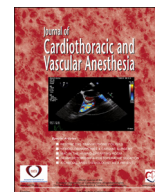




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Original Article

Comparative Study Between Conventional Fasting Versus Overnight Infusion of Lipid or Carbohydrate on Insulin and Free Fatty Acids in Obese Patients Undergoing Elective On-pump Coronary Artery Bypass Grafting. A Prospective Randomized Trial

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Objectives: Postoperative insulin resistance represents a major component of postoperative metabolic disorder. The authors compared the effects of preoperative infusion of lipid emulsion or carbohydrate to conventional preoperative fasting on postoperative insulin and free fatty acid (FFA) levels.

Design: A prospective randomized double-blinded study.

Settings: Tertiary university hospital.

Participants: Sixty-three patients undergoing coronary artery bypass grafting.

Intervention: Participants were randomized into 3 equal groups. Group G received 500 mL of glucose 10% (50 g glucose). Group L received 100 mL of 2% lipid emulsion (soybean 30%, medium chain triglycerides (TG) 30%, olive oil 25%, fish oil 15%, and 20 mg vitamin E). Group C fasted overnight except for clear fluids allowed until 4 hours preoperatively. Serum insulin at the start of infusion (T₁), 1-hour preinduction (T₂), on admission to the intensive care unit (T₃), after 24 hours of admission (T₄), and after 48 hours of admission (T₅), and FFA at T₁ and T₂ were measured. Serum very-low-density lipoprotein (VLDL), serum TG, and blood sugar were all measured (T₁-T₄). Bypass time, ischemic time, need for inotropic support, and length of intensive care unit stay also were measured.

Measurements and Main Results: At the end of infusion FFAs were significantly lower in the L group (1.1 ± 0.76 mg/dL) compared with G (1.64 ± 0.85 mg/dL) and C groups (1.48 ± 0.76 mg/dL). Insulin levels were significantly lower in the L group compared with levels in the G and C groups at T₂, T₃, and T₄. Also, TG, VLDL, and random blood sugar levels decreased significantly at T₂, T₃, and T₄ in the L group compared with the other 2 groups and compared with baseline value within the same group.

Conclusion: Preoperative lipid infusion lowered postoperative FFA, insulin, TG, VLDL, and random blood sugar in obese patients undergoing coronary artery bypass grafting surgeries.

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Key Words: perioperative fasting; CABG surgery; insulin resistance; SMOF lipids

THE ADVERSE METABOLIC EFFECTS of preoperative fasting have been studied comprehensively. Fasting depletes

liver glycogen reserves, increases whole-body protein catabolism, elevates plasma fatty acids concentrations, and increases resting energy expenditure.¹ Although insulin level often increases, blood glucose also increases due to the development of insulin resistance. Conventional preoperative fasting time may aggravate insulin resistance and cause hyperglycemia, especially if it lasts longer than the expected 6 to 8 hours as it

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may reach as long as 10 to 16 hours.² Insulin resistance occurs both in hepatic and extrahepatic tissues, mainly muscles. Endogenous glucose production is increased and the uptake of glucose in the periphery is reduced.³

In adipose tissue, insulin resistance increases lipolysis, which increases free fatty acid (FFA) flux with further aggravation of insulin resistance through the alteration of the insulin-signaling pathway. The reduction of this accelerated lipolysis is a target for the treatment of insulin resistance.⁴

Fasting insulin and glucose levels are believed to serve as surrogate measures of insulin sensitivity and secretion, and preloading the patient with oral carbohydrates could reduce stress in cardiac surgical patients.^{5,6}

Patients with insulin resistance may benefit from medium chain triglycerides (MCTs) as they do not depend on carnitine palmitoyltransferase-1 (CPT-1); an enzyme needed to facilitate their mitochondrial entry for oxidation. In humans, MCTs have controversial impact on insulin resistance, insulin concentration, and blood glucose. Also, fish oil was found to alter blood glucose homeostasis through its effect on glucose transporter 4 (GLUT4), the transporter of glucose to the skeletal muscles, and the activation of the Adenosine monophosphate (AMP) kinase with its consequences on blood glucose homeostasis.⁷⁻⁹

The aim of this study was to compare the effects of overnight infusion of lipid or carbohydrate solution compared with conventional overnight fasting on insulin levels and FFAs in obese patients undergoing elective first time on-pump coronary artery bypass grafting (CABG) Fig 1.

Patients and Methods

After approval of the institutional research ethical committee and obtaining a written informed consent, 63 patients scheduled for elective on-pump CABG from September 2014 to July 2016 participated in this prospective, randomized double-blinded study.

Computer-generated random numbers randomized participants into 3 equal groups (21 each) and closed opaque envelopes were used for concealment.

- **Group I (G group):** Patients received 500 mL of glucose 10% containing 50 g of glucose and providing patients with 200 Kcal with an osmolarity of 556 milliosmol/L.
- **Group II (L group):** Patients received 100 mL of SMOF lipid Fresenius Kabi (soybean E) containing 20 g of lipid and provides patients with 200 Kcal with an osmolarity of 380 milliosmol/L.
- **Group III (C group):** Patients fasted overnight from 11:00 pm to 9:00 am except for clear fluids, which were allowed until 5:00 am (4 hours preoperatively).

Included in the study were adult patients (≥ 18 years) with American Society of Anesthesiologists class II-III, body mass index 30 to 40, and New York Heart Association functional capacities I-II, undergoing elective on-pump CABG. All patients were classified as type IIa World Health

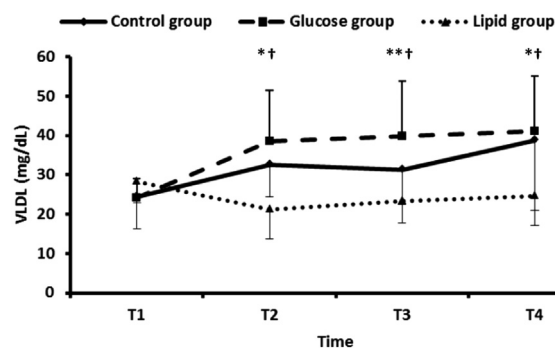


Fig 1. Triglycerides. T₁, at start of infusion; T₂, 1 hour before induction; T₃, on ICU admission; T₄, 24 hours after admission. *Significance between control group and lipid group. †Significance between glucose group and lipid group.

Organization (WHO)/Fredrickson classification of primary hyperlipidemias.¹⁰

Patients with diabetes mellitus, patients on fibrates, patients with type I, IIb, III, IV, and V WHO/Fredrickson classification of primary hyperlipidemias, patients with a history of allergic reactions to fish, egg yolk containing foods, peanut or soy products, and patients with carbohydrate or fat intolerance also were excluded. Also excluded from the study were patients with redo and emergency procedures, those with left ventricular ejection fraction less than 40%, and patients with renal or hepatic dysfunction defined as blood results more than double the upper reference value.

Infusion bottles and lines were sealed with dull silver foil papers by a pharmacist who was blinded to group allocation and were given by nursing staff blinded to the contents of the bottles. After all, the investigators who collected the samples were blinded to the content of the bottles and group allocation.

Group I (G group) (N = 21) patients received 500 mL of glucose 10% containing 50 g of glucose providing patients with 200 Kcal with 556 mosmoles/L. Flow rate of the infusion was 62.5 mL/h. Group II (L group) (N = 21) patients received 100 mL of SMOF lipid Fresenius Kabi (soybean 30%, MCTs 30%, olive oil 25%, fish oil 15%, and 20 mg vitamin E) containing 20 g of lipids, which provided patients with 200 Kcal with osmolarity of 380 mosmoles/L with a flow rate of infusion of 12.5 mL/h. Using Pilot A2 syringe pumps, study drugs in both groups were infused over a period of 8 hours (12:00-8:00 am) and all surgeries started at 9:00 am.

Group III (C group) patients fasted overnight before surgery for 10 hours starting from 11:00 pm until 9:00 am. Clear fluids (plain water, apple juice, or tea without milk) were allowed until 5:00 am according to the Practice Guidelines for Preoperative Fasting: An Updated Report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters.¹¹

Nutritional Plan for All Patients the Day Before Surgery

The day before surgery all patients received a nutritional regimen that provided them with 1,300 Kcal for females of group I-G and II-L and 1,500 Kcal for males of the same

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