Commonly Prescribed Salt Intake in Continuous Ambulatory Peritoneal Dialysis Patients Is Too Restrictive: Results of a Double-Blind Crossover Study

ADRIAN FINE, BUNNY FONTAINE, and MADGE MA
Section of Nephrology, St. Boniface General Hospital, Winnipeg, Manitoba, Canada.

Abstract. Salt restriction in continuous ambulatory peritoneal dialysis (CAPD) patients is widely prescribed and thereby may reduce quality of life. It is presumed that this has a beneficial effect on BP and reduces the need for hypertonic dialysate. However, this has never been formally evaluated. A double-blind crossover study of placebo versus sodium chloride pills (60 mEq of sodium per day) is presented in 20 stable CAPD patients, 10 of whom were hypertensive. Dietary sodium was quantified throughout the study by 3-d dietary histories and remained unaltered throughout. There was a clinically unimportant but statistically significant rise in BP with added salt: 135/77 to 144/82 (P < 0.05). No rise in BP occurred in the hypertensive patients. Weights, use of hypertonic dialysate, and BP medications remained unaltered throughout the study. In conclusion, 200 mEq of sodium per day, i.e., a normal sodium intake, is easily tolerated in stable CAPD patients, and the recommended sodium intake commonly prescribed is too restrictive. (J Am Soc Nephrol 8: 1311–1314, 1997)

Significant variation exists in recommended sodium intake for continuous ambulatory peritoneal dialysis (CAPD) patients. The American Dietetic Association recommends 130 to 170 mEq/d (1), which is similar to the amount of 140 to 175 mEq/d recommended by others (2). A recent textbook recommends similar sodium intake only if the patient can use hypertonic solutions (3). In spite of these recommendations, some centers are more restrictive, reducing intake to 85 to 130 mEq/d (4). One-third of 11 CAPD units in North America that we surveyed before conducting this study restricted sodium intake to <170 mEq/d. In contrast to the findings above, others recommend no salt restriction (5).

Because the normal average Western diet contains 175 to 204 mEq of sodium per day (6), the prescribed sodium intake in many units for many patients is restrictive. This may have a negative impact on the quality of life for some patients.

The diversity of these dietary recommendations could be due to several factors. There is a wide variation between reported values for net dialysate sodium removal; one report of 250 mEq/d (7) contrasts with another report of 129 mEq/d (8). A more recent report has values very similar to this latter amount (9). Only one of these reports has quantified sodium intake (9). None has reported the effects of altering sodium intake in these patients, specifically, whether this would affect BP, fluid gain, and strength of dialysate used.

Therefore, we decided to add 60 mEq of sodium per day to the usual diet of CAPD patients and to assess its effect on BP and weight. Because of the potential for poor dietary tolerance of added salt in patients used to salt restriction, combined with the difficulty in controlling for the amount added, we performed a double-blind crossover study of placebo versus salt pills.

Materials and Methods

Patients

Before the study, we assessed the clinic records of the previous three outpatient visits on 15 patients to determine the number of patients required to be able to detect statistically significant changes in BP and weight. The number required was 20. Thirty-two CAPD patients whose overall medical condition was stable were included in the study. Hypertension and dietary noncompliance were not contraindications. Patients were excluded from the study for the following reasons: (1) poorly controlled BP (diastolic patients > 100, n = 4); (2) difficulty staying edema-free (n = 2); (3) medication noncompliance (n = 4); (4) considered by us to be unable to keep an accurate dietary history or to record their own BP (n = 10); (5) use of 4.25% dialysate in 75% or more of their usual cycles (n = 2); (6) refusal to be in the study (n = 3); or (7) on CAPD for less than 4 mo (n = 6). The most common reason for exclusion was geographical distance between our unit and the patient’s home (n = 20). Approximately 40% of our CAPD patients live outside Winnipeg, some as far as 500 miles away. The study required four 24-h dialysate plus urine collections, as well as home visits by our research nurse, thereby excluding many non-Winnipeg patients. Our CAPD population was 83 at the start of the study. Therefore, only a very small number of patients were excluded on the basis of severe hypertension or fluid problems. The conclusions from this study are applicable to the majority of CAPD patients.

Dialysate sodium was 132 mEq/L in all patients. After a 3-wk washout period, patients were randomized by our pharmacy to receive either gelatin capsules of placebo or 60 mEq of sodium (as NaCl) divided into three doses taken after meals. Physician, patient, and study nurse were blinded. Tablets were taken for 6 wk followed by...
another 3-wk washout and then crossed over for an additional 6 wk (Figure 1). Throughout the 18-wk study, patients recorded two weights and three BP per week. Patients were trained by the study nurse to take their own BP. In the last week of each period, five readings a day for 3 d were taken. BP were taken by an electronic sphygmomanometer in a sitting position in the mid-morning and mid-afternoon with no significant exercise having taken place within 30 min. The study nurse visited the patients at home to assess accuracy of these determinations. Mean values were calculated from values obtained on the last week of the washout periods and the last week of salt/placebo periods. At the end of each period, 3-d dietary intakes were recorded by the patients who had received verbal and written instructions on how to measure and record such information. Then, 24-h dialysate and urine collections were obtained. Any change in dialysate regimen was recorded daily by the patients. Patients were closely monitored by weekly phone calls from the study nurse.

The 3-d diet records were analyzed using the Beaver Foods Nutrient Database, which consists of the Canadian Nutrient File (10). The accuracy of this method for quantifying dietary intakes has been validated previously (11,12). Sodium concentrations in dialysate and urine were measured by flame photometer and performed in duplicate.

Twelve patients, six on salt pills and six on placebo, could not complete both arms of the study for the following reasons: gastrointestinal symptoms (5), itch (1), depression (1), poor record keeping (1), patient decision for no identifiable reason (2), and patient concern about their BP based on single BP readings (2). In one of these two patients, the diastolic BP did not exceed 85, and in the second patient systolic BP did not exceed 160. Their data have been excluded. Twenty patients completed the entire study. The high dropout rate warrants further discussion. This protocol placed considerable demands on these patients, beyond the usual rigors of home dialysis, and in our view, five to six of the dropouts were related to a general apathy that developed during the study. The gastrointestinal symptoms may in part be related to the highly artificial manner in which the salt was given, but the strict design of the study mandated the procedure. To our surprise, two of the five patients whose gastrointestinal intolerance led to withdrawal from the study developed those symptoms when taking placebo. The withdrawal from the study should therefore not be taken as a sign of intolerance to added salt.

Statistical Analyses
The results were analyzed by the Hill and Armitage test for crossover clinical trials (13). First, a carryover effect was tested for; when not present, a treatment effect was then tested for. Because the baselines did not differ between the two treatment periods, we did not have to carry out an analysis for variables adjusted for washout (i.e., baselines). For BP change in the hypertensive subgroup and net sodium losses (urine plus dialysate), significance was also assessed by paired Wilcoxon rank sum test. Results are given as mean ± SD.

Results
Seventy percent of the patients were men. The mean age was 61 ± 13. Ten patients were hypertensive on medication. The primary renal diseases were the usual found in North American dialysis units (Table 1).

Systolic BP rose from 135 ± 19 (placebo) to 144 ± 21 (P = 0.021), and diastolic BP rose from 77 ± 8 (placebo) to 82 ± 12 (P = 0.045) (Table 2). In subgroup analysis in the 10 patients who were hypertensive (Table 3), the rise in systolic BP approached significance (P = 0.08; Hill and Armitage), but was not significant (P > 0.10) by Wilcoxon rank sum test. There was no change in diastolic BP (P = 0.29, Wilcoxon rank sum test).

Patients' weights were unaffected by ingesting excess salt (72 ± 10 [placebo] versus 72 ± 11 kg). None of the hypertensive patients had to adjust their medications during the salt period, and no nonhypertensive patient became hypertensive (BP greater than 160/90) requiring treatment during that pe-

![Figure 1. Schematic representation of study design.](image-url)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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<tbody>
<tr>
<td>n</td>
<td>20</td>
</tr>
<tr>
<td>M/F</td>
<td>14/6</td>
</tr>
<tr>
<td>Age</td>
<td>61 ± 13</td>
</tr>
<tr>
<td>Duration of dialysis (mo)</td>
<td>15 ± 15</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10</td>
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<tr>
<td>Primary renal disease</td>
<td></td>
</tr>
<tr>
<td>glomerulonephritis</td>
<td>5</td>
</tr>
<tr>
<td>polycystic kidney disease</td>
<td>3</td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td>7</td>
</tr>
<tr>
<td>hypertension</td>
<td>3</td>
</tr>
<tr>
<td>pyelo/reflux</td>
<td>2</td>
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</tbody>
</table>

* M, male; F, female.
period. During the salt phase, 4 of 20 patients increased their dialysate strength, and 1 patient decreased it. The corresponding numbers during the placebo period were three patients who increased their dialysate strength and one patient who reduced the strength. Thus, there was no measurable change in dialysate strength due to extra salt ingestion.

Because alterations in dietary sodium between periods could affect the results, dietary sodium intake was obtained. Sodium intake did not vary during the study (137 ± 28 [placebo] versus 134 ± 45 [after NaCl] mEq/d) in the entire group, nor did it change in the hypertensive group (Table 3).

There was a wide variation in dialysate and urinary sodium values (Table 4). Dialysate plus urinary sodium loss was 155 ± 108 mEq/24 h at the end of the placebo period and 207 ± 88 mEq/24 h during the salt period. Urinary sodium losses were 20 ± 24 and 28 ± 30 mEq/d in the same periods, respectively (NS). Although the dialysate plus urinary sodium losses increased by 52 mEq/d during the salt period, this was not significant (P = 0.15, Hill and Armitage; P = 0.24, Wilcoxon) due to the wide variation between patients and within patients. Alteration of ultrafiltration volume by salt was not statistically significant (Table 4).

### Discussion

Quality of life is significantly affected for dialysis patients, and undoubtedly, dietary restrictions can be a major contributing factor. The realization that a significant number of patients do not comply with dietary salt restriction and yet remain clinically stable partially prompted this study. The finding of a wide variation in recommended sodium intakes in the literature and between units in our preliminary telephone survey, combined with the fact that the issue has not been scientifically explored further, also prompted the study.

Our results clearly demonstrate that a total sodium intake of approximately 200 mEq/d is easily tolerated and does not lead to edema or the necessity to use stronger dialysate. Although a higher sodium intake results in a statistically significant rise in BP, these increases are probably not clinically significant, i.e., do not approach hypertensive values. Even hypertensive patients maintained healthy BP levels when taking this extra salt and did not require additional medication.

The design of this study was similar to other studies showing an effect of added (14) or reduced (15,16) sodium intake on BP in nonrenal patients. We empirically extended both the washout and treatment periods by 50% from that used in the study by Masioli et al. (14) because there are no reported data on sodium balance in CAPD patients. The lack of carryover effect supports this experimental design.

With regard to BP determinations, we had to have a research design that was practical and minimally onerous to the patient. Although ambulatory BP recording would have been ideal, it was deemed impractical and too expensive for this study. We followed the recommendations of Padfield et al., who have confirmed the validity and reproducibility of five home BP readings per day for 3 d (17,18). The number of BP readings far exceeded the usual in most previously described studies of the effect of sodium on BP (14–16).

Although there was a statistically significant increase in BP with added salt, BP clearly remained within the range considered normal and did not warrant therapeutic intervention. The question is whether this increase in BP is clinically important. Adjusted stroke mortality rate is identical with diastolic patients in the ranges of 76 to 78 mmHg and 81 to 83 mmHg (19).

