EXPERIMENTAL ALCOHOLISM INDUCES PHOSPHORUS AND MAGNESIUM DEFICIENCY IN SKELETAL MUSCLE

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INTRODUCTION

Structural, electrochemical and biochemical derangements of skeletal muscle are exceptionally common findings in patients with severe, chronic alcoholism. Collectively, these abnormalities represent alcoholic myopathy. Studies conducted in our laboratories during the past eight years on patients and experimental animals suggest that skeletal muscle is consistently damaged by chronic exposure to ethanol\textsuperscript{1-4}. In brief, prominent findings include a substantial depression of muscle cell phosphorus and magnesium content, while calcium is markedly elevated. As occurs in any injured cell, contents of sodium and chloride are elevated, while potassium tends to be reduced. These changes in muscle cell composition may occur either with or without elevated serum levels of creatine phosphokinase (CPK) activity.

Recently, we have developed a model of chronic alcoholism in the dog which successfully avoids the common problem of malnutrition\textsuperscript{1,5}. Utilizing this model, we have shown derangements of canine skeletal muscle ionic composition after 8 weeks of alcohol ingestion which duplicate the changes seen in skeletal muscle of severe, alcoholic patients. In addition, we have demonstrated that these derangements of skeletal muscle ionic composition were accompanied by increases in active sodium transport of skeletal muscle microsomal preparations\textsuperscript{1,5}.

In the studies reported herein we were interested in ascertaining the effects of more prolonged ethanol consumption on skeletal muscle ionic composition and active sodium transport activity. In particular, we were interested in determining the temporal pat-
terns of skeletal muscle electrolyte and divalent ion compositional changes induced by ethanol in the absence of malnutrition. Since internal sodium and potassium concentrations are regulated by the membrane-bound Na,K-ATPase, the enzymatic equivalent of the sodium pump, we were also interested in determining the temporal relationships between skeletal muscle electrolyte concentrations and active sodium transport. Finally, since active sodium transport requires the expenditure of metabolic energy, we were interested in ascertaining if changes in active sodium transport were supported by changes in skeletal muscle respiration.

METHODS

Eleven healthy dogs (20-30 Kg) were selected for study based on their willingness to consume a nutritious, synthetic diet mixed with ethanol. Only dogs that totally consumed the twice daily portions throughout the twelve days were selected for study. Following the selection process, the dogs were returned to diet plus water for a six week control period. Thereupon the experimental period began with the dogs consuming 3.2 gm ethanol/Kg body weight mixed with diet twice daily.

On the day preceding the period of ethanol administration and again at 1, 2, 3, 4 and 7 months the dogs were anesthetized with sodium thiopental, intubated, and the resting transmembrane electrical potential difference of skeletal muscle cells (Em) was determined in situ using Ling-Gerard type electrodes on the gracilis muscle by techniques previously described. 12-20 individual fiber potentials were obtained for each animal and the average calculated for each measurement. Following the measurement of the membrane potential, muscle samples were obtained from the contralateral gracilis muscle for electrolyte and mineral content, Na,K-ATPase activity, and muscle cell respiration.

Muscle wet, dry and fat-free dry weights and contents of sodium, potassium, chloride, magnesium, calcium and phosphorus were determined as previously described. Total water content of muscle samples was determined gravimetrically on samples after vacuum drying at 80°C. Using the chloride distribution which in turn is calculated from the membrane potential (Em) and extracellular chloride content, the intracellular concentrations of sodium, potassium, and chloride were calculated using previously described equations.

Skeletal muscle microsomal fractions were prepared essentially as described by Asano et al except the second homogenization step was eliminated. The ATPase assay conditions were as previously described except the reaction was carried out in 1.0 ml and terminated by the addition of 0.2 ml of iced 30% TCA. The ortho-