Measuring partial body potassium in the legs of patients with spinal cord injury: a new approach

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Wielopolski L, Ramirez LM, Spungen AM, Swaby S, Asselin P, Bauman WA. Measuring partial body potassium in the legs of patients with spinal cord injury: a new approach. J Appl Physiol 106: 268–273, 2009. First published November 20, 2008; doi:10.1152/japplphysiol.90435.2008.—Patients with acute spinal cord injury (SCI) with paralysis experience rapid and marked muscle atrophy below the level of the lesion. Muscle is lost above the lesion due to enforced bed rest associated with immobilization. Presently, there is no viable method to quantify muscle loss between the time of injury to the initiation of rehabilitation and remobilization. Furthermore, to assess the efficacy of any physical or pharmacological intervention necessitates the ability to accurately determine the impact of these treatments on muscle mass and function. Our results are presented from measurements of regional potassium (K) in the legs of persons with chronic SCI. The intracellular body K, comprising ~97% of the total body K, is indicative of the metabolically active cell mass, of which over 50% is located in the skeletal muscle (SM). To assess regional variations in SM mass in the legs, a partial body K (PBK) system designed for this purpose was placed on a potentially mobile cart. The SM mass measured by PBK in an able-bodied control cohort (n = 17) and in patients with chronic SCI (n = 21) was 17.6 ± 0.86 and 11.0 ± 0.65 kg, respectively, a difference of ~37.5%. However, the difference in the lean tissue mass of the legs obtained by dual-energy absorptiometry (DXA) in the same cohorts was 20.5 ± 0.86 and 15.5 ± 0.88 kg, respectively, or a difference of ~24.4%. PBK offers a novel approach to obtain regional K measurements in the legs, thus allowing the potential for early and serial assessment of muscle loss in SCI subjects during the acute and subacute periods following paralysis. The basic characteristics and performance of our PBK system and our calibration procedure are described in this preliminary report.

Because of the difficulties of undertaking sophisticated regional body composition analysis immediately after the catastrophic traumatic event, there is limited knowledge of the soft-tissue changes. In longitudinal studies of 31 SCI patients using dual-energy x-ray absorptiometry (DXA), Wilmet et al. (26) found that there was a rapid 15% decrease in lean mass of the legs within 1 year; notably, patients with spastic paralysis, in which motor control is nonvoluntary, lost less lean mass in their legs than did those with flaccid paralysis. Patients realized a 30% increase in lean mass in the arms after 6 mo of rehabilitation (26); however, because initial measurements were made ~10 wk after the acute event, this apparent increase may have been the result of an equivalent loss (i.e., 30%) in LT immediately postinjury. Spungen et al. (19) using DXA studied monozygotic twins discordant for chronic SCI and found no difference in the lean (or fat) tissue in the arms of the twin pairs, also supporting the likely possibility that the increase in the LT of the arms reported by Wilmet et al. (26) was merely a return to baseline/preinjury status. Rossier et al. (14) studied 17 subjects with SCI within 1 mo after injury and again 2 to 12 mo later demonstrated a significant depletion of potassium and loss of weight of lean body mass. Individuals with chronic SCI have a lower energy expenditure that is directly related to the level of neurological deficit and their LT mass. Spungen et al. (17, 18) reported a relationship between metabolic rate and body cell mass in 12 SCI patients. The greater the loss of lean body tissue, the greater the decline in their resting metabolic rate (19). Mollinger et al. (9) also described a 12–29% reduction from the predicted values for basal energy expenditure (BEE) in 48 people with SCI; those with higher levels of injury and, presumably, less LT mass exhibited the larger reductions in BEE.

In acute stress, nitrogen wasting may occur despite aggressive nutritional support. Streat et al. (20) reported that eight patients with sepsis in an intensive care unit who received ample caloric and protein intake lost 1.5 kg of body protein over 10 days. This study and others strongly suggest that there may be substantial losses in lean body tissue during severe states of stress or injury. In such catabolic states, endogenous anabolic hormones, growth hormone, and testosterone are markedly depressed. These anabolic hormone levels are also low in persons with acute and chronic SCI (1, 3, 4, 10, 21, 22). Thus an unfavorable metabolic milieu may contribute to the loss of muscle tissue caused by paralysis and immobilization.

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Preliminary results of a comparison of two cohorts: healthy SCI would be beneficial in devising and testing treatments to preserve muscle mass.

Potassium (K) is an essential element in the human body, totaling ~140 g in adults (16), of which ~97% is intracellular. To maintain the proper potential of the cell membrane, the amount of K is tightly controlled homeostatically and is distributed uniformly within the metabolically active cells (16). Consequently, K is a very good indicator of the body cell mass (BCM) and of intracellular water (11). We propose to use regional potassium measurements of the legs to directly measure the BCM and the changes in the SM mass affected by the SCI. Our partial body potassium (PBK) system is mounted on a cart and in the future has the potential to be wheeled beside the patient’s bed; Wielopolski et al. (25) earlier constructed a stationary system for measuring K in the arm. We demonstrate here the suitability of our leg PBK system and report the preliminary results of a comparison of two cohorts: healthy controls and patients with chronic SCI.

