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Original article

Cost analysis of Omega-3 supplementation in critically ill patients with sepsis

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SUMMARY

Introduction: Nutritional supplement of omega-3 fatty acids have been proposed to improve clinical outcomes in critically ill patients. While previous work have demonstrated that omega-3 supplementation in patients with sepsis is associated with reduced ICU and hospital length of stay, the financial impact of this intervention is unknown.

Objective: Perform a cost analysis to evaluate the impact of omega-3 supplementation on ICU and hospital costs.

Methods: We extracted data related to ICU and hospital length of stay from the individual studies reported in a recent systematic review. The Cochrane Collaboration tool was used to assess the risk of bias in these studies. Average daily ICU and hospital costs per patient were obtained from a cost study by Kahn et al. We estimated the ICU and hospital costs by multiplying the mean length of stay by the average daily cost per patient in ICU or Hospital. Adjustments for inflation were made according to the USD annual consumer price index. We calculated the difference between the direct variable cost of patients with omega-3 supplementation and patients without omega-3 supplementation. 95% confidence intervals were estimated using bootstrap re-sampling procedures with 1000 iterations.

Results: A total of 12 RCT involving 925 patients were included in this cost analysis. Septic patients supplemented with omega-3 had both lower mean ICU costs ($15,274 vs. $18,172) resulting in $2897 in ICU savings per patient and overall hospital costs ($17,088 vs. $19,778), resulting in $2690 in hospital savings per patient. Sensitivity analyses were conducted to investigate the impact of different study methods on the LOS. The results were still consistent with the overall findings.

Conclusion: Patients with sepsis who received omega-3 supplementation had significantly shorter LOS in the ICU and hospital, and were associated with lower direct variable costs than control patients. The 12 RCTs used in this analysis had a high risk of bias. Large-scaled, high-quality, multi-centered RCTs on the effectiveness of this intervention is recommended to improve the quality of the existing evidence.

1. Introduction

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection [1]. It is among the most common global causes of emergency admission to the Intensive Care Unit (ICU) [3,4] and the leading cause of morbidity or mortality in critical care environments [5,6]. 1.5 million people in the U.S are diagnosed with sepsis every year [7]. Patients admitted to the ICU with sepsis are also have prolonged length of stay (LOS) [8]. Since ICU is the most resource demanding unit in nearly every hospital, there are significant costs associated with patients that require longer LOS in ICU [4,9].

In 2013, sepsis was the most expensive condition treated in the United States accounting for $23.7 billion dollars or 6.2% of all hospital expenditures [10]. As the aging population continues to

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increase in developed countries, the prevalence of sepsis and its associated high costs also escalates and places further financial pressure on the healthcare system. Immune nutrition management in septic patients is a cost-effective and comparatively new area of research in critical care that aims to recover a functioning immune system [11,12]. Many studies have demonstrated promising effects of omega-3 supplementation in patients with severe sepsis, believed to be due to its anti-inflammatory properties [11–16].

A recent systematic review by Lu et al. assessed the health outcomes of omega-3 supplementation in ICU patients with sepsis [16]. Their analysis has shown a significant reduction in hospital and ICU LOS with administration of omega-3 [19]. While this review investigated the health outcomes of Omega-3 in septic patients, the financial impact of Omega-3 supplementation was not examined. We evaluated the impact on ICU and hospital costs by conducting a cost analysis on omega-3 supplementation in this patient population.

2. Methods

We extracted individual length of stay in ICU and in hospital from the data reported by 12 prospective, randomized control trials involving 925 critically ill patients with sepsis included in the systematic review from Lu et al. [19]. The Cochrane Collaboration tool was used to assess the risk of bias in these studies [19].

We performed a cost analysis to compare hospital and ICU costs of omega-3 supplementation, as compared to costs of control patients. We pooled hospital and ICU LOS data from the 12 RCTs in Lu et al. using a random effect model [19]. Average daily hospital and ICU costs per patients were obtained from the study by Kahn et al. [20], a retrospective cohort study of all patients undergoing invasive mechanical ventilation for 48 h or longer in one tertiary care teaching hospital in Pennsylvania. We focused on one type of cost: direct variable costs. We defined direct variable costs as total hospital costs excluding overhead, staff salary and equipment costs. According to Kahn et al. [20], direct variable costs can be used to estimate immediate cost-savings as a result of reduced LOS.

