Potassium, Sodium and Magnesium Contents in Skeletal Muscle of Renal Stone-Formers: A Study in an Area of Low Potassium Intake†

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Abstract

Skeletal muscles surgically obtained from the stone-former group (external oblique muscle; n = 202, 82 males & 120 females), control group I (external oblique muscle; n = 5, all males), control group II (rectus abdominis muscle; n = 23, all females) and control group III (quadriceps femoris muscle; n = 11, all males) were analyzed for potassium (K), sodium (Na) and magnesium (Mg) contents. Muscle samples were digested with 65 per cent HNO_3 and determined for K, Na and Mg by an atomic absorption spectrophotometer. The results of analysis showed the mean K, Na and Mg (±S.D.) contents in µmol per one gram of fresh tissue of the stone-former group, control groups I, II and III were 73.5±16.6, 51.3±13.4 and 6.6±1.3, 77.5±3.9, 43.9±9.9 and 7.2±0.5, 83.8±27.5, 49.4±24.1 and 6.7±1.8 and 85.0±17.1, 48.5±12.1 and 6.8±1.3. Among these variables, only the K content of control group III was higher significantly ($p<0.05$) than that of the stone-former group. In the stone-former group, regression analysis showed significant correlations between K and Mg contents ($r = 0.856$, $p < 0.001$) and K and Na contents ($r = -0.325$, $p < 0.001$). Due to no available data of the external oblique, we made a comparison of our results to the soleus type of skeletal muscle of normal subjects reported by Dorup *et al* and found that the external oblique muscle had lower mean contents of K and Mg but a higher Na content than those of the soleus. Our results were similar to the K and Mg depleted muscles obtained from the patients receiving long-term treatment with diuretic drugs. The results suggest that most of our subjects in both the stone-former and the 3 control groups were in a state of K and Mg depletion. The causes may be multifactorial, for instance low intake, high sweat loss and the existence of environmental inhibitor (s) for K transport like vanadium.

Key word : Muscle Potassium, Muscle Sodium, Muscle Magnesium, Renal Stone-Formers

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Data on blood and urine biochemistry revealed that people in the rural northeast of Thailand might be in a state of K depletion(1-3). This is further supported in part by the results of a K balance study, where its high positive value suggested there was a physiological retention of K compensating for the body K deficit(3). The environmental temperature in this region is always above 30°C, especially during the hot season. Thus, a considerable amount of K loss *via* sweat is inevitable(3). Since people in this region have a very low K intake(2), its combination with high K loss *via* sweat would further aggravate their K status. We, therefore, were interested in performing analysis directly for the K content of their skeletal muscles, the main reservoir of body K(4,5). In human subjects, Mg and K contents of skeletal muscle are closely correlated(6-8). This is because Mg regulates the transport of K across the cell membrane through controlling the Na, K-ATPase activity(9). The enzyme uses Mg as a cofactor, and transports $2K^+$ into the cell in exchange for $3Na^+$ out of the cell. Therefore, the metabolism of K, Mg, and Na are intimately interrelated in that Mg deficiency would finally cause a decrease in cellular K and an intracellular accumulation of Na. In this communication, therefore, the data of Mg and Na contents of the studied muscle specimens are also shown.

SUBJECTS AND METHOD

This research project was approved by the Faculty of Medicine Ethical Committee, and all subjects gave informed consent before inclusion into the project.

Muscle specimens and the subjects

There were four groups of participating subjects, a stone-former group and three control groups. Since we were unable to obtain muscle specimens from completely normal healthy subjects, we decided to use subjects with renal tumor as control group I, ovarian tumor or myoma uterus as control group II and a bone fracture from an accident as control group III (after healing of the bone fracture, they were re-admitted to the hospital to remove fixed plates and screws). A muscle piece of about 0.1-0.2 g was surgically removed during the operations on each subject and kept frozen until analysis. While the external oblique muscle type was obtained from stone-former and control group I subjects, the rectus abdominis and quadriceps femoris types were from control groups II and III, respectively. Only muscle specimens obtatined by the author S.B. during the year 1997-1998 at the Khon Kaen Regional Hospital were collected.

K, Na and Mg analysis

The muscle specimens, after thawing, were placed on filter papers to blot off excess fluid and contaminated blood. The samples were dissected, while lying on the papers, free of visible fat and connective tissues. They were cut into 2-4 small pieces of about 0.02-0.05 g. These muscle samples were then weighed and transfered into conical 15 ml centrifuge tubes containing 0.5 ml of 65 per cent HNO_3 (analytical grade). The samples were then digested by heating in a water bath for about 5 min. After cooling, the HNO_3 digested samples were then diluted to 10 ml with deionized water. The diluted samples were centrifuged briefly, and then determined for K, Na, and Mg using an atomic absorption spectrophotometer(10). To minimize any contamination that might occur, the muscle samples were digested, diluted, and centrifuged in the same centrifuge tubes.

RESULTS

Details of subjects & sites of stone in urinary tract

Some details of the participants in all study groups are shown in Table 1. They comprised 202 stone-former patients (120 females, 82 males) and 5 males, 23 females and 11 males of control groups I, II and III, respectively. Their age and body weight were not significantly different. Furthermore, with regard to body K status, their serum K levels were all in the normal range. Though the difference in percentage of hypokalemic serum was clearly seen among groups, i.e., from 0 per cent in the control group I to as high as 20 per cent in the stone-former group, this probably reflected a great difference in population size among groups. Their main occupation as subsistence farmer clearly indicated that they were from rural communities.

For the stone-former group, the majority of them had a stone at one site of the urinary tract, i.e., kidney (renal calculi, RC), ureter (ureteric calculi, UC) or bladder (vesicle calculi, VC).

K, Na, and Mg contents of the muscles

The results of muscle analysis for K, Na and Mg contents, expressed as means (±S.D.) in

Table 1. Descriptions of studied subjects and sites of stones found in urinary tract.

	Stone-former subjects			Control subjects		
	Male	Female	Total	Group 1, male	Group 2, female	Group 3, male
No. of cases	82	120	202	5	23	11
Age, year, mean±S.D.	45.2±12.8	40.8±13.4	42.6±13.2	47±6	48.4±10	42.2±9
Weight, Kg, mean±S.D.	57.8±9.8	52.7±8.8	54.8±9.2	57±6	58.3±9	55.3±11
Serum, mEq/L, mean±S.D.	3.9±0.4	3.9±0.4	3.9±0.4	4.0±0.3	3.9±0.5	4.1±0.3
% Hypokalemia	11.42	20.50	10.96	0	6.22	8.11
Occupation						
Subsistence farmer	68	113	181	3	15	8
Labourer	2	2	4	-	6	2
Other	12	5	17	2	2	1
No. of stone sites						
One site (RC/UC/VC)*	54 (66%)	92(77%)	146 (72%)	-	-	-
Two sites (Bilat RC/Bilat UC/UC+VC /RC+UC/RC+VC)*	26 (32%)	26 (21%)	52 (26%)	-	-	-
Three sites (RC+UC+VC/Bilat RC+UC)*	2 (2%)	2 (2%)	4 (2%)	-	-	-

* RC, renal calculi ; UC, ureteric calculi ; VC, vesicle calculi ; Bilat RC, bilateral renal calculi.

Table 2. Means (±SD) of K, Na and Mg contents of skeletal muscle obtained from stone-former and three control groups.

Subjects (muscle type)	Mean ± SD, µmol / g wet wt		
	K	Na	Mg
Stone –former (external oblique)			
Male (n = 82)	76.9±16.4	49.3±12.6	6.9±1.2
Female (n = 120)	72.4±18.2	53.8±13.6	6.4±1.3
Total (n = 202)	73.5±16.6	51.3±13.4	6.6±1.3
Controls			
Group I (external oblique, n = 5)	77.5±3.9	43.9±9.9	7.2±0.5
Group II (rectus abdominis, n = 23)	83.8±27.5	49.4±24.1	6.7±1.8
Group III (quadriceps femoris, n = 11)	85.0±17.1*	48.5±12.1	6.8±1.3

* VS stone-former, $p < 0.05$

µmol / g wet wt, are shown in Table 2. In comparison among groups for these mean values, only the K content of the control group III (85.0±17.1) was significantly higher ($p<0.05$) than those of the stone-former group (73.5±16.6).

