



EDITORIAL

Evidence supports nutritional support

Introduction

Nutritional support has long been one of the most controversially discussed therapeutic interventions in modern medicine. In fact more than 20 years ago, *Koretz* wrote a noteworthy article: "What supports nutritional support?",¹ outlining that we do not have enough information to make evidence based decisions about indications of nutritional support. However, since then the situation has considerably changed.

There is excellent evidence that undernutrition is an independent risk factor for higher morbidity, increased length of hospital stay, higher readmission rates, delayed recovery, lower quality of life as well as higher hospital costs and higher mortality.²

Similarly the evidence about the effectiveness of nutritional support has grown considerably within the last decades. Therefore, the European Society for Clinical Nutrition and Metabolism (ESPEN) has decided to publish evidence-based guidelines on enteral nutrition to evaluate benefits and risks of enteral nutrition in a predefined reproducible way. These guidelines represent the most comprehensive evaluation of enteral nutrition yet. In 10 chapters the role of enteral nutrition in different indications has been evaluated. Furthermore, ethical and methodological aspects of enteral nutrition are dealt with in separate chapters.

These guidelines form a consensus among a group of experts in clinical nutrition but also in their individual specialties to which nutritional support is applied. In establishing the guidelines the consensus group followed the internationally accepted recommendations of the Scottish Intercollegiate Guidelines Network (SIGN)³ for guideline development. These regulate composition of consensus groups, systematic evaluation of the literature and the process of finding a consensus as described in the methods section.

However, since most of the chapters of the guideline deal with very specific questions of timing, route of application and a composition of enteral nutrition solutions, it appears necessary to discuss some basic issues in this editorial.

What are relevant questions? It is still not clear for all clinical conditions if nutritional support can counteract the negative effects of undernutrition and starvation, or if disease inherent catabolism renders substrate supplementation inefficient. Therefore, it is important to evaluate the effect of nutritional support specifically in different disease states. Similarly the amount and composition of substrates needed, the route of application and the appