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Parenteral nutrition and protein sparing after surgery: do we need glucose?

Thomas Schricker[a,*], Sarkis Meterissian[b], Francesco Donatelli[a], George Carvalho[a], Louise Mazza[a], Leopold Eberhart[c], Linda Wykes[d], Franco Carli[a]

[a]*Department of Anesthesia, McGill University Montreal, Canada H3A 1A1*
[b]*Department of Surgery, McGill University Montreal, Canada H3A 1A1*
[c]*Department of Anesthesia and Intensive Care Medicine, Philipps University Marburg, 35043 Marburg, Germany*
[d]*School of Dietetics and Human Nutrition, McGill University Montreal, Canada H3A 1A1*

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Abstract

Although capable of inducing an anabolic state after surgery, parenteral nutrition, including glucose, leads to hyperglycemia. Even moderate increases in blood glucose are associated with poor surgical outcome. We examined the hypothesis that amino acids, in the absence of glucose supply, spare protein while preventing hyperglycemia. In this prospective study, 14 patients with colonic cancer were randomly assigned to undergo a 6-hour stable isotope infusion study (3 hours of fasting followed by 3-hour infusions of amino acids, Travasol [Baxter, Montreal, Canada] 10% at 0.02 mL · kg^{-1} · min^{-1}, with or without glucose at 4 mg · kg^{-1} · min^{-1}) on the second day after colorectal surgery. Protein breakdown, protein oxidation, protein balance, and glucose production were assessed by stable isotope tracer kinetics using L-[1-^{13}C] leucine and [6,6-$^{2}H_2$]glucose. Circulating concentrations of glucose, cortisol, insulin, and glucagon were determined. The administration of amino acids increased protein balance from −16 ± 4 μmol · kg^{-1} · h^{-1} in the fasted state to 16 ± 3 μmol · kg^{-1} · h^{-1}. Combined infusion of amino acids and glucose increased protein balance from −17 ± 7 to 7 ± 5 μmol · kg^{-1} · h^{-1}. The increase in protein balance during nutrition was comparable in the 2 groups (P = .07). Combined administration of amino acids and glucose decreased endogenous glucose production (P = .001) and stimulated insulin secretion (P = .001) to a greater extent than the administration of amino acids alone. Hyperglycemia (blood glucose, 10.1 ± 1.9 μmol/L) occurred only in the presence of glucose infusion. In summary, excluding glucose from a short-term feeding protocol does not diminish the protein-sparing effect of amino acids and avoids hyperglycemia.

1. Introduction

The immediate period after colorectal surgery is characterized by semistarvation due to anorexia and/or restricted oral food intake for medical reasons. Unless nutrients are provided in amounts sufficient to match the demands of catabolism, rapid net loss of lean tissue ensues. Thus, the primary goal of perioperative nutritional support is to attenuate protein wasting by optimizing nutrient delivery within the constraints of major organ function [1].

Parenteral nutrition, that is, the intravenous provision of anabolic substrates together with energy represents a therapeutic modality to achieve this goal. The metabolic efficacy of intravenous feeding strategies using combined glucose and amino acid infusions is well documented in patients undergoing gastrointestinal surgical procedures [2,3]. Although capable of producing nitrogen retention after abdominal surgery, parenteral nutrition, including the administration of glucose, leads to hyperglycemia [3]. As a result of impaired insulin sensitivity, a typical feature of the endocrine response to surgical tissue trauma [4], exogenous glucose increases the blood glucose concentration even when given in small hypoenergetic amounts [5,6]. Considering the detrimental effects of hyperglycemia on outcome, any disturbance of glucose homeostasis by nutritional interventions gains clinical importance, particularly in the surgical patient population [7,8].

The present study was designed to examine whether amino acids, in the absence of additional energy supply, spare protein while avoiding hyperglycemia as observed during the administration of glucose. We therefore assessed the kinetics of protein and glucose metabolism 2 days after

* Corresponding author. Tel.: +1 514 9341934x34883; fax: +1 514 8431698.
E-mail address: thomas.schricker@mcgill.ca (T. Schricker).

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colorectal surgery in the fasted state and during a 3-hour infusion of amino acids with or without glucose.

2. Materials and methods

2.1. Patients and ethics

The study was approved by the ethics committee of the Royal Victoria Hospital, Montreal, Quebec, Canada. Informed consent was obtained from 14 patients with localized colorectal carcinoma scheduled for elective trans-abdominal resection. None of the patients had significant cardiac, hepatic, renal, or metabolic disease. No subject had developed recent weight loss or had a plasma albumin concentration of less than 35 g/L.

The patients were randomly allocated to a group receiving intravenous amino acids (n = 7) or a group receiving intravenous amino acids and glucose (n = 7).

