TOTAL BODY WATER, TOTAL EXCHANGEABLE SODIUM AND POTASSIUM
IN PATIENTS WITH CONVALESCENT ACUTE MYOCARDIAL
INFARCTION ONE TO TWO MONTHS AFTER ONSET

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Total exchangeable sodium (Nae), potassium (Ke), and total body water (TBW) were measured by the multiple isotope dilution method, in 10 healthy subjects (normal), 10 patients with congestive heart failure (CHF), and 47 patients with acute myocardial infarction (AMI), 1–2 months after onset. According to Killip’s classification, 29 patients with AMI were classified as class I, and 18 patients were classified as class II and III (referred to as class II & III). No differences were found in plasma and urine sodium and potassium concentrations. By the multiple isotope dilution method, significant elevations in Nae/BSA (body surface area) were observed in the following order: normal, class I, class II & III and patients with CHF. Compared with normal subjects, Nae/BSA and Nae/Ke were elevated in class I patients. Elevations of Nae/Ke and TBW/BSA in both class II & III patients with AMI and patients with CHF indicated severe cardiac impairment. Both Nae/BSA (p = 0.60) and Ke/BSA (p = 0.71) had negative and positive correlations with the left ventricular ejection fractions (EF) measured by catheterization in 20 patients with AMI. This indicates a major sodium and water retention mechanism due to impaired cardiac function in AMI. It is worth noting that conspicuous abnormalities in body fluid compositions, particularly in class I patients with AMI as well as class II & III, remained despite no evidence of cardiac failure.

It is essential to treat acute myocardial infarction (AMI) by emergency procedures for severe distress caused by cardiac failure and arrhythmia immediately after onset. Recent medical progress makes recovery possible for patients with AMI. However, the contractility of infarcted myocardium is reduced to some extent, as seen in innumerable studies.1–3 Little work has been done to study the body fluid composition of patients with AMI. However, multiple isotope dilution studies have shown disturbed body fluid volume and composition of sodium and potassium in patients with congestive heart failure (CHF) due to valvular and hypertensive heart diseases.4–9

This paper describes the first multiple isotope dilution study on total exchangeable sodium, total exchangeable potassium and total body water in patients with AMI, particularly 1–2 months after onset.

SUBJECTS AND METHOD

Forty-seven patients with AMI, 10 patients with CHF and 10 subjects without any signs of heart disease were employed in this study. The

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TABLE I NUMBER OF PATIENTS, AGE, SEX, AND, SODIUM AND POTASSIUM CONCENTRATIONS OF SERUM AND URINE, IN NORMAL SUBJECTS, AND PATIENTS WITH AMI AND CHF

<table>
<thead>
<tr>
<th>Number (57) (Male/Female)</th>
<th>Age (Years)</th>
<th>Plasma (mEq/L)</th>
<th>Urine (mEq/24 hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Na</td>
<td>K</td>
</tr>
<tr>
<td>N</td>
<td></td>
<td>31.3 ± 14.7</td>
<td>141.9 ± 2.8</td>
</tr>
<tr>
<td>C I</td>
<td>10 (5/5)</td>
<td>56.7 ± 9.6</td>
<td>142.0 ± 2.3</td>
</tr>
<tr>
<td>C II &amp; III</td>
<td>10 (3/7)</td>
<td>59.8 ± 9.3</td>
<td>141.2 ± 2.1</td>
</tr>
<tr>
<td>CHF</td>
<td>18 (13/5)</td>
<td>59.1 ± 11.8</td>
<td>138.3 ± 3.5*</td>
</tr>
</tbody>
</table>

Values are shown as mean ± S.D.M. * = Statistically significant (p < 0.02) compared with the values of normal subjects. Abbreviations: N = Normal subjects; C I = Patients with AMI assigned to Killip’s class I; C II & III = Patients with AMI in Killip’s classes II and III; CHF = Patients with congestive heart failure due to valvular diseases and dilated cardiomyopathy.

47 patients with AMI had been admitted to the Coronary Care Unit of Iwate Medical University Hospital, and diagnosed as AMI based on ECG findings and serum heart-related enzymes (creatinine kinase, transaminase and lactic dehydrogenase). According to studies by Killip et al.2,3 patients with AMI occurring immediately after onset can be divided into the following 4 classes: Killip’s class I, patients with AMI showing no lung congestion. In this study there were 29 such patients. Killip’s class II, those showing moderate CHF with audible humid rales to almost half of the lungs. Class III, those with severe pulmonary edema and audible humid rales in over 50% of the lungs. In this study, 19 patients fitting both class II and III are referred to together as “class II & III", to better balance class I in number. Patients in serious cardiogenic shock, Killip’s class IV, were not employed in this study.