Fig. 1 shows the distribution of oblique muscle K, Na, and Mg contents in comparison with the corresponding mean values of the soleus muscle reported by Dorup et al(6). There were 25 (12.38%), 12 (5.94%) and 198 (98.02%) specimens of the oblique muscle which had K, Mg and Na contents equal to or higher than those of the soleus muscle.

Further comparison with other data is also made and shown in Table 3, where our mean values of K and Mg contents of the oblique muscle of all groups were compatible with the values found in the muscles of those subjects on long-term diuretc treatment(6-8).

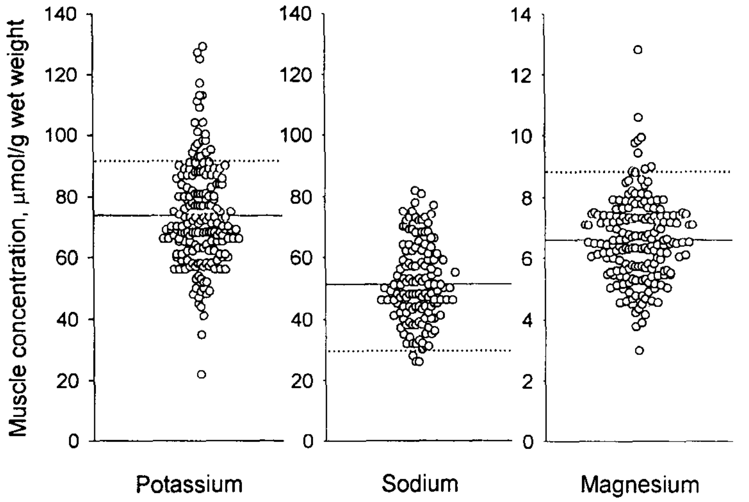

Fig. 1. Distribution of potassium, sodium and magnesium contents of external oblique muscles obtained from 202 stone-formers. Horizontal solid lines are means of each content. For comparison, means of the corresponding parameters of the soleus muscle reported by Dorup et al[8] are also shown (dotted lines).

Table 3. Comparison of K and Mg contents of the skeletal muscles of this study with other reports. The muscle specimens were obtained from patients receiving long-term diuretic treatment for arterial hypertension (AHT), congestive heart failure (CHF), control (CT), and stone-former (ST) subjects.

Study	Mg (µmol/g wet wt)				K (µmol/g wet wt)				Muscle type
	CT	AHT	CHF	ST	CT	AHT	CHF	ST	
Dyckner & Wester, 1978 (7)	9.3	8.1	7.9	-	92.0	80.8	77.5	-	Vastus lateralis
Dorup et al, 1988 (10)	9.5	8	7	-	91.7	77.7	69.4	-	Vastus lateralis
Dorup & Clausen, 1998 (6)	9.5	5.8	-	-	91	59.7	-	-	Vastus lateralis
Dorup et al, 1993 (8)	9.3	7.9	7.4	-	92.2	78.7	76.2	-	Vastus lateralis
This report	7.2	-	-	6.6	77.5	-	-	73.5	External Oblique
	6.7	-	-	-	83.8	-	-	-	Rectus abdominis
	6.8	-	-	-	85.0	-	-	-	Quadriceps femoris

Relations between K and Mg and K and Na

It is well recognized that the cellular regulation of these three electrolytes is closely interrelated[6,7]. Regression analysis for the stone-former group showed significant correlation between the muscle contents of K and Mg ($r = 0.856$, $p < 0.001$) as well as K and Na ($r = -0.325$, $p < 0.001$) as shown in Fig. 2 and 3, respectively. No correlation was observed either between the muscle Na and Mg contents, as well as serum K and the muscle K content. These observations were similar to those reported by others[6,7].

