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[Intervention Review]

# Enteral versus parenteral nutrition and enteral versus a combination of enteral and parenteral nutrition for adults in the intensive care unit

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## ABSTRACT

### Background

Critically ill people are at increased risk of malnutrition. Acute and chronic illness, trauma and inflammation induce stress-related catabolism, and drug-induced adverse effects may reduce appetite or increase nausea and vomiting. In addition, patient management in the intensive care unit (ICU) may also interrupt feeding routines. Methods to deliver nutritional requirements include provision of enteral nutrition (EN), or parenteral nutrition (PN), or a combination of both (EN and PN). However, each method is problematic. This review aimed to determine the route of delivery that optimizes uptake of nutrition.

### Objectives

To compare the effects of enteral versus parenteral methods of nutrition, and the effects of enteral versus a combination of enteral and parenteral methods of nutrition, among critically ill adults, in terms of mortality, number of ICU-free days up to day 28, and adverse events.

### Search methods

We searched CENTRAL, MEDLINE, and Embase on 3 October 2017. We searched clinical trials registries and grey literature, and handsearched reference lists of included studies and related reviews.

### Selection criteria

We included randomized controlled studies (RCTs) and quasi-randomized studies comparing EN given to adults in the ICU versus PN or versus EN and PN. We included participants that were trauma, emergency, and postsurgical patients in the ICU.

### Data collection and analysis

Two review authors independently assessed studies for inclusion, extracted data, and assessed risk of bias. We assessed the certainty of evidence with GRADE.

### Main results

We included 25 studies with 8816 participants; 23 studies were RCTs and two were quasi-randomized studies. All included participants were critically ill in the ICU with a wide range of diagnoses; mechanical ventilation status between study participants varied. We identified 11 studies awaiting classification for which we were unable to assess eligibility, and two ongoing studies.

Seventeen studies compared EN versus PN, six compared EN versus EN and PN, two were multi-arm studies comparing EN versus PN versus EN and PN. Most studies reported randomization and allocation concealment inadequately. Most studies reported no methods to blind personnel or outcome assessors to nutrition groups; one study used adequate methods to reduce risk of performance bias.

### Enteral nutrition versus parenteral nutrition

We found that one feeding route rather than the other (EN or PN) may make little or no difference to mortality in hospital (risk ratio (RR) 1.19, 95% confidence interval (CI) 0.80 to 1.77; 361 participants; 6 studies; low-certainty evidence), or mortality within 30 days (RR 1.02, 95% CI 0.92 to 1.13; 3148 participants; 11 studies; low-certainty evidence). It is uncertain whether one feeding route rather than the other reduces mortality within 90 days because the certainty of the evidence is very low (RR 1.06, 95% CI 0.95 to 1.17; 2461 participants; 3 studies). One study reported mortality at one to four months and we did not combine this in the analysis; we reported this data as mortality within 180 days and it is uncertain whether EN or PN affects the number of deaths within 180 days because the certainty of the evidence is very low (RR 0.33, 95% CI 0.04 to 2.97; 46 participants).

No studies reported number of ICU-free days up to day 28, and one study reported number of ventilator-free days up to day 28 and it is uncertain whether one feeding route rather than the other reduces the number of ventilator-free days up to day 28 because the certainty of the evidence is very low (mean difference, inverse variance, 0.00, 95% CI -0.97 to 0.97; 2388 participants).

We combined data for adverse events reported by more than one study. It is uncertain whether EN or PN affects aspiration because the certainty of the evidence is very low (RR 1.53, 95% CI 0.46 to 5.03; 2437 participants; 2 studies), and we found that one feeding route rather than the other may make little or no difference to pneumonia (RR 1.10, 95% CI 0.82 to 1.48; 415 participants; 7 studies; low-certainty evidence). We found that EN may reduce sepsis (RR 0.59, 95% CI 0.37 to 0.95; 361 participants; 7 studies; low-certainty evidence), and it is uncertain whether PN reduces vomiting because the certainty of the evidence is very low (RR 3.42, 95% CI 1.15 to 10.16; 2525 participants; 3 studies).