The CHF group consisted of 10 patients with 6 mitral valvular diseases, 3 mitral and aortic valvular diseases and 1 idiopathic dilated cardiomyopathy, all of whom had shown CHF at the time of admission. Diagnoses were based on heart murmurs, echocardiograms, cardiophonograms and cardiac catheterizations including myocardial biopsies. Most cardiac conditions were situated between classes II and III, according to the New York Heart Association’s classification.10 In addition, 10 subjects with normal cardiac functions were used in this study. The diagnoses were pneumonia in 2 cases, urinary tract infection in 2 cases, and gastric ulcer in 2 cases. Four others were volunteers. All patients with AMI and CHF received a fixed diet containing 120 mEq/day of salt after hospitalization.

One to two months after onset of AMI, the patients with AMI were maintained on daily regimens of nitrate (isosorbide dinitrate 20–80 mg) and calcium antagonists (verapamil 80–120 mg, diltiazem 90–120 mg and/or nifedipine 30–40 mg). Killip’s class II & III patients showed no signs of CHF and edema even without digitalis and diuretics. The patients with CHF, receiving daily digitalis (digoxin 0.25 mg) and furosemide (40–80 mg), were non-edematous and well compensated when determinations of body fluid compositions were made. No abnormal renal functions, including serum creatinine (0.63 ± 0.22 mg/dl, M ± S.D.M.), were found in the subjects with AMI.

Total exchangeable sodium (Nae), total exchangeable potassium (Ke) and total body water (TBW) were determined by the multiple isotope dilution method.11 All isotopes of 3-H for TBW, 24-Na for Nae and 42-K for Ke determinations were purchased from The Japan Radioisotope Society (Tokyo). Intravenous injections of 100 µCi 3-H, and oral administrations of both 24-NaCl 150 µCi and 42-KCl 150 µCi were given to the patients at 10:00. Twenty-two-hour urine was collected from 10:00 on administration day until 08:00 the following morning. The next morning a 2-hour urine was collected from 08:00 to 10:00; blood was drawn from the forearm vein at 10:00. Concentrations of sodium and potassium in all plasma and urine, including the 2-hour urine, were determined by flame-photometry.

The radioactivity (counts per min, cpm) of 3-H in urine and plasma, including the standard solution, was estimated by a liquid scintillation counter (Beckman, LS-3155T). The radioactivi-
ties of 24-Na and 42-K in urine and plasma were estimated using a well-typed scintillation counter (Aloka, Type F3-3A). Nae, Ke and TBW were calculated as follows: 11

\[
\text{Nae (mEq)} = \frac{24-\text{Na (cpm) administered} - 24-\text{Na (cpm) excreted}}{24-\text{Na (cpm/L) in plasma/Na (mEq/L) in plasma}}
\]

\[
\text{Ke (mEq)} = \frac{42-\text{K (cpm) administered} - 42-\text{K (cpm) excreted}}{42-\text{K (cpm) in 2-hour urine/K (mEq) in 2-hour urine}}
\]

\[
\text{TBW (L)} = \frac{3-\text{H (cpm) administered} - 3-\text{H (cpm) excreted}}{3-\text{H (cpm/L) in plasma}}
\]

Renin activity, anti-diuretic hormone (ADH) and aldosterone in plasma were simultaneously measured using commercial radioimmunoassay kits, after blood collection at 06:00. With informed written consent the 20 patients with AMI (class I: 12 cases and class II & III: 8 cases) received intracardiac catheterization within 7 days of these multiple isotope dilution studies; the left ventricular ejection fraction (EF) was calculated using Dodge's method. 12

**RESULTS**

The average age and gender composition of the 4 groups (normal, class I, class II & III and CHF), together with the sodium and potassium concentrations in plasma and urine are shown in Table 1. There were no significant differences in the sodium and potassium concentrations of plasma and urine, except in the CHF group where plasma sodium concentrations were low.

Values of Nae per body surface area (Nae/BSA) of normal subjects (1531.4 ± 67.4, mean ± S.E.M.) were lower than those of the other groups and increased in the following order;
Fig. 2. Total body water to body surface area (TBW/BSA, L/m²) shown in the left figure and total exchangeable sodium to total exchangeable potassium (Nae/Ke) shown in the right figure measured by multiple isotope dilution method in normal healthy subjects, and patients with AMI and CHF. Values are shown as mean ± S.E.M. and p value are examined. Abbreviations: N = Normal healthy patients; C I = Patients with AMI assigned class I according to KILLIP T et al; C II & III = Patients with AMI class II and III according to KILLIP T et al; CHF = Patients with congestive heart failure due to valvular disease and idiopathic dilated cardiomyopathy.

Fig. 3. Relations between total exchangeable sodium per body surface area (Nae/BSA, mEq/m²) and left ventricular ejection fraction (E.F., %) (left), and total exchangeable potassium per body surface area (Ke/BSA, mEq/m²) and E.F. (right) in 20 patients with AMI.

class I, 1839.8 ± 54.3; class II & III, 2396.1 ± 88.1; and CHF, 3367.8 ± 424.1 mEq/m². All mutual significant Nae/BSA differences among the groups are as shown in Fig. 1.

In comparison with normal subjects (900.5 ± 49.6 mEq/m²), Ke/BSA progressively decreased in class I (661.3 ± 54.3), class II & III (638.5 ± 61.5) and CHF (521.2 ± 42.8). Ke/BSA in the CHF group was significantly lower than that in class I (Fig. 1).