METHODS

Subjects. Volunteers were drawn from three groups: 17 healthy able-bodied subjects, 10 subjects with paraplegia, and 11 subjects with tetraplegia. These last two cohorts were analyzed separately and as a single combined SCI group. The groups were of similar age and weight; time after injury (duration of injury, DOI) and body mass index (BMI) are also presented (Table 1). There were four obese subjects in both the control (BMI > 30 kg/m²) and SCI (BMI > 26 kg/m²) groups (17, 23). The study was approved by the Institutional Review Board of the James J. Peters Veterans Affairs Medical Center, and informed consent was obtained from subjects before initiating the testing.

Potassium measurement and analysis. Potassium measurement is based on the long-lived, ~10^9-yr half-life, natural radioisotope ^{40}K that is in a dynamic equilibrium of 0.0117% with the two stable isotopes of K, viz., ^{39}K and ^{41}K (2). A complex decay scheme to the ground state of ^{40}Ar emits isotopically monoenergetic 1.46-MeV gamma rays at a rate of ~200 gamma rays/s per gram of natural K. In our mobile PBK system, gamma rays are detected by four standard thallium-doped sodium iodide (NaI[Tl]) detectors that form a detection cavity and stand in a lead shielding block that reduces the background radiation. The system is mounted on a cart that is adjacent to the lower end of a bed. The positioning tray for the subject has been inserted into the counting chamber. A setup for partial body potassium measurement of the legs (thighs and calves) filled with deionized water placed inside the detection cavity and stand in a lead shielding block that reduces the background radiation. The system is mounted on a cart that is adjacent to the lower end of a bed. The positioning tray for the subject has been inserted into the counting chamber.

Innovative Methodology

Partial Body Potassium in the Legs in SCI

Fig. 1. A setup for partial body potassium measurement of the legs. The system is mounted on a cart that is adjacent to the lower end of a bed. The positioning tray for the subject has been inserted into the counting chamber.

Table 1. Demographic characteristics of the control, SCI-paraplegia, SCI-tetraplegia, and SCI-combined groups

<table>
<thead>
<tr>
<th></th>
<th>Controls (n = 17)</th>
<th>SCI-Paraplegia (n = 10)</th>
<th>SCI-Tetraplegia (n = 11)</th>
<th>SCI-Combined (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, yr</strong></td>
<td>43.7</td>
<td>52.5</td>
<td>50.2</td>
<td>51.3</td>
</tr>
<tr>
<td><strong>DOI, yr</strong></td>
<td></td>
<td>10.6</td>
<td>13.5</td>
<td>12.0</td>
</tr>
<tr>
<td><strong>Weight, kg</strong></td>
<td>86.6</td>
<td>29–65</td>
<td>23–71</td>
<td>23–71</td>
</tr>
<tr>
<td><strong>BMI, kg/m²</strong></td>
<td>28.0</td>
<td>16.8</td>
<td>20.5–36.9</td>
<td>18.6–36.9</td>
</tr>
</tbody>
</table>

SCI, spinal cord injury; DOI, duration of injury; BMI, body mass index. SCI-combined group refers to SCI subjects with paraplegia and SCI subjects with tetraplegia.
converted into grams potassium in the legs by dividing \( K_N \) by the slope of the calibration line

\[
K_{\text{Legs}} = \frac{K_N}{m_{\text{cal}}}
\]  

Thus evaluated, the net potassium signal is proportional to the potassium mass in subject’s legs that subsequently is converted into the SM mass. The linearity of the signal with K content has been published elsewhere and is not discussed here (5, 12, 15).

Similarly, in a preliminary attempt to study the effect of obesity on the K signal, a 2.5-cm-thick cylinder filled with plain water was mounted around each leg of a BOMAB phantom, simulating a layer of fat in which K is not present.

Finally, we compared PBK results with those obtained from DXA. For this purpose the DXA images were acquired on a GE Lunar Prodigy Advance DXA. (GE Lunar enCore2004, version 8.8, Madison, WI). Software algorithms were applied to isolate the legs’ ROI for quantification of LT mass. The legs were graphically displayed, and the operator adjusted the final cut lines on each subject. All cuts were performed by a single investigator to avoid interrater variability.