### Enteral nutrition versus enteral nutrition and parenteral nutrition

We found that one feeding regimen rather than another (EN or combined EN or PN) may make little or no difference to mortality in hospital (RR 0.99, 95% CI 0.84 to 1.16; 5111 participants; 5 studies; low-certainty evidence), and at 90 days (RR 1.00, 95% CI 0.86 to 1.18; 4760 participants; 2 studies; low-certainty evidence). It is uncertain whether combined EN and PN leads to fewer deaths at 30 days because the certainty of the evidence is very low (RR 1.64, 95% CI 1.06 to 2.54; 409 participants; 3 studies). It is uncertain whether one feeding regimen rather than another reduces mortality within 180 days because the certainty of the evidence is very low (RR 1.00, 95% CI 0.65 to 1.55; 120 participants; 1 study).

No studies reported number of ICU-free days or ventilator-free days up to day 28. It is uncertain whether either feeding method reduces pneumonia because the certainty of the evidence is very low (RR 1.40, 95% CI 0.91 to 2.15; 205 participants; 2 studies). No studies reported aspiration, sepsis, or vomiting.

### Authors' conclusions

We found insufficient evidence to determine whether EN is better or worse than PN, or than combined EN and PN for mortality in hospital, at 90 days and at 180 days, and on the number of ventilator-free days and adverse events. We found fewer deaths at 30 days when studies gave combined EN and PN, and reduced sepsis for EN rather than PN. We found no studies that reported number of ICU-free days up to day 28. Certainty of the evidence for all outcomes is either low or very low. The 11 studies awaiting classification may alter the conclusions of the review once assessed.

## PLAIN LANGUAGE SUMMARY

### Delivery of nutrition (food) to critically ill adults other than by the person eating and swallowing the food/nutrition

#### Background

Critically ill adults in the intensive care unit (ICU) are at an increased risk of malnutrition because the body responds to serious illness or injury by increasing the metabolic rate. Also, the person's feeding routine may be disrupted because they are unconscious or too ill to feed themselves or eat normally. This means alternative ways to ensure people receive adequate nutrition must be used. People may be given artificial nutrition in three ways: enteral feeding (through a tube placed into the stomach or small intestine; parenteral feeding (through a tube inserted into a vein whereby nutrients enter the bloodstream directly); or by a combination of both routes. This review compared the effects of these routes.

#### Study characteristics

The evidence is current to 3 October 2017. We included 25 studies with 8816 participants who had trauma, emergency, medical or postsurgical conditions and were in the ICU. Eleven studies are awaiting classification (because we did not have enough details to assess them) and two studies are ongoing. Included studies compared enteral feeding with parenteral feeding, or with combined enteral and parenteral feeding.

## Key results

Studies reported the number of people who died from any cause at different time points. We found no evidence that enteral feeding compared to parenteral feeding or compared to a combination of routes was more or less likely to reduce the number of deaths in hospital, within 90 days and 180 days. We found evidence from three small studies that fewer people died within 30 days when feeding was given through combined enteral and parenteral routes. No studies reported number of ICU-free days up to day 28 (i.e. length of stay in the ICU by taking account of expected participant loss because of death) and one study reported that the feeding route did not affect the number of ventilator-free days.

We found no evidence that enteral feeding compared to parenteral feeding was likely to increase or decrease cases of aspiration (the entry of materials such as food from the digestive system to the lungs) or pneumonia (swelling of the tissue in one or both lungs that is usually caused by a bacterial infection). Enteral nutrition may reduce sepsis (a life-threatening condition that arises when the body's response to infection causes injury to its own tissues and organs), although evidence was from studies of people with different conditions (such as trauma, medical, or postsurgical conditions). We found that fewer participants vomited if they were given parenteral feeding rather than enteral feeding, although there were few studies with very few reported events.

## Certainty of the evidence

It was not possible for researchers to mask the ICU staff to the type of feeding route, which may have biased the findings, and study authors did not consistently report good study methods. People in each study had different types of critical illness (such as trauma, medical, or postsurgical conditions) which may have affected how they responded to the type of feeding route, and there were limited data for many of our measurements. We believed that the certainty of the evidence was low or very low.

## Conclusion

We found insufficient evidence to determine with confidence whether one feeding route was better at reducing the number of deaths, the number of ventilator-free days, and side effects. No studies reported number of ICU-free days up to day 28. Evidence was of low and very low certainty, and we could not be confident in the findings of our review.