EFFECTS OF HYPERTHYROIDISM ON GLUCOSE, GLUTAMINE AND KETONE-BODY METABOLISM IN THE GUT OF THE RAT

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Abstract—1. The metabolism of glucose, glutamine and ketone-bodies was studied in the small intestine of rats after 5 days of hyperthyroidism.

2. Portal-drained visceral bloodflow increased by 20.1% (P < 0.05) in hyperthyroid rats and was accompanied by a decrease in the arteriovenous concentration difference of glucose (25.7%, P < 0.05), glutamate (22.9%, P < 0.05), alanine (20.9%, P < 0.05) and ammonia (28.6%, P < 0.05) and an increase in that of glycine (37.2%, P < 0.05), lactate (28.9%, P < 0.05) and ketone-bodies (163.2%, P < 0.001).

3. The gut of hyperthyroid rats showed increased rates of extraction of glucose, lactate and ketone-bodies.

4. Enterocytes isolated from hyperthyroid rats showed increased rates of utilization of glucose and ketone-bodies but that of glutamine were decreased.

5. The maximal activities of hexokinase, 6-phosphofructokinase, pyruvate kinase, citrate synthase and oxoglutarate dehydrogenase were increased (by 13.7–36.2%) in intestinal mucosal scrapings of hyperthyroid rats, whereas the activity of glutaminase was decreased (22.1–31.4%).

6. It is concluded that hyperthyroidism increases the rates of utilization of glucose and ketone-bodies but decreases that of glutamine (both in vivo and in vitro) by the epithelial cells of the small intestine.

INTRODUCTION

Hyperthyroidism is associated with several metabolic changes including enhanced gluconeogenesis, glycogenolysis, lipid mobilization and ketogenesis together with increased protein breakdown; the latter results in negative nitrogen balance and muscle wasting (for reviews see Ingbar and Woebner, 1981; Hedges et al., 1987). Moreover, hyperthyroidism is accompanied by increases in gastric emptying, intestinal motility, diarrhoea and steatorrhoea (for reviews see Ingbar and Woebner, 1981; Levin, 1969).

The major site of metabolism of glutamine in the non-hepatic splanchnic bed is the mucosa of the small intestine, which is characterized by a high rate of glutamine utilization (Windmueller, 1984). Most of the energy required by these cells is provided by the oxidation of glucose and glutamine in the fed-state and of glutamine and ketone bodies in the starved state (Asby and Ardawi, 1988). Studies have been carried out on the metabolic changes of the small intestine in catabolic conditions such as surgery (Soubra et al., 1987), uncontrolled diabetes (Ardawi, 1988), endotoxaemia (Austgen et al., 1991), sepsis (Ardawi et al., 1990) and hypothyroidism (Ardawi and Jalalah, 1991). However, the effects of hyperthyroidism on the metabolism of glutamine and other fuels (i.e. glucose and ketone-bodies) by the gut are unknown. This study was designed to determine the effects of hyperthyroidism on the extent of metabolism of glucose, glutamine and ketone-bodies by the gut of the rat. Rates of utilization have been obtained from arteriovenous concentration differences across the small intestine (together with bloodflow data). In addition, the rates of glucose, glutamine and ketone bodies utilization by isolated incubated enterocytes have been investigated. Finally, the maximal activities of key enzymes in the pathways of glucose, glutamine and ketone bodies utilization in intestinal mucosa have also been determined.

MATERIALS AND METHODS

Animals

Male Wistar albino rats (200–215 g) were supplied by King Fahd Medical Research Center, College of Medicine and Allied Sciences, King Abdulaziz University, Jeddah, Saudi Arabia. The animals were maintained on a standard diet (commercial rat cubes containing w/w approx. 18% protein, 3% fat, 77% carbohydrate and 3% organic salt mixture with a vitamin supplement; Grain Silos and Flour Mills Organization, Jeddah, Saudi Arabia) and water ad libitum, and were kept in a controlled environment (constant temperature 24°C, and a light cycle of 12 hr on/12 hr off). Animals were divided into two groups: a hyperthyroid group (n = 98) and a euthyroid control group (n = 98).

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