RESULTS

Because the natural background may fluctuate, we monitored the reproducibility of the background in a single location and the net K counts from a phantom for a year. We noticed that one of the detectors was misaligned and because the four detectors are connected to a summing amplifier, small fluctuations affected the counts between two fixed channels. Once the detector was aligned with the other detectors, there was a significant reduction in the percent standard deviation (SD) by a factor of five. The plots with the results are displayed where the mean and SD in the ROI for the period following alignment are 19,804 ± 399, 37,257 ± 572, and 17,495 ± 522, respectively, for the background, total, and net counts (Fig. 4). Figure 4 also plots the means and the SDs before the alignment; the reduction in the SD is apparent by comparing the daily background counts before and after alignment. For a mobile system, the background may also vary from room to room.

To evaluate for obesity, we wrapped the phantom with a 2.5-cm layer of insulating water, a fraction of the K gamma rays emitted from the leg scatter in this extra outer layer losing energy and registering in the Compton region (see Fig. 2). Thus the losses in the ROI are partially compensated for by gains registered in the Compton region, with some being totally lost due to multiple scatterings. To gauge the scatter, three different set-ups for phantom measurements were obtained: 1) water phantom with an overlay, 2) phantom with K, and 3) phantom with K and an outer layer; the counts of the three energy regions (i.e., Compton, ROI, and HE) for these phantom measurements are presented (Table 2). In this simple...
model, the signal in the ROI is reduced by 36%. However, by combining the Compton and ROI regions, the reduction in the signal is only 20%. Furthermore, the error in the K net counts in the ROI with the overlay, 2.13%, is reduced to 1.30% when using both regions. Finally, using both regions improves the K signal relative to the natural K background, i.e., signal-to-noise ratio improves when using both regions due to availability of more data. Linear attenuation of a narrow photon beam through 2.5 cm of water at K energy lowers the signal only by 14%, clearly underestimating the mean free path length through the outer layer. During these experiments the third HE region above the ROI remains unchanged, demonstrating that there were no changes in the counting system.

The distributions of the SM mass in the legs were determined by PBK, and the LT mass was determined by DXA for control and SCI subjects (Fig. 5). The mean values, SDs, and ranges for PBK and DXA are reported (Table 3). A conversion factor of 3 g K/kg SM, from grams potassium to kilograms skeletal muscle mass (6), was used (Fig. 5; Table 3). We noted that LT mass is slightly larger than the SM mass because of the additional tissues in the former. The SM mass of the legs by PBK was 37.5% lower in the combined SCI group than of the control group ($P < 0.0001$), whereas the difference in LT mass by DXA between SCI and control groups was only 24.4% lower ($P = 0.003$). Similarly, PBK measurements provided greater discrimination between the groups with paraplegia and tetraplegia than did DXA.

Plotting the PBK results against DXA, SM mass by PBK is generally lower than LT mass by DXA, as expected, with the majority of the subjects falling below the 1:1 line (Fig. 6). The values obtained by PBK are approximately 60–90% of the value of the LT mass value by DXA. However, the correlation between PBK and DXA in the combined control and SCI groups is significant ($r^2 = 0.325$ and $P = 0.0002$), albeit weak. We would expect the regression lines to be at least parallel to the 1:1 line, suggesting a possible offset by either PBK or DXA or both. The underestimation of the LT mass by DXA in SCI subjects compared with SM mass by MRI was reported by Modlesky et al. (8). This would skew the regression line in Fig. 6 in the expected direction, that is, more parallel to the 1:1 line. It is appreciated, however, that PBK detectors were over the upper leg whereas the DXA ROI included the proximal and distal leg, from the crotch down.

**DISCUSSION**

The results demonstrated the possibility of using a PBK system for monitoring SM mass in patients with chronic SCI. The difference between SM masses in the SCI and control subjects determined by PBK is ~1.5 times larger (37.5 vs. 24.4%) than that recorded for LT masses by DXA. The PBK
system is passive involving no external radiation, and it capitalizes on radioactive $^{40}$K in equilibrium with natural K as an indicator of the SM mass. By contrast, the DXA system involves external radiation, albeit small. Our present system, which was mounted on a cart, was heavily shielded. However, with further shielding redesign and optimization, it should be possible to make the entire system more flexible to be used at the bedside during the acute and subacute phase of SCI. Data processing for quantitative analysis can be improved using the Compton and ROI regions or, alternatively, using library least-squares (LLS), resulting in a better monitoring system (13). While our experiments with the overlaying water layer in the phantom overestimate the signal’s self-attenuation from that expected in obese subjects, including the Compton region in the analysis lowered the effect of obesity by reduction in signal loss from 36% to 20%. In addition, improvements in spectral analysis using LLS analysis may ease the requirements for loss from 36% to 20%. In summary, a PBK system mounted on a cart for monitoring K of the lower extremities was constructed and applied to persons with chronic SCI and able-bodied controls. The system has the potential to provide immediate, highly specific, and more sensitive monitoring of SM atrophy in immobilized individuals. It is envisioned that this system, unlike DXA and other nonmobile body compositional techniques, may be used at bedside to test the efficacy of a physical or pharmacological intervention to preserve muscle mass immediately after lower extremity paralysis.

GRANTS

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