al.[10] reported that treatment of humans with Azosemide or Furosemide resulted in significant elevation of the renin–angiotensin–aldosterone (RAA) system and antidiuretic hormones, and that the pattern of responses showed a mirror image relationship to the time course of percent change in circulating blood volume, indicating that a decrease in circulating blood volume plays an important role in stimulation of the RAA system after treatment with Azosemide or Furosemide. The same investigators, however, reported that stimulation of the RAA system and antidiuretic hormones was less marked after treatment with Azosemide than after Furosemide. In the present study, which involved long-term observation of a large number of patients, no significant difference was noted in these aspects between the two drugs.

The second problem is stimulation of the RAA system following treatment with loop diuretics[11,12]. Yoshida et al.[13] compared the survival of Dahl high-salt heart failure model rats after treatment with Azosemide with that after treatment with Furosemide, and found that survival was significantly longer in the Azosemide treatment group and that two indicators of sympathetic nervous system, i.e. myocardial and the blood level of norepinephrine, were affected much less by Azosemide than by Furosemide.

Tomiyama et al.[14] also carried out a crossover study comparing Azosemide with Furosemide in 19 patients with chronic heart failure, and reported that the change in heart rate, as measured by the 24-h Holter ECG (an indicator for sympathic nerve system), improved significantly in the Azosemide treatment group compared with the Furosemide treatment group. Direct comparison of the present study with these previous studies is not possible because we did not analyze neurohumoral factors. However, urinary protein excretion, corrected for creatinine, rose in the present study after treatment with Furosemide. In view of the lack of significant change in blood pressure, this change in urinary protein excretion probably reflects elevation in glomerular pressure due to stimulation of the RAA system following rapid diuresis, etc.

Regarding influences on uric acid, a previous study comparing Azosemide with Forosemide in patients with various edematous diseases revealed no significant difference between the two groups[8]. On the other hand, since urinary uric acid excretion is reduced less by Azosemide than by Furosemide[15,16], the blood uric acid level is reported to be significantly lower after treatment with Azosemide than after Furosemide treatment[17]. Like thiazides, loop diuretics are likely to induce hyperuricemia[18] and need to be used carefully. Regarding the cause of the hyperuricemia seen after diuretic treatment, it has been reported that, during prolonged use of diuretics, a chronic decrease in bodily fluid reduces the reverse leakage of uric acid from the renal interstitium into the renal tubules, and leads to elevation of the blood uric acid level[19]. In any event, it seems likely that reduction of urinary uric acid excretion is involved in the onset of secondary hyperuricemia due to diuretics. In the present study, blood uric acid level rose after treatment with each of these two drugs, although the elevation was not significant.

Serum creatinine rose significantly after treatment with Azosemide, but the degree of increase was relatively small. The same parameter also tended to rise after treatment with Furosemide, but the elevation was mild. There was no significant difference between serum creatinine level after treatment with Azosemide and that after treatment with Furosemide, but possible changes in this parameter need close attention when using these drugs in patients with compromised renal function.

We now discuss the patients' quality of life and their compliance with treatment. In our experience, Furosemide often reduces the quality of life of outpatients because its potent and rapid diuretic activity often causes symptoms such as pollakiuria. It is not uncommon for patients to omit taking the drug on days when they visit the clinic in order to prevent the frequent need for urination on the way to the clinic. In most studies, the unidentified complaints specific to diuretics were halved by the use of Azosemide instead of Furosemide[4,20]. In the present study, however, no significant difference in this aspect was noted between the two drugs. However, when they were asked to name their preferred drug, a slightly higher percentage of patients selected Azosemide. In other words, more patients considered Azosemide to be less disturbing to their daily lives. In the present study, no significant difference was noted between the two drugs. This result seems to be closely related to the finding of Miyazaki et al.[21] that the biological half-life of Furosemide in blood was extended by Furosemide treatment in dogs with renal failure in a study designed to investigate the pharmacokinetics and diuretic action of Furosemide in normal dogs and dogs with experimentally induced renal failure. In the present study, involving patients with compromised renal function , it seems likely that the blood level of Furosemide (a drug primarily excreted via the kidneys[22]) tended to shift toward the right (i.e. it tended to remain longer in the high range), resulting in a long-lasting diuretic action resembling that of azosemide. This probably led to the finding of no differ-

ence between the two drugs in any of the indicators analyzed.

Thus, although efficacy and safety differed little between Azosemide and Furosemide (no significant difference), 35% of the patients expressed the desire to continue treatment with Azosemide.

Conclusions

A crossover study comparing the short-acting loop diuretic Furosemide with the long-acting loop diuretic Azosemide was carried out in 34 patients with chronically compromised renal function. There was no significant difference between the two drugs in biochemical parameters, hematological parameters, parameters of urinalysis, and responses to a questionnaire on unidentified complaints specific to diuretics, suggesting that efficacy and safety differ little between the two drugs. When asked about their preferred drug, the percentage of patients selecting Furosemide (30%) was close to the percentage selecting Azosemide (35%). Azosemide merits consideration as an alternative drug for patients with chronic kidney disease.

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慢性腎臓病患者における長時間作用型と短時間作用型ループ利尿薬の効果と安全性の検討

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要　約

慢性腎臓病患者において，長時間作用型ループ利尿薬（アゾセミド），と短時間作用型（フロセミド）の効果と安全性を比較検討した。

現在ループ利尿薬を服用している血清Ｃｒ値1.5mg/dl 以上の外来患者を対象とし，文書にて同意を得られた34名を対象とした。投与薬剤の順番をランダム化して，アゾセミドまたはフロセミドを，１－２ヶ月毎に交互に投与した。

その結果，アゾセミド60mg とフロセミド40mg を同等力価と考えて交互に投与した場合，血圧，体重，尿量，尿中 Na 排泄量に差はなく，血液検査データ，尿中電解質などにも差は無かった。尿蛋白量はアゾセミド投与後に有意に減少した（p=0.0556）。アンケート調査では，手のつれがアゾセミド投与後に多い傾向であったが，どちらの薬剤を服用したいかは，フロセミド30％，アゾセミド35％，どちらともいえないが35％であった。

以上より，慢性腎臓病患者における有効性，安全性ともアゾセミドはフロセミドと同等であると考えられた。

キーワード：CKD，慢性腎不全，フロセミド，アゾセミド

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