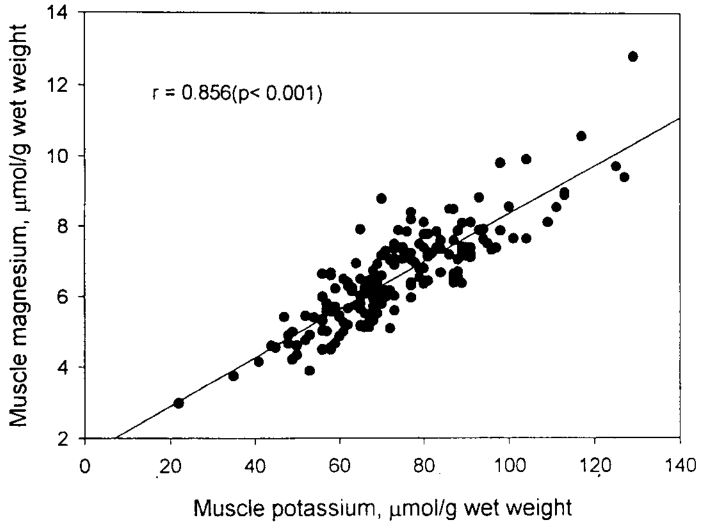

Fig. 2. Relationship between potassium and magnesium contents of the external oblique muscles obtained from 202 stone-formers.

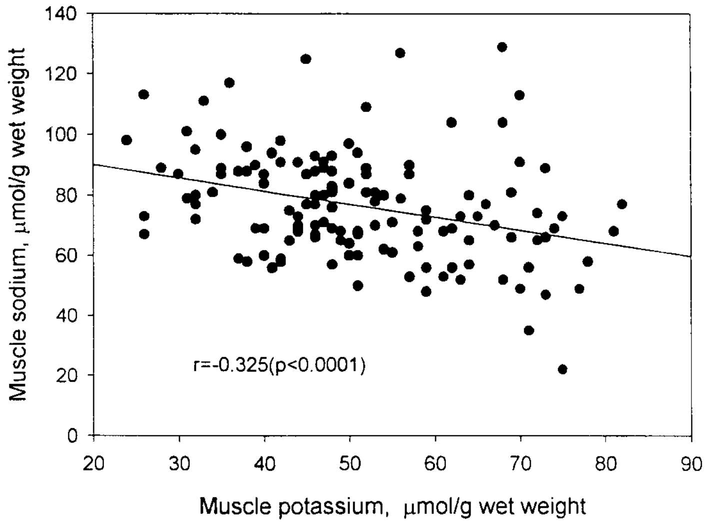

Fig. 3. Relationship between sodium and potassium contents of the external oblique muscles obtained from 202 stone-formers.

DISCUSSION

Though the main store of K in the body is skeletal muscle, variation in K contents between different sites and muscle groups has been clearly demonstrated(10-14). In human subjects, Dorup *et al*(6) showed that fast-twitch muscle had significantly more K and Mg content than the low-twitch one. Since we used the external oblique type as a representative for the skeletal muscle and there is no existing data on K & Mg contents of this muscle type, we, therefore, compared the results with the data of the same low-twitch muscle, i.e. the soleus (6-10). We found that the mean values of K and Mg content of the external oblique muscle of our stone subjects were much lower. The results suggest that most of our stone subjects had both low K and Mg content in their skeletal muscles, at least of the external oblique type. For K, the findings are compatible with our previous data, which showed that people in this region had low K intake, high sweat K loss[2] and frequently a high prevalence of hypokalemia and hypokaliuria[1-3]. It has been demonstrated that individual tissues of experimental rats vary in their susceptibility to dietary deficiency of K, with skeletal muscle being most severely affected (e.g. K in thigh muscle reduced by 48 per cent upon feeding with K deficient fodder for two weeks), whereas the liver and brain were apparently unaffected[11,12]. If this is true for human subjects, it therefore suggests that low intake is an important cause for K depletion seen in the external oblique muscle of our subjects. If we compared the results with other reports (Table 3), K and Mg contents in the muscle of our stone subjects were similar to those of the K and Mg depleted muscles commonly found among the long-term diuretic treatment patients[7,8]. Our control subjects of all three groups, in general, also showed similar results. Though the mean K content of control group II was higher and that of control group III significantly higher than that of the stone-former group, all these mean K values were still lower than those reported by others[7,8,10]. The variability in K content seen among these control groups most probably reflects their difference in muscle types studied, as observed by others[10,13,14]. These findings suggest that all groups of our subjects were affected similarly by the same environmental factors causing K depletion. The results supported our previous repeated observations that both stone and normal subjects residing in the same rural area had similar blood and urine biochemistry[1-3]. It has been demonstrated that an animal fed Mg-deficient fodder showed reduced concentrations of not only Mg but also K in muscle[6]. The low Mg content in the muscles of our subjects, therefore, further suggested that the cause of K depletion was not only from the low intake but probably also secondary to Mg deficiency. To confirm this role of Mg, its intake and excretion among these people should also be assessed in future studies.