There was no significant difference in TBW/BSA between normal healthy subjects (17.9 ± 0.7) and class I (18.5 ± 0.6 L/m²). TBW/BSA of both class II & III (23.1 ± 1.0) and CHF
Body Fluid Composition in AMI

(24.4 ± 1.2 L/m²) were abnormally elevated (Fig. 2).

As shown in Fig. 2, progressive elevations of Nae/Ke in the normal, class I, class II & III and CHF groups were 1.74 ± 0.10, 3.18 ± 0.26, 4.20 ± 0.41 and 5.58 ± 0.99, respectively. There were significant mutual disparities among the groups, except between the class II & III and CHF.

The EF was negative-correlated with both Nae/BSA (r = -0.60) and TBW (r = -0.45), while there was a positive relationship (r = 0.71) between EF and Ke/BSA in the 20 patients with AMI who received intracardiac catheterizations. (See Fig. 3)

Plasma ADH was elevated along with both the increase of Nae (r = 0.47) and TBW (r = 0.40). Plasma aldosterone was slightly positive-correlated with the amount of urine potassium (r = 0.48).

DISCUSSION

AMI with severe chest pain, arrhythmia and heart failure is associated with transmural or non-transmural necrotic changes of the myocardium. The necrotic myocardium gradually replaces fibrous tissues, accompanied by more or less reduced cardiac function and regional myocardial immobility. In our patients with AMI fitting Killip's class I to III, as previously described, the plasma levels of sodium and potassium determined by flame-photometry were within normal limits.

The Nae, Ke and TBW levels estimated in this study were fairly invariable and reliable, and were consistent with other studies. The Nae, Ke and TBW determinations showed a clear distinction between the patients with AMI and normal healthy subjects. As the cardiac functions deteriorated, the Nae per BSA increased in the following order: (1) normal, (2) class I, (3) class II & III, and (4) CHF.

A contrary downward slope of Ke/BSA was observed in the same order. The decrease of Ke/BSA in class II & III was interpreted as follows: First, the increase of kidney potassium excretion, which is secondarily involved in the stimulated hormonal systems of renin, angiotensins and aldosterone. Second, a concomitant fall of body potassium with loss of body cell mass, which contributes to the severity of cardiac dysfunction as shown by White et al. The extracellular fluid from which body cell mass can be inferred was not determined in this study. Those findings validate Killip's AMI classification and suggest that in patients with AMI, body fluid composition remains unbalanced in spite of asymptomatic states. Marked body potassium depletion in patients with CHF taking furosemide was assumed to be caused by furosemide therapy in addition to profound heart failure.

Studies have shown that Nae/TBW in edematous and non-edematous patients with CHF is higher than that in edematous patients due to hepatic and renal failure. Farber et al concluded that this increase of Nae is based on increased levels of sodium in the intracellular space as well as extracellular space. The elevations of Nae/BSA in class II & III patients with AMI in our study were very marked, almost equaling the levels in patients with CHF. Furthermore, a significant elevation of TBW/BSA appeared in non-edematous class II & III patients with AMI as well as in the CHF group. A possible explanation for this is the massive sodium retention, and water retention in intra- and extra-cellular spaces, that occurred in patients with AMI.

It is important to note that even in class I patients with AMI, whose cardiac functions were not so reduced, an increase in Nae/BSA and decrease in Ke/BSA were found. Thus, body electrolyte composition remains affected for long periods in class I patients with AMI, and their stabilized conditions could turn for the worse. At the same time, the increase in TBW/BSA of class I patients with AMI did not match the Nae/BSA increase. Therefore, it is likely that sodium accumulation exceeds that of water, and that body fluid disorders are due primarily to electrolyte accumulation, rather than water retention. However, in the AMI patients at 1–2 months after onset, it is a difficult to choose between sodium and water for an initial fluid disorder evoked immediately after onset.

In heart failure, reduced myocardial contractility is regarded as the most likely cause of sodium and water retention by the kidneys. This can be explained by the following theory of diminished "effective" plasma volume. The kidneys perceive the reflexion of the left atrium volume receptor, which detects impaired cardiac pumping. This causes the kidneys to retain sodium and water, as though plasma volume were diminished, even when the actual volume may be normal or high. In class I patients with AMI, who showed no signs of CHF and were presumed to be mildly impaired, the cause of sodium re-

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tention, as observed by the Nae/TBW increase, is attributable to the immobile infarcted myocardium, in spite of the small size of damaged area.

It is commonly accepted that worsening cardiac pump function causes much sodium and water retention in kidneys. Thus, it is not surprising that we found a negative correlation ($r = -0.60$) between Nae/BSA and the EF, and a positive correlation ($r = 0.71$) between Ke/BSA and the EF in our patients with AMI. Regarding plasma aldosterone and ADH, it is of secondary importance to evaluate the roles of Nae, Ke and TBW from the weak correlations among them.

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