We estimated hospital and ICU costs by multiplying weighted LOS with respective average daily cost per patient. For ICU costs, we obtained the daily direct variable costs as follows (in US Dollars [USD]): ICU day 1 $3678, day 2 $1057, day 3 $839, day 4 $834, and day 5 $690 onward. Hospital cost was $249/day. We calculated difference in costs by subtracting hospital costs, ICU costs and total direct variable costs from patients with Omega-3 supplements to patients without supplements. 95% confidence intervals (CIs) were estimated using bootstrap re-sampling procedures with 1000 iterations. We inflated all costs to 2017 USD using the annual consumer price index reported by the Bureau of Labor Statistics [21].

The impact of different study methods on LOS was investigated. Three sensitivity analyses were performed to examine the impact of studies conducted after 2010, administration of a placebo and double blinding.

3. Results

12 out of 17 studies [22–33] in the Lu et al. meta-analysis reported data on ICU length of stay and 4 studies [22,27,29,30] reported the overall hospital length of stay. 925 patients in total were included in the meta-analysis. This data was abstracted and included in this cost analysis.

3.1. Quality assessment

8 out of 12 studies were judged to have a “high” risk of bias while the remaining 4 were “unclear” for the risk of bias. Quality of evidence was assessed by GRADE was “very low” for ICU Length of Stay.

3.2. ICU LOS

Comparisons between septic patients receiving omega-3 supplementation and controls are depicted in Table 1a. 10 out of 12 studies (83%) reported shorter ICU LOS among patients receiving omega-3 supplementation. The mean ICU LOS for the omega-3 supplement group was 12.8 days (95% CI: 8.9–16.7) compared to 16.2 days (95% CI: 11.7–20.7) in the control arm. Subsequently, septic patients supplemented with omega-3 spend on average 3.8 (95% CI: 2.09–5.49; $P < 0.00001$; $I^2 = 80\%$) fewer ICU days than the patients without supplements.

3.3. Hospital LOS

4 out of the 12 studies ($n = 216$) reported difference in hospital LOS between patients receiving omega-3 supplementation and control patients (Table 1b). 3 of these studies found that patients receiving omega-3 supplements experienced shorter hospital LOS than those who did not. The mean hospital LOS for the omega-3 supplements was 18.7 days (95% CI: 9.8–27.7), as compared to 21.5 days (95% CI: 16.2–26.7) in the control group. Patients receiving omega-3 supplementation spend 6.5 (95% CI: −2.9–16.0; $P < 0.0001$; $I^2 = 87\%$) fewer days in hospital than the control patient group.

3.4. Cost analysis

The cost analysis determined the mean cost per patient based on the mean ICU and hospital LOS from each study. Cost comparison between the intervention and the control group is depicted on Table 2. Based on data reported, 10 out of 12 studies have shown significant cost saving benefits associated with lower ICU LOS. The average cost of ICU admissions is $15,274.30 (IQR: 11,744–19,368) per omega-3 supplemented septic patient compared to $18,171.57 (IQR: 14,592–21,085) per control patient (Table 3a). The difference in ICU cost savings was $2897.27 (95% CI: 2589.45–3885.06) between the two groups (Table 4). 3 out of 4 RCTs demonstrated significantly lower hospital spending in the omega-3 supplemented patients versus the control group (Table 2). The average cost of hospital admission in omega-3 supplemented patients was $17,087.68 (IQR: 12,287.83–17,595.23) per patient whereas cost per control patient was $19,777.92 (IQR: 15,069.80–22,957.73) (Table 3b). The total cost difference between the two groups was $2690.24 (95% CI: 888.62–2953.16) (Table 4).

Table 4 illustrates the average cost savings per sepsis patient in the ICU and hospital and the potential cost savings if 250, 500, 750 or 1000 septic patients were admitted in those settings.

3.5. Sensitivity analysis

The sensitivity analysis results are displayed in Table 3a for ICU costs and Table 3b for hospital costs. For ICU difference in costs, the sensitivity analyses excluded 3 RCTs prior to 2010 (MD = -$2727; 95% CI: −2890.99, −2561.64, $I^2 = 0\%$), 3 trials that did not use placebos for the control group (MD = -$3171; 95% CI: −3499.67, −2877.03, $I^2 = 53\%$) and 9 studies that were not double blinded (MD = -$3277; 95% CI: −4767.42, −1871.40, $I^2 = 40\%$). The same sensitivity analyses were performed for hospital cost differences. Trials conducted prior

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