The fact that Mg deficiency is followed by K deficiency indicates that Mg plays a regulatory role for cellular K homeostasis[6]. Transportation of K across the membrane is an active process requiring Na, K-ATPase activity and Mg as the cofactor[9]. For each ATP hydrolysis, the process moves 2 K^+ inward in exchange for the 3Na^+ outward from the cell. Thus cellular depletion of Mg could lower the enzyme activity resulting in decreased cellular K with a concomitant accumulating of Na intracellularly. Our findings of the unusually high muscle Na content and the significant reverse relationship between Na and K contents supported the hypothesis. Analysis of cadavers has also shown that the K depletion is associated with an increase in total body Na regardless of the presence or absence of edema[15]. If this is true, K depletion secondary to Mg deficiency should be associated with urinary K wasting due to the low activity of Na,K-ATPase. In our case, however, low urinary K excretion was always seen in both normal and stone-formers[1-3], which already confirmed our data of the low K intake[2].

In our previous reports we frequently showed that erythrocyte Na,K-ATPase in certain northeast Thai population groups was both low in activity and in number[16-18]. Vanadium (V) is known to inhibit various enzymes including H, K-ATPase and Na, K-ATPase[19] and the level of this trace element is high in the soil of the northeast region of Thailand. A considerable amount of V was also detected in the urine and the tissues of people in this region[20]. Sitprija *et al* have postulated that certain metabolic diseases commonly found in this area are probably attributed to the inhibition of Na, K-ATPase and H, K-ATPase activity by V[21]. Recently, in studies among 7 Thai population groups, Tosukhowong *et al* demonstrated that a group of adult males from the northeast region had a low activity of erythrocyte Na, K-ATPase and suggested an acquired disorder probably from the inhibititory effect of V or other unknown inhibitor (s)[17]. The role of the inhibitor, therefore, was another potential contributing factor causing K depletion among the northeastern Thai population.

In conclusion, the causes of K depletion among our subjects are probably multifactorial; including low K intake, Mg depletion, the presence of natural inhibitor (s) for K transportation and finally high sweat K loss. Though the effects of inhibitor (s) cannot be overcome, to improve their K status, people residing in this area should be encouraged to take not only food with high K[22,23], but also high Mg content[23]. Extra supplements of both electrolytes should be taken for the groups of people who potentially sweat highly, i.e. construction workers, farmers and other labourers. In the literature, these people were the high risk groups reported to have a high prevalence of those metabolic diseases commonly found in the region(20,21).

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ปริมาณโปแทสเซียม โซเดียมและแมกนีเซียมในกล้ามเนื้อลายของผู้ป่วยโรคนิ่วไต : กรณีศึกษาในพื้นที่ที่ได้รับโปแทสเซียมในอาหารต่ำ