With regard to systolic BP, the adjusted stroke mortality in the range 142 to 150 mmHg is 0.8/10,000 patient years higher than in the range 132 to 136 mmHg. Whether this is statistically significant is unclear, but it is only a minor effect (equivalent to 0.8 patients dying out of 1000 [dialysis] patients followed for 10 yr).

With regard to cardiovascular mortality, several reports conclude that the ideal diastolic BP in hypertensive patients, from the coronary risk point of view, is 84 to 89 mmHg (20,21) and that the rate of adjusted coronary mortality is virtually identical in the diastolic BP ranges found in our study (19). However, it should be noted that there are no comparable data in uremic patients.

### Table 2. The effects of added salt on weight, BP, and dietary salt intake in 20 CAPD patients

<table>
<thead>
<tr>
<th>Category</th>
<th>Placebo</th>
<th>Salt</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>72 ± 10</td>
<td>72 ± 11</td>
<td>0.76</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>135 ± 19</td>
<td>144 ± 21</td>
<td>0.021</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>77 ± 8</td>
<td>82 ± 12</td>
<td>0.045</td>
</tr>
<tr>
<td>Dietary sodium intake (mEq/d)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>137 ± 28</td>
<td>134 ± 45</td>
<td>0.20</td>
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</table>

* Excludes the added sodium chloride.

### Table 3. The effects of added salt on weight, BP, and dietary salt intake in the subgroup of 10 hypertensive CAPD patients

<table>
<thead>
<tr>
<th>Category</th>
<th>Placebo</th>
<th>Salt</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>75 ± 9</td>
<td>76 ± 11</td>
<td>0.25</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>140 ± 21</td>
<td>153 ± 14</td>
<td>0.08</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>79 ± 7</td>
<td>84 ± 11</td>
<td>0.18</td>
</tr>
<tr>
<td>Dietary sodium intake (mEq/d)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>142 ± 28</td>
<td>134 ± 28</td>
<td>0.44</td>
</tr>
</tbody>
</table>

* Excludes the added sodium chloride.
Dietary sodium intake records are remarkably accurate and give values within 85 to 90% of the measured intake (22). In healthy subjects, approximately 85% of sodium intake is recovered in the urine (22). There are no data for the percentage of ingested sodium recovered in the dialysate of CAPD patients. The percentage recovery of sodium in dialysate plus urine in our patients is within 15% of the calculated intake. Although the measured output of sodium went up by approximately the same amount as the added salt pills, this was not statistically significant due to the very large SD of 24-h dialysate sodium determinations. It should be noted that the dietary sodium was not strictly controlled immediately before the dialysate/urine collections, but instead the patients continued on their usual modest sodium restriction. Large day-to-day variations in sodium intake occurred in these patients (data not given) mandating 3-to-5-d food diaries. This variation is similar to previous reports (23,24). Indeed, in healthy subjects the intraindividual variation in 24-h urinary sodium is so large that it would require 14 to 16 collections per patient to identify high and low sodium intakes (23,24). Furthermore, the impact of the coefficient of variation (2.5%) of sodium determinations is far greater in 24-h dialysate collections than in corresponding 24-h urine collections due to the fact that the number would be multiplied by 8 to 10 L (of spent dialysate) rather than 1 to 2 L (of urine). Therefore, the wide SD in our study is to be expected and might have been reduced with far more rigid control of sodium intake for several days before each collection period. However, this would have been contrary to the primary aim of the study, which was to assess the safety of added salt to the usual diet of these CAPD patients.

Our study, primarily designed to assess the clinical safety of allowing increased salt intake in CAPD patients, has shown no deleterious effect of a normal salt intake in these patients over 6 wk. Although longer-term studies may now be warranted, it seems reasonable to suggest that the recommended sodium intake for these patients be made less restrictive. Reducing dialysate sodium concentration (which has been shown to significantly increase salt removal; reference 9) could be an option for those patients desiring even larger salt intakes.

Acknowledgments

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References