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Propofol sedation substantially increases the caloric and lipid intake in critically ill patients

Mélanie Charrière R.N. [a], Emma Ridley R.N. [b,c], Jennifer Hastings M.D. [d], Oliver Bianchet M.D. [d], Carlos Scheinkestel M.D. [d], Mette M. Berger M.D., Ph.D. [a,*]

[a] Service of Intensive Care Medicine, University Hospital (CHUV), Lausanne, Switzerland
[b] ANZIC RC, Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia
[c] Nutrition Department, The Alfred Hospital, Melbourne, Australia
[d] Intensive Care Unit, The Alfred Hospital, Melbourne, Australia

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ABSTRACT

Objective: The amount of lipid delivered to patients varies considerably depending on the non-nutritional intake from sedation, and on the feeding solution. The aim of this study was to quantify the magnitude and proportion of lipids and energy provided from propofol sedation in intensive care unit (ICU) patients.
Methods: This was a retrospective analysis of prospectively collected data in consecutive patients admitted to the ICUs of two university hospitals. Inclusion criterion included an ICU stay >5 d. Data were collected for a maximum of 10 d. Propofol sedation using 1% or 2% propofol solutions was defined as >100 mg/d. Nutritional management was per protocol in both centers, recommending enteral feeding. Data are shown as means ± standard deviation.
Results: In all, 701 admissions (687 patients, ages 59 ± 16 y, SAPS II 51 ± 17) and 6485 d, including 3484 propofol sedation days were analyzed. Energy targets were 1987 ± 411 kcal/d; mean energy delivery was 1362 ± 811 kcal/d (70% ± 38% of prescription) including propofol and dextrose. Enteral feeding dominated (75% of days) and progressed similarly in both ICUs. Mean propofol sedation dose was 2045 ± 1650 mg/d, resulting in 146 ± 117 kcal/d. Fat from propofol constituted 17% of total energy (up to 100% during the first days). Fat delivery (40 ± 23 g/d: maximum 310 g/d) was significantly increased by the combination of propofol sedation, the 1% solution, and high-fat–containing feeds. In survivors, high-fat proportion was associated with prolonged ventilation time ($P < 0.0001$).
Conclusion: Propofol sedation resulted in large doses of lipids being delivered to patients, some receiving pure lipids during the first days. As the metabolic effects of high proportions of fat are unknown, further research is warranted.

Introduction

Over the past 3 decades, sedation has considerably evolved in critical care with the appearance of short-acting agents such as propofol. Conversely, there has been little evolution in commercial enteral nutrition (EN) solutions regarding nutrient composition. The focus of such EN solutions is mainly on total energy, glucose in the context of glucose control, and recently on protein intake, but with little concern regarding lipid [1]. In the critically ill, the commercial EN and parenteral nutrition (PN) solutions may deliver ≤55% of total energy as lipids. This is in contrast with recommendations for healthy individuals to avoid fat intake >35% of total energy, aiming at reducing cardiovascular risk [2]. However, such recommendations do not exist for critically ill patients. There are only general guidelines that recommend that daily fat should not exceed 1 to 1.5 g/kg [3], whereas data supporting this range are few. The knowledge about the effects of higher amounts of lipid over prolonged periods come from studies investigating the effects of ω-3 fatty acids on intensive care unit (ICU) outcome: The trials used a

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* Corresponding author. Tel.: +41 (0)21 31 42 095; fax: +41 (0)21 31 43 045.
E-mail address: mette.berger@chuv.ch (M. M. Berger).

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high-dose (55% of energy) long-chain triacylglycerol (LCT) solution as comparative and showed poorer outcomes with the higher lipid-containing feeds [4]. Furthermore, studies in critically ill burn patients show that feeds with fat content reduced to 15% of total energy result in less infectious complications compared with feeds with 30% fat [5].

There has been increasing awareness regarding additional energy provision from non-nutritional sources, such as dextrose from drug dilution and hydration, citrate from dialysate solutions, and lipid from the sedative agent propofol [6–8]. When these nonnutritional energy sources are added to artificial nutrition delivery, overfeeding may result. Propofol comes as lipid emulsion composed of either pure LCT soya lipid emulsion or a balanced mixture of medium-chain triacylglycerols and LCTs. It is generally solubilized as a 1% or 2% solution. Its use, particularly in high doses, increases the overall proportion of fat provided to the patient [8,9].

Alterations of lipid metabolism are frequent during critical illness [10], and hypertriglyceridemia is observed in nearly 45% of patients who require >3 d of ICU treatment. Hypertriglyceridemia reflects a global liver dysfunction that has several causes including overfeeding. Propofol and its accompanying lipid emulsion are the strongest risk factors for hypertriglyceridemia, stronger than total energy, glucose, and lipid intake from feeding [8]. Moreover, hypertriglyceridemia, may occur during the rare but life-threatening propofol infusion syndrome (PRIS) [11].

The present study aimed to quantify the quantity of lipid and the proportion of both energy and lipids that resulted from propofol sedation in critically ill patients requiring artificial nutrition in two distinct ICU settings.