2.2. Anesthesia and surgical care

Epidural catheters were inserted in one of the thoracic vertebral levels between T10 and T12 of patients on arrival in the anesthetic room. Bilateral sensory block to ice and pin prick from thoracic dermatome level 6 to lumbar dermatome level 1 was achieved with bupivacaine 0.5% and was maintained during the operation with boluses of bupivacaine 0.25% (approximately 10 mL/h). General anesthesia was induced by propofol and continued with 35% nitrous oxide in oxygen and isoflurane at end-tidal concentrations of 0.3 to 0.4 vol% to achieve tolerance of the endotracheal tube and to prevent awareness. All patients received a bolus of 10 mL/kg normal saline before induction followed by 5 $mL \cdot kg^{-1} \cdot h^{-1}$ during surgery. Blood losses were replaced with Pentaspan (Bristol-Myers Squibb, Montreal, Quebec, Canada). All patients received hypoenergetic nutritional supplementation with glucose from 08:00 AM to 08:00 PM on the first postoperative day (100 mL/h glucose 5% equivalent to approximately 1046 kJ [250 kcal]) followed by the infusion of NaCl 0.9% (100 mL/h).

Sensory blockade from T8 to L3 was maintained postoperatively by a continuous epidural infusion of 0.1% bupivacaine supplemented with 3 μg/mL fentanyl administered at a rate between 8 and 14 mL/h. Pain treatment was adjusted to obtain a numerical analogue score at rest of less than 4 (numerical analogue scale from 0 = no pain to 10 = worst pain imaginable).

2.3. Parenteral nutrition

On the second postoperative day, after a 3-hour period of fasting, patients received a 10% amino acid solution without electrolytes (Travasol, Baxter, Montreal, Canada) either alone or together with crystallized beet sugar (10% dextrose anhydrous, Avebe, Foxhol, Holland) at 4 $mg \cdot kg^{-1} \cdot min^{-1}$ for 3 hours. The rate of amino acid infusion was set at 0.02 $mL \cdot kg^{-1} \cdot min^{-1}$ (equivalent to approximately 2.9 $g \cdot kg^{-1} \cdot day^{-1}$) to achieve plasma amino acid concentrations at least 2-fold above basal level [9]. The composition of Travasol (in micromoles per milliliter), which was verified before each administration, was as follows: proline 35, threonine 34, glycine 217, alanine 207, valine 36, methionine 37, isoleucine 34, leucine 45, tyrosine 2, phenylalanine 35, tryptophan 9, lysine 38, histidine 26, and arginine 57. The dextrose solution was prepared by the local pharmacy under sterile conditions and tested for sterility, stability, and absence of pyrogens before infusion. Beet dextrose was chosen because of its low carbon 13 content and therefore the lack of significant alteration of $^{13}CO_2$ enrichment in expired air [10]. Previous studies showed that the infusion of a solution containing beet dextrose and amino acids does not perturb baseline $^{13}CO_2$ enrichment in humans [11].

2.4. Experimental protocol

Plasma kinetics of leucine and glucose were determined by a primed constant infusion of tracer quantities of L-[1-^{13}C]leucine (99% ^{13}C) and [6,6-$^{2}H_2$]glucose (99% ^{2}H, Cambridge Isotope Laboratories, Cambridge, MA). Sterile solutions of labeled isotopes were prepared in the hospital pharmacy and kept at 4°C until administration. All tests were performed in the fasted state beginning at 08:00 AM on the second postoperative day. A superficial vein in the dorsum of the hand was cannulated and the cannula kept patent with saline 2 $mL \cdot kg^{-1} \cdot h^{-1}$. A second vein in the contralateral arm was cannulated to provide access for the infusion of the stable isotopes. Blood and expired air samples were collected before the infusion to determine baseline enrichments. Priming doses of $NaH^{13}CO_3$ 1 μmol/kg, L-[1-^{13}C]leucine 4 μmol/kg, and [6,6-$^{2}H_2$]glucose 22 μmol/kg were administered and followed immediately by continuous infusions of L-[1-^{13}C]leucine 0.06 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ and [6,6-$^{2}H_2$]glucose 0.22 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ lasting 6 hours. Toward the end of each 3-hour study period, 4 blood and expired breath samples were collected at 10-minute intervals. Each blood sample was transferred to a heparinized tube, centrifuged at 4°C (3000*g*, 15 minutes), and stored at −70°C. Breath samples were collected in a 2-L latex bag and transferred immediately to 20-mL vacutainers.

2.5. Gaseous exchange

Indirect calorimetry (Datex Deltatrac, Helsinki, Finland) was performed in the last hour of the fasted and fed states. The subjects were lying in a semi-recumbent position (20°) breathing room air in the ventilated hood, for 20 minutes on each occasion. Oxygen consumption ($V\dot{O}_2$) and carbon dioxide production ($V\dot{C}O_2$) were measured, and the respiratory quotient was calculated. An average value of $V\dot{O}_2$, $V\dot{C}O_2$, and respiratory quotient was taken, with a coefficient of variation of less than 10%.

2.6. Analytical methods

2.6.1. Isotopic enrichments

Plasma [1-^{13}C]α-ketoisocaproate (α-KIC) enrichment was determined by electron impact selected-ion monitoring