Review Article

Impact of propofol sedation on inadequate energy and protein intake in critically ill patients receiving nutrition support: a narrative literature review and synthesis

Impacto da sedação por propofol na inadequação da oferta energética e proteica em pacientes críticos em terapia nutricional: uma revisão integrativa

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ABSTRACT

Introduction: This study aimed to analyze the impact of propofol sedation on inadequate energy and protein intake in critically ill patients receiving nutrition support (NS). **Methods:** A systematic search was conducted in PubMed, Virtual Health Library, Embase, and Cochrane in June 2025. Only original studies with critically ill patients who used propofol while receiving NS and that provided data on energy and/or protein intake were included. Studies with pediatric populations and those whose full texts were not available were excluded. **Results:** Ten studies published between 2005 and 2024 were included. The number of participants ranged from 22 to 687. Most studies were retrospective (70%) and utilized a single-center design (90%). Propofol sedation significantly affected nutritional adequacy, with heterogeneous effects on energy provision and more consistently contributing to exceeding lipid targets and inadequate protein provision. Switching from 1% to 2% propofol and administering protein boluses may help minimize these inadequacies. **Conclusion:** These findings highlight the need for individualized NS for critically ill patients, including strategies to minimize nutrition inadequacy during propofol use, as well as for original studies assessing the clinical impact of propofol-associated nutritional inadequacy and new strategies to mitigate it.

RESUMO

Introdução: Pacientes críticos apresentam aumentado risco de desnutrição. No entanto, a adequação da terapia nutricional (TN) ainda é um desafio, principalmente em relação à oferta energética-proteica insuficiente. Um fator menos discutido, porém, é o impacto das calorias não nutricionais (CNN) nessa inadequação. O propofol é um dos principais contribuintes para o aporte de CNN em unidades de terapia intensiva (UTIs) e, por vezes, para evitar hiperalimentação durante seu uso, a vazão da nutrição enteral é reduzida, culminando em oferta proteica inadequada. Nesse contexto, este estudo buscou analisar o impacto da sedação por propofol na inadequação da oferta energética e proteica em pacientes críticos. **Método:** Essa foi uma revisão integrativa de estudos originais indexados nas bases PubMed, BVS, Embase e Cochrane, com buscas realizadas em junho de 2025. **Resultados:** Dez estudos publicados entre 2005 e 2024 foram incluídos. O número de participantes variou de 22 a 687. A maioria dos estudos teve delineamento retrospectivo (70%) e caráter unicêntrico (90%). A sedação por propofol impactou significativamente a adequação da oferta nutricional. O impacto ocorreu de maneira heterogênea quanto à oferta energética. Também houve exacerbação da meta lipídica e suboferta proteica. A troca de propofol 1% para 2% e a administração de bolus de proteína podem ser estratégias para minimizar essa inadequação. **Conclusão:** Os achados reforçam a necessidade da TN individualizada na UTI, bem como de estudos originais que se proponham a verificar o impacto clínico da inadequação nutricional associada ao uso de propofol e de novas estratégias de mitigação para esse cenário.

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INTRODUCTION

Nutritional therapy is an essential part of intensive care, as critically ill patients are at increased risk of malnutrition due to several factors related to disease severity, such as persistent inflammation, hypercatabolism, and anabolic resistance[1]. These changes often result in loss of muscle mass, which is associated with negative outcomes, such as prolonged hospital stay, impaired wound healing, delayed weaning from mechanical ventilation, and reduced quality of life and functional capacity[2]. However, despite its importance, the patients' clinical condition, as well as necessary clinical interventions, can make adequate nutrient delivery a challenge in intensive care units (ICU), whether due to the need to interrupt enteral nutrition (EN) for procedures or due to feeding intolerance, hemodynamic instability, and the use of high-dose vasoactive drugs, among other factors[3,4]. A less discussed issue, however, is the impact of non-nutritional calories (NNC) on nutritional adequacy. NNC are additional calories provided without nutritional purpose, often as part of medications, mainly propofol[5].

Propofol is a sedative widely used in ICU due to its rapid onset of action and short half-life, which allows for daily awakening and spontaneous breathing trials[6]. It has a lipid-based formulation. Its most commonly used emulsion is 1% proporfol (10 mg/ml) and it provides 1.1 kcal/ml[2]. High doses of propofol may substantially increase patients' caloric intake and are therefore often considered in the calculation of energy provision[6]. However, the strategy commonly adopted to avoid energy overfeeding is to reduce the EN infusion rate, which may result in inadequate protein delivery[6]. Disregarding NNC derived from propofol may lead to total energy delivery far exceeding requirements, particularly during the acute phase of critical illness, potentially resulting in organic and metabolic complications related to overfeeding, such as refeeding syndrome, hyperglycemia, hypertriglyceridemia, pancreatitis, and hepatic steatosis[7-9].

In this context, this review aims to synthesize and analyze data from original studies to assess the impact of propofol sedation on the adequacy of energy and protein intake in critically ill patients receiving nutrition support (NS).

METHODS

This review was conducted following the the Scale for the Assessment of Narrative Review Articles (SANRA) and the methodological steps proposed by Whittemore et al.[10] and Oermann et al.[11]: (1) identification of the problem; (2) literature search; (3) data evaluation; (4) data analysis; and (5) presentation of the results, focusing not only on describing the findings but also on critically and comparatively analyzing their results and implications for NS in critically ill patients.

Research question

This study aimed to examine the impact of propofol sedation on the adequacy of energy and protein intake in critically ill patients receiving NS. To do so, the PECO strategy (population, exposure, comparison, and outcome) was used. The population was critically ill patients receiving NS. The exposure was propofol sedation. The comparison was based on absence of propofol sedation or different doses of the drug. The outcome included the adequacy of energy and protein intake.

Search strategies

A systematic search was conducted in June 2025 across PubMed, *Biblioteca Virtual em Saúde (BVS)*, Embase, and Cochrane using DeCS and MeSH descriptors, boolean operators, and other database-specific search specifications. The specific search strategies are described in Table 1.

Inclusion and exclusion criteria

Only original studies with critically ill patients who used propofol while receiving NS and that provided data on energy and/or protein intake of these patients were included. Studies with pediatric populations, as well as those whose full texts were not available, even after direct contact with the authors, were excluded.

Study selection

Search results were exported to an artificial inteligence-powered online platform (Rayyan AI) for automatic identification and manual review of duplicate studies. The independent screening of the studies was conducted by the two authors in four steps on the platform, following the pre-established inclusion and exclusion criteria: (1) blind, independent screening of titles and abstracts; (2) resolution of conflicts in cases of disagreement; (3) blind, independent full-text screening; and (4) resolution of conflicts after full-text review.

Data extraction and organization

Data from the selected studies were manually extracted using a structured form in Google Forms and analyzed in Google Sheets. The extracted information included: authors, year of publication, study title, objectives, population, exposure, comparison, outcomes or variables related to nutritional adequacy, main results concerning nutritional adequacy, main conclusions, study limitations, and conflict-of-interest statements.

Table 1 – Search strategies by database.

Database	Search Strategy
PUBMED	("Propofol"[Supplementary Concept] OR Propofol[Title/Abstract]) AND ("Parenteral Nutrition, Total"[MeSH Terms] OR "Nutrition Therapy"[MeSH Terms] OR "Enteral Nutrition"[MeSH Terms] OR "Protein Deficiency"[MeSH Terms]) AND ("Critical Care"[MeSH Terms] OR "Critical Illness"[MeSH Terms])
BVS (*Biblioteca Virtual em Saúde*)	("Propofol") AND ("Nutrição Parenteral Total" OR "Terapia Nutricional" OR "Nutrição Enteral" OR "Deficiência de Proteínas") AND ("Cuidados Intensivos" OR "Estado Terminal")
EMBASE	(('propofol':ti,ab)) AND (('total parenteral nutrition':ti,ab OR 'nutrition therapy':ti,ab OR 'enteral nutrition':ti,ab OR 'protein deficiency':ti,ab)) AND (('intensive care':ti,ab OR 'critical illness':ti,ab))
COCHRANE	(propofol) AND ("total parenteral nutrition" OR "nutrition therapy" OR "enteral nutrition" OR "protein deficiency") AND ("intensive care" OR "critical illness")

Synthesis and analysis of results

The results were summarized descriptively and analytically, presenting absolute numbers and percentages whenever possible, to identify patterns and divergences among the reviewed studies.

RESULTS

The searches retrieved 117 studies. Throughout the selection process, 107 were excluded, and 10 were included in the review. The detailed selection flow diagram is presented in Figure 1.

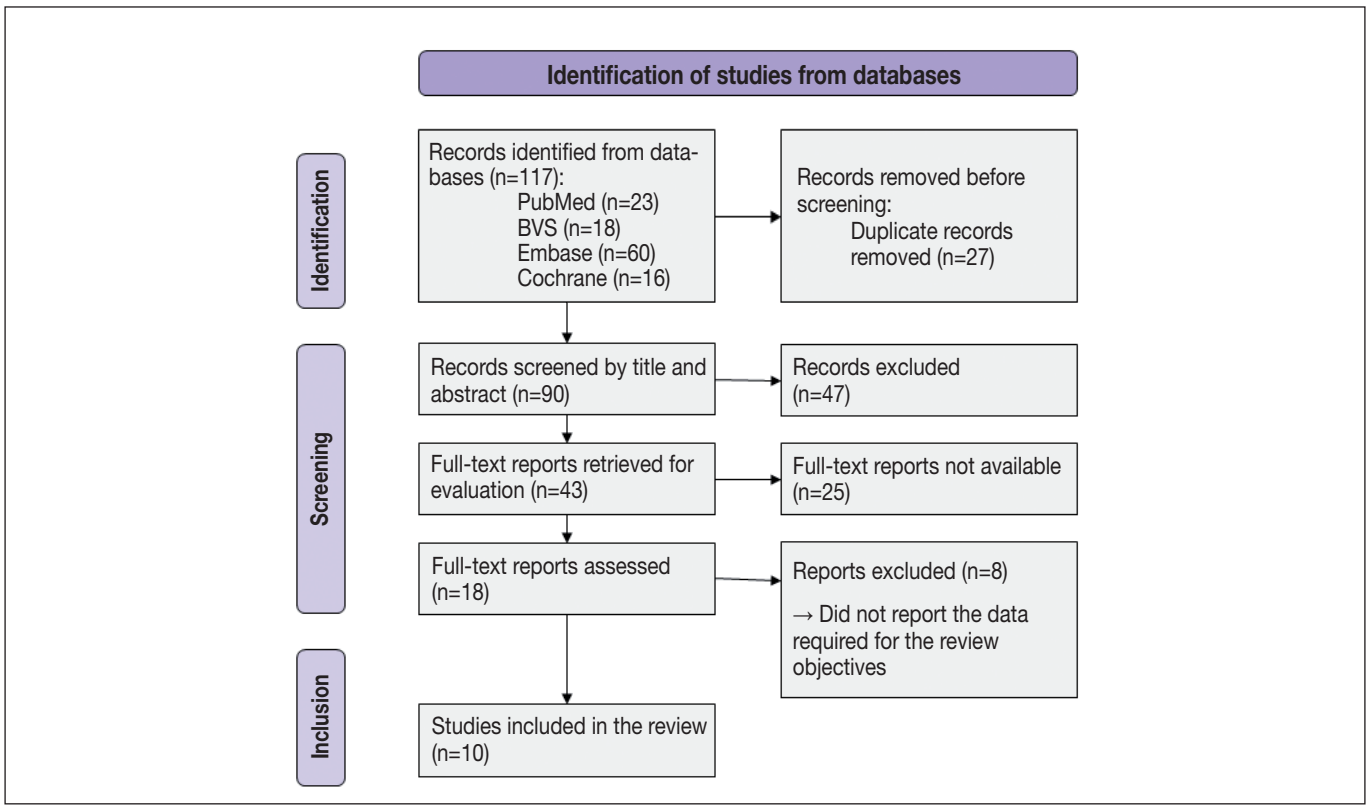

Figure 1 - *Study selection flowchart.*

The included studies were published between 2005 and 2024, and the number of participants ranged from 22 to 687. Most had a retrospective design (70%; n=7) and were single-center (90%; n=9). Other study characteristics are presented in Table 2.

All studies reported, through different variables, the adequacy of energy intake; eight (80%) reported protein adequacy and five (50%) reported lipid adequacy. Propofol contribution to total lipid intake was observed in four (40%) studies, and to total energy intake in

Table 2 – Characteristics of the studies included in the review.

	Author (year)	Study design	Objective	Population	Patients included (n)
I	Taylor, Bowles & Jewkes (2005)[12]	Prospective observational; single-center	To determine if reducing EN to accommodate calories from 1% propofol results in suboptimal nitrogen delivery (<80% of target).	Adult ICU patients on MV, receiving 1% propofol	85
II	Rai et al. (2010)[13]	Retrospective cohort; single-center	To assess the adequacy of EN in septic patients on MV with and without shock.	Adults admitted to the ICU with sepsis, on MV for ≥3 days	43
III	Charriere et al., (2017)[14]	Retrospective observational (prospective database); multicenter	To quantify lipid delivery and the proportion of energy and lipids from propofol sedation in critically ill patients on NS in two ICU.	Adult ICU patients on MV for >5 days	687
IV	Buckley et al., (2021)[15]	Retrospective observational; single-center	To quantify calories from propofol and EN and compare protein delivery using a protein bolus protocol vs. a traditional approach with isocaloric conventional EN.	Adult ICU patients with TBI, on EN, and receiving propofol for ≥2 days	51
V	Buckley et al., (2021)[16]	Retrospective observational; single-center	To assess the protein requirements of critically ill patients on MV with COVID-19.	Adults admitted to the ICU with COVID-19, on MV within the first 7 days	22
VI	Terblanche; Remmington, (2021)[17]	Retrospective pre-post observational; single-center	To assess the effect of switching from 1% to 2% propofol on protein delivery.	Adults in a cardiothoracic ICU for ≥72 h, on propofol for ≥3 days, and on NS	100 - 50 in the 1% group; - 50 in the 2% group.
VII	Pastrana, Zúñiga & Barca (2022)[18]	Prospective cohort; single-center	To assess the nutritional adequacy of EN in a general hospital ICU.	Adult ICU patients on EN	26
VIII	Viana et al. (2022)[19]	Prospective, comparative of consecutive cohorts; single-center	To compare metabolic and nutritional variables between patients with and without COVID-19 to identify issues related to the management of these patients, with an emphasis on energy balance.	Adults in a persistent critical illness program, in the ICU, on MV for >10 days	104 - 52 with COVID-19; - 52 withaut COVID-19.
IX	Vieira & Castro (2023)[5]	Retrospective observational; single-center	To assess the relevance of calories derived from propofol in patients with COVID-19.	Adult ICU patients with COVID-19, on MV, and EN	51
X	Popoff et al. (2024)[20]	Retrospective observational; single-center	To quantify NNC in relation to energy recommendations during the acute phase of ICU patients on MV with ARDS due to COVID-19.	Adults admitted to the ICU for ARDS due to COVID-19	157

EN = enteral nutrition; ICU = intensive care unit; MV = mechanical ventilation; NS = nutrition support; TBI = traumatic brain injury; NNC = non-nutritional calories; ARDS = acute respiratory distress syndrome.

eight (80%). Frequencies of other outcomes are shown in Table 3. None of the authors reported conflicts of interest.

There was considerable variation in propofol's energy contribution, ranging from negligible values[13,15] to significant amounts exceeding 500 kcal/d[12]. Its use was associated with energy prescriptions below target in one study[12], and it contributed to excessive total energy intake in others[13,15,20]. Some patients exceeded lipid targets[12,14,17-19,20], with most studies reporting inadequate protein intake[5,12,16,18,19], even after mitigation strategies[15,17,20]. The most frequently cited mitigation strategy was switching propofol from 1% to 2%[5,12,14,17]. One study suggested administering protein boluses in an isocaloric regimen[15], while another mentioned the development of water-soluble propofol as an alternative[20] (Table 4).