Methods

The study was designed as a bicentric retrospective analysis of prospectively collected data of consecutive patients admitted to the ICUs of two teaching hospitals (Alfred Hospital [AH], Melbourne, Australia and the Centre Hospitalier Universitaire Vaudois [CHUV], Lausanne, Switzerland). Inclusion criterion was a ventilation time >5 d and an ICU stay >5 d, with no exclusion criteria. Patients were identified through hospital databases. The study was conducted from August 2011 to March 2012 at CHUV and from January 2012 to December 2012 at AH. Data were collected from ICU admission until day 10 of an ICU stay or ICU discharge (whichever occurred first). Data obtained included demographic and admission data, nutrition assessment information (including energy and protein targets), and daily nutrition therapy data, including the mode of nutrition, delivery of energy, and lipid amounts from propofol and feeds. Lengths of mechanical ventilation and ICU stay and outcome were recorded. We did not record infectious complications.

The protocol was reviewed by the Commission Cantonale d'Ethique pour la Recherche sur l'être humain (CHUV) and by Human Research Ethics Committee at The Alfred Hospital (AH). In both institutions, a low-risk ethics approval was obtained and the requirement for consent was waived due to the absence of intervention and low-risk nature of the project.

Propofol sedation days were defined as any 24-h period with ≥100 mg of propofol any day with less being aggregated with the "nonpropofol days." The centers used different formulations of propofol: a 1% solution at AH (Fresofol 1%, Fresenius Kabi, Australia: 1.1 kcal/mL, 100 mg propofol delivery of 11 kcal as LCT) and a 2% solution at CHUV (Propofol Lipuro, BBraun, Crissier, Switzerland: 0.5 kcal/mL, 100 mg propofol delivery of 5 kcal). This difference meant that for the same dose of propofol, AH patients received twice the amount of fat.

Nutrition therapy was as per evidence-based nutrition guidelines in both ICUs, and EN was systematically favored. Energy targets were set differently: At AH the Schofield equation with added stress factors was used [12], whereas CHUV used mainly a weight-based target (25 kcal/kg daily), or in patients >70 y the Harris–Benedict predicted value times 1.2. Both centers used indirect calorimetry on occasions in patients requiring specific nutrition therapy (burns, trauma, transplantation, obesity, malnutrition). The choice of the EN formula was as per standard practice at each site: The composition of the three most frequently used EN solutions per center is depicted in Table 1. At CHUV only, blood triacylglycerols (TGs) are determined twice weekly as part of routine care.

For each patient, the mean fat intake and proportion of energy intake from fat was calculated. High-fat delivery was defined to occur when >45% of total energy was supplied as fat, and excessive fat delivery when >55% of total energy was supplied as fat.

Statistical analysis

Variables are reported as numbers or percentages; normally distributed variables are reported as mean ± standard deviation, and non-normally distributed variables are reported as median (interquartile range [IQR]). Comparisons between sites were carried out using χ^2 tests for discrete variables, and two-way analysis of variances for continuous variables repeated over time. Single regressions were calculated between fat doses and outcome variables. Significance was considered at the level of $P < 0.05$. Statistical package, JMP Version 10, was used (SAS Institute Inc. Cary, NC, USA).

Results

In all, 701 admissions of 687 patients met the inclusion criteria, resulting in 6485 study days. The demographic characteristics of the population are reported in Table 2. The mean age was 59 ± 16 y, and body mass index was 27.2 ± 6.9 kg/m^2. Patients were significantly younger and heavier at AH. The two largest diagnostic categories were cardiovascular (19% and 23.6%, respectively, per site) and trauma and musculoskeletal pathologies (higher at AH with 45% versus 3% at CHUV).

Propofol sedation

Of the 6485 study days, 3484 (53.7%) were with propofol sedation (1623 and 1861 d propofol from CHUV and AH, respectively). Overall, 2045 ± 1650 mg/d propofol were provided during the 10 d of the study, corresponding to 85 mg/h propofol with a large inter-ICU and interpatient variability (Fig. 1B). The median propofol dose was 1290 mg/d at AH and 2400 mg/d at CHUV ($P < 0.0001$). Propofol was most intensively used during the first 3 d: The proportion of overall energy provided by propofol sedation is shown in Figure 2. As the result of the 1% or 2% propofol emulsion, despite significantly higher propofol dose at CHUV, the median amount of energy resulting from the sedation was lower at CHUV (AH: 136 kcal/d [IQR 61–253]; CHUV: 108 kcal/d [IQR 40–178]; $P < 0.001$). Energy from propofol was the unique source of kcal in several patients for a few days. Overall, propofol sedation contributed 17% as a mean of total energy delivery per day over the study period.

Nutrition therapy

Overall, 75% of days were on EN: 17.4% of days were without nutrition for multiple reasons. Indirect calorimetry was used to adjust the energy target in 79 patients (21 AH, 51 CHUV) and repeated in some patients (N = 109 studies). The mean daily energy target for the population was 1987 ± 411 kcal. The energy target was higher at AH ($P = 0.0001$) as result of the use of the Schofield equation and a younger cohort (Figure 3). The mean daily amount of energy delivered from all sources at both sites was 1362 ± 811 kcal corresponding to 81% of prescription. Other nutritional information is provided in Table 3.

Fat delivery

Median fat delivery was 39 g/d (IQR 31–56) increasing to 43 g/d (IQR 35–59) on propofol days. Maximal daily fat intake was 310 g/d. Figure 1A shows total lipid delivery. Expressed per kg of body weight per day, the cumulated nutrition-propofol intake represents a median of 0.53 g/kg daily with (IQR 0.27–0.76) with maximal values in both centers of 2.11 and 2.31 g/kg. This represents 31% (IQR 20–40) of total energy. Considering all days,