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ได้ทำการวิเคราะห์หาปริมาณโปแทสเซียมในกล้ามเนื้อลายที่ได้จากการผ่าตัดของกลุ่มผู้ป่วยโรคนิ่วไต (กล้ามเนื้อ external oblique จำนวน 202 ชิ้น จากผู้ป่วย 82 รายและผู้หญิง 120 ราย) กลุ่มเปรียบเทียบที่ 1 (กล้ามเนื้อ external oblique จำนวน 5 ชิ้น จากผู้ชายทั้งหมด) กลุ่มเปรียบเทียบที่ 2 (กล้ามเนื้อ rectus abdominis จำนวน 23 ชิ้นจากผู้หญิงทั้งหมด) และกลุ่มเปรียบเทียบที่ 3 (กล้ามเนื้อ quadriceps femoris จำนวน 11 ชิ้น จากผู้ชายทั้งหมด) ทำการย่อยสลายตัวอย่างชิ้นเนื้อด้วยกรดไนตริก (HNO_3) 65% แล้ววัดหาระดับโปแทสเซียม โซเดียม และแมกนีเซียม ด้วยเครื่อง atomic absorption spectrophotometer ผลการวิเคราะห์พบว่าในตัวอย่างชิ้นเนื้อสด 1 กรัม มีปริมาณเฉลี่ย (±S.D.) ของโปแทสเซียม โซเดียมและแมกนีเซียมตามลำดับคิดเป็นจำนวนไมโครโมลเท่ากับ 73.5±16.6, 51.3±13.4 และ 6.6±1.3 สำหรับกลุ่มผู้ป่วยโรคนิ่วไตเท่ากับ 77.5±3.9, 43.9±9.9 และ 7.2±0.5 สำหรับกลุ่มเปรียบเทียบที่ 1 เท่ากับ 83.8±27.5, 49.4±24.1 และ 6.7±1.8 สำหรับกลุ่มเปรียบเทียบที่ 2 และ เท่ากับ 85.0±17.1, 48.5±12.1 และ 6.8±1.3 สำหรับกลุ่มเปรียบเทียบที่ 3 การวิเคราะห์ทางสถิติพบว่าเฉพาะค่าเฉลี่ยของปริมาณโปแทสเซียมของกลุ่มเปรียบเทียบที่ 3 มีค่าสูงกว่าของกลุ่มผู้ป่วยนิ่วไตอย่างมีนัยสำคัญทางสถิติ ($p<0.05$) ในกลุ่มผู้ป่วยนิ่วไตเองพบว่าค่าโปแทสเซียมมีความสัมพันธ์กันเชิงบวกกับค่าแมกนีเซียม ($r = 0.856$, $p < 0.001$) ในขณะที่ค่าโปแทสเซียมมีความสัมพันธ์กันเชิงลบกับค่าโซเดียม ($r = -0.325$, $p<0.001$) เนื่องจากยังไม่เคยมีรายงานมาก่อนเกี่ยวกับการวิเคราะห์กล้ามเนื้อลายชนิดนี้ คณะวิจัยจึงทำการเปรียบเทียบผลที่ได้กับกล้ามเนื้อลายชนิด soleus ของคนปกติ ที่รายงานโดย Dorup et al ซึ่งก็พบว่าค่าเฉลี่ยของโปแทสเซียมและแมกนีเซียมของกล้ามเนื้อลายชนิด external oblique มีค่าต่ำกว่าของชนิด soleus ชัดเจน ส่วนค่าโซเดียมก็สูงกว่าอย่างเห็นได้ชัด โดยผลของการวิเคราะห์กล้ามเนื้อในการศึกษาครั้งนี้จะคล้ายกับของกล้ามเนื้อที่ขาดโปแทสเซียมและแมกนีเซียมในผู้ป่วยโรคความดันโลหิตสูงที่ได้รับยาขับปัสสาวะเป็นระยะเวลานาน ๆ ผลการศึกษาในครั้งนี้จึงเป็นการชี้ให้เห็นว่าประชากรที่นำมาศึกษาทั้งกลุ่มผู้ป่วยนิ่วไตและกลุ่มเปรียบเทียบทั้ง 3 กลุ่มต่างกำลังอยู่ในภาวะพร่องทั้งโปแทสเซียมและแมกนีเซียมเป็นส่วนใหญ่ซึ่งสาเหตุน่าจะมาจากหลาย ๆ ปัจจัย เช่น ได้รับแร่ธาตุทั้งสองจากอาหารน้อย มีการสูญเสียไปทางเหงื่อสูง รวมทั้งอาจมีสารยับยั้งในธรรมชาติไปยับยั้งกระบวนการขนย้ายโปแทสเซียมเข้าสู่เซลล์ เช่น แร่ธาตุแวนาเดียม

คำสำคัญ : โปแทสเซียมในกล้ามเนื้อ, โซเดียมในกล้ามเนื้อ, แมกนีเซียมในกล้ามเนื้อ, โรคนิ่วไต

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