Table 3 – Synthesis of the analyzed outcomes in the reviewed studies

Outcome (assessment variables)	Studies	n	%
Energy delivery adequacy (% of target, kcal/kg, or kcal/d)	I-X	10	100
Protein delivery adequacy (% of target, g/kg/d, or NB)	I, IV, V, VI, VII, VIII, IX, X	8	80
Lipid delivery adequacy (diverse criteria)	I, III, VI, VII, VIII	5	50
Propofol dose/infusion rate (mL/h, mg/d)	I, III, VI, VIII, X	5	50
Duration of propofol use (days)	III, VI, IX	3	30
Energy contribution of propofol (kcal, kcal/kg/d, or % of TEI)	I, II, III, IV, V, VI, IX, X	8	80
Lipid contribution of propofol (g, g/kg/d, % of total lipid delivery, or % of TEI)	III, VI, VII, X	4	40
Comparison between 1% and 2% propofol	I, III, VI, IX	4	40

NB = nitrogen balance; TEI = total energy intake.

Table 4 –Synthesis of integrated results on the impact of propofol on nutritional delivery adequacy in critically ill patients

Synthesis variables	Key integrated results	Studies
Energy contribution of propofol	Propofol energy delivery ranged from 0 to 528 kcal/day, with median values between ~200 and 350 kcal. Some studies reported 5-6 kcal/kg/d (range: <1–15 kcal/kg/d), while others reported 15–27% of TEI.	I-X
Energy delivery inadequacy	Propofol was associated with energy prescription below requirements (81%) in one study, whereas others showed that patients on propofol exceeded total energy targets, reaching 101–126%. Other studies reported that patients failed to reach targets regardless of propofol use.	I, II, III, IV, VI, VII, IX, X
Macronutrient imbalance (lipid excess)	Propofol use contributed 17.5–48% of total lipid intake in some studies and led to lipid delivery up to twice that of individuals not receiving propofol. Lipid delivery ranged from 41.65% to 100% of TEI on certain days, exceeding the target in 36–38.5% of cases. Impairments in glucose and protein delivery were also reported.	I, III, VI, VII, VIII, X
Protein intake inadequacy	Propofol use was associated with protein/nitrogen delivery below requirements (90% to <80%) in one study. In another, patients receiving more propofol had a significantly higher cumulative protein deficit (p = 0.0077), though no direct association with the drug was established. Other studies reported protein inadequacy regardless of propofol concentration or strategies to increase protein intake.	I, IV, V, VI, VII, VIII, IX, X
Strategies to mitigate propofol's nutritional impact	Switching from 1% to 2% propofol was the most cited strategy, resulting in lower energy and lipid delivery (reducing cases exceeding lipid targets from 36% to 2% in one study), higher protein delivery and a significant increase in the proportion of patients reaching nitrogen and glucose targets. Protein bolus administration was also used, doubling protein delivery compared to conventional isocaloric formulas. Finally, one study mentions the potential development of a water-soluble propofol.	I, III, IV, VI, IX, X

TEI = total energy intake.

DISCUSSION

The reviewed studies showed that propofol sedation can significantly impact nutritional intake adequacy in critically ill patients. Its impact was heterogeneous regarding energy intake and more consistent in contributing to exceeding lipid targets and suboptimal protein intake.

Propofol energy contribution

The energy contribution of propofol ranged from 0 to 528 kcal/day [12,13], or from <1 to 15 kcal/kg/d[15], with most studies reporting median values of approximately 200 to 350 kcal/d[5,16,17,20] or 5 to 6 kcal/kg[15,16]. This variation can be explained by individual differences in propofol dosages, which range from 0.3 to 4 mg/kg/h for sedation in ICU[21,22], and the resulting infusion rate, which is influenced by patient weight and emulsion concentration. The percentage of total energy intake (TEI) attributable to propofol, which ranged from 15% to 27%[5,20], also varies according to individual energy intake.

Energy intake inadequacy

Propofol was associated with energy prescriptions below requirements (81%) in the study by Taylor et al.[12], which is consistent with the findings of Terblanche & Remmington[17], who observed that the group receiving 1% propofol received, on average, less energy from NS to avoid overfeeding (13.4 kcal/kg [SD=5.6] vs 15.7 kcal/kg [SD=5.1]; p=0.03). This practice of reducing the EN infusion rate to prevent energy overfeeding, especially during high doses of propofol, is mentioned by Buckley et al.[15] as the rationale for exploring alternative approaches, since simply reducing EN may lead to macronutrient inadequacy, with a higher lipid proportion and suboptimal protein and carbohydrate delivery, as observed by Taylor et al.[12].

Other studies also reported overall energy delivery below target: 81% in the study by Charriere et al.[14] and 86% in the study by Vieira & Castro[5]. The latter considered sedation-derived calories of minor relevance but acknowledged that they could reach significant levels in some cases. Terblanche & Remmington[17] reported that, regardless of propofol concentration, patient groups failed to meet nutritional targets because they received a lower EN volume than prescribed. This discrepancy between prescribed and delivered volumes is often attributed to procedural interruptions and gastrointestinal intolerance[17,18]. However, in critically ill patients, interruptions also occur due to hemodynamic instability and the use of high-dose vasoactive drugs[3,4]. Additionally, Pastrana et al.[18] identified the non-individualized institutional EN protocol, which used standard formulas and standardized volume progression, as a contributing factor for only half of the participants reaching their energy targets during the first seven days.

Conversely, some studies observed energy overfeeding associated with propofol use[13,20]. Popoff et al.[20] reported that all patients who received energy above target (6.9% of participants) received propofol, with an average of 267 kcal (SD=123) from the drug. During the first week, patients receiving propofol received significantly more calories than their peers (4163 kcal [SD=1911] vs 2096 kcal [SD=2032]; p<0.001). Similarly, Rai et al.[13] observed that 73.68% of patients using propofol exceeded energy requirements, receiving 101% to 126% of the target on at least one day during the first week. This highlights the importance of accounting for NNC in NS calculations to prevent overfeeding. Current NS guidelines for critically ill patients recommend starting with a lower caloric intake and gradually increasing to meet targets by the third or fourth day[1,23]. High doses of propofol may contribute to overfeeding by increasing TEI, especially during the acute phase of critical illness, a period associated with significant endogenous energy production[1,23].

Macronutrient imbalance

Another observed factor was an imbalance in macronutrient adequacy, particularly due to increased lipid intake. In some studies, the lipid intake from propofol accounted for 17.5% to 48% of total lipid intake[18,20].

In this context, Taylor et al.[12] observed that lipid intake accounted, on average, for 51% of TEI, with 20% of patients exceeding 2 g/kg/d. Although that study used a maximum recommended intake of 2.6 g/kg/d, current guidelines recommend an upper limit of 1 g/kg/day for intravenous lipid infusion, with tolerance up to 1.5 g/kg/d[2]. However, the authors did not differentiate between lipid sources (i.e., EN and propofol). Similarly, Pastrana et al.[18] reported an increase in lipid intake from 30% to 41.65% of TEI, while Viana et al.[19] observed significantly higher lipid intake in patients with COVID-19, with 38.5% exceeding 1 g/kg/d compared to their peers (p=0.002), as a result of receiving significantly higher doses of propofol (p<0.001).

Concordant results were described by Terblanche & Remmington[17], who compared 1% and 2% propofol; the group receiving 1% propofol had, on average, higher lipid intake (0.9 g/kg/d [SD=0.39] vs 0.72 g/kg/d [SD=0.21]; p=0.034), with 36% exceeding 45% of TEI from lipids. Similarly, Popoff et al.[20], when comparing patients with and without propofol sedation, found that those receiving propofol had significantly higher lipid intake (197 g [SD=109] vs 78 g [SD=100]; p<0.001). Finally, in the study by Charriere et al.[3], lipids were the sole energy source on 5.5% of the study days.

This imbalance is expected, as propofol, owing to its lipophilic nature, is formulated in a lipid emulsion and provides 0.1 g of lipids per ml[21]. Therefore, particularly at higher doses

or when combined with high-fat enteral formulas or total parenteral nutrition, propofol may significantly increase lipid intake, disrupting macronutrient balance[12,19,20] and increasing the risk of hypertriglyceridemia, lipid overload syndrome, and pancreatitis[8,24,25].

Protein intake inadequacy

Regarding protein intake, most studies reported inadequacy or deficits relative to target values[5,12,15-20], which may be partly explained by the previously mentioned strategy of reducing EN infusion rates to avoid overfeeding during propofol use[15]. This strategy reduces calories from nutritional therapy, which may result in adequate TEI but suboptimal protein and, at times, glucose/carbohydrate intake[12].

In the study by Buckley et al.[16], patients who achieved neutral or positive nitrogen balance received significantly more calories from EN (1450 kcal/d [SD=389] vs 767 kcal/d [SD=633]; p=0.029; 15 kcal/kg/d[2] vs 9 kcal/kg/d[8]; p=0.046) and, consequently, more protein (1.2 g/kg/d [SD=0.4] vs 0.8 g/kg/d [SD=0.8]; p=0.046), despite no difference in calories derived from propofol sedation (212 kcal/d [SD=202] vs 189 kcal/d [SD=303]; p=0.728; 2 kcal/kg/d [SD=2] vs 2 kcal/kg/d [SD=3]; p=0.776). Similarly, Viana et al.[19] observed that patients receiving higher doses of propofol received less protein than their peers (0.93 g/kg/d vs 1.03 g/kg/d; p=0.020), resulting in a higher median cumulative protein deficit over 20 days (-532 g [IQR=-820 to -330] vs -370 g [IQR=-545 to -153]; p=0.0077), although both groups exceeded the -300 g cutoff.

Conversely, but still consistent with the previous observation, Popoff et al.[20] found that despite overall protein intake being close to zero during the first three days, the propofol group received more protein on average (192 g [SD=125] vs 104 g [SD=129]; p<0.001). This difference may be partly explained by the higher caloric intake from nutritional therapy in this group compared with their peers (2393 kcal [SD=1431] vs 1500 kcal [SD=1922]; p<0.001). This pattern was also observed in the study by Terblanche & Remmington[17]. Although overall protein intake remained below target, the group receiving 2% propofol received significantly more protein (73.05 g/d [SD=25.16] vs 62.8 g/d [SD=24.68]; p=0.04) and more calories from NS (15.7 kcal/kg/d [SD=5.1] vs 13.4 kcal/kg/d [SD=5.6]; p=0.03).

Pastrana et al.[18] also observed a critical protein deficit, with an intake of 0.44 g/kg/d during the first seven days and only 12.55% of TEI derived from protein, compared with the study's reference target of 24%. This finding was partly attributed to propofol use and to an institutional NS protocol not tailored to individual patient needs. Other studies also reported inadequate protein intake but did not directly relate it to propofol use or make direct group comparisons; for instance, Vieira & Castro[5] reported an overall protein target adequacy of 88%.

Mitigation strategies

Buckley et al.[15] tested protein bolus supplementation while maintaining isocaloric intake, aiming to mitigate the effects of reducing EN infusion rates to avoid overfeeding during propofol use. This strategy resulted in protein delivery ranging from 24% to twice that of conventional or high-protein formulas. Patients achieved an average intake of 1.2 g/kg/d by the third day. However, this still represented a 25% to 30% deficit relative to the study's target of 2 g/kg/d. The authors attributed this deficit to procedural interruptions, as documented in other studies[3,4,17,18], and, in 20% of cases, to gastric intolerance without optimized treatment due to a national shortage of erythromycin at the time.

Other studies also tested or cited mitigation strategies[5,12,14,15,17,20], the most common being switching from 1% to 2% propofol (20 mg/ml), as doubling the concentration halves lipid and energy delivery for the same drug dose. This was demonstrated in the study by Charriere et al.[14], in which patients from the hospital using 2% propofol received significantly fewer calories from sedation (108 kcal/d [IQR=40–174] vs 136 kcal/d [IQR=61–253]; p<0.001), despite receiving significantly higher doses (2400 mg/d vs 1290 mg/d; p<0.0001). With this switch, Taylor et al.[12] observed better adequacy relative to nitrogen targets (98% [IQR=91–106] vs 85% [IQR=76–93.5]; p<0.0001), with a significant reduction in the proportion of patients with intake below 80% of the target (4.7% vs 35.3%; p=0.014). Likewise, fewer patients failed to achieve carbohydrate targets (15.3% vs 47.1%; p<0.001), and the proportion of lipids in TEI was lower (44% [IQR=42–46] vs 52% [IQR=47–56.5]; p<0.0001). In the study by Terblanche & Remmington[17], the 2% propofol group had significantly fewer patients exceeding 45% of TEI from lipids (2% vs 36%; p=0.003).

Despite the apparent benefits of 2% propofol, its availability might be a significant limitation. Although this concentration is available in several countries[6], others face supply constraints. In Brazil, for instance, only one manufacturer has regulatory approval from the National Health Surveillance Agency (ANVISA) for this concentration[21]. Moreover, regulatory constraints exist, such as in the United States, where this concentration was temporarily authorized for emergency use in 2020 during the COVID-19 pandemic, but the authorization was revoked in 2022 following the manufacturer's request, citing the intention to discontinue supply[26].

An important concern when both concentrations are available is the risk of accidental overdose if concentrations are confused or exchanged[27,28]. In addition, Regier

et al.[28] noted that the 2% propofol formulation does not contain ethylenediaminetetraacetic acid (EDTA), which could increase the risk of bacterial growth if directly contaminated. Furthermore, they highlight that, unlike the 1% formulation, the 2% version contains medium-chain triglycerides (MCT). Consequently, continuous infusion may pose a higher risk for pregnant patients, as animal studies have shown an increased risk of neural tube defects and embryonic abnormalities. However, the presence of EDTA and MCT appears to vary by manufacturer rather than concentration. In the package inserts of products available in Brazil, for example, only two of four mention EDTA in 1% propofol[29,30], and one reports the presence of MCT in both concentrations[21].

Only one study mentioned the possibility of developing water-soluble propofol[20], although this suggestion is limited by the molecule's highly lipophilic properties. Nevertheless, studies are exploring this alternative through new water-soluble molecules that act as propofol prodrugs[30,31].

Limitations of the reviewed studies

Regarding the limitations of the reviewed studies, most authors cited retrospective, observational, or single-center designs[5,12,15-17,20]. Others noted small sample sizes or sample specificity[5,13,14,16,17,19,20], limiting the generalizability of the findings. Furthermore, some studies reported estimated nutritional requirements and deficits due to the inability to use or lack of availability of indirect calorimetry[12,19,20]. Additionally, Taylor et al.[12] cited the indirect measurement of nitrogen balance. Charriere et al.[14] noted the use of different sedation protocols and enteral formulas across hospitals. Buckley et al.[15] highlighted a national shortage of erythromycin that resulted in increased gastric intolerance.

Furthermore, two studies cited limitations related to the COVID-19 pandemic: Pastrana et al.[18] were unable to implement a new NS protocol based on study findings due to ICU reorganization to accommodate only COVID-19 patients, and Viana et al.[19] reported massive staffing changes, including physicians and nurses lacking ICU-specific training and dietitians working off-site due to pandemic-related restrictions.

Limitations and strengths of this review

This review also had limitations, namely the exclusion of some studies due to the unavailability of full texts, even after contacting the authors. The fact that most included studies did not primarily aim to assess the nutritional impact of propofol sedation, resulting in a lack of specific data on nutritional adequacy or propofol dosage in some cases. Consequently, limited data on the clinical or metabolic impact of these findings available.

Regarding its strengths, this review was conducted with high methodological rigor, without restrictions on publication period or language. Nevertheless, it presents contemporary data, with most included studies published within the last five years.

CONCLUSION

This review identified that calories derived from propofol sedation can contribute to a significant proportion of the nutritional requirements of critically ill patients. Such intake may be associated with both the exacerbation of energy and lipid intake and the underdelivery of NS, particularly protein, in the presence of inadequate strategies and protocols. On the other hand, the use of 2% propofol, as well as tailored NS with the administration of protein boluses, may represent viable alternatives to mitigate this inadequacy while other pharmacological alternatives are not yet available.

These findings reinforce the need for individualized NS for critically ill patients, as well as for original studies to assess the clinical impact of nutritional inadequacy associated with propofol use and to investigate new mitigation strategies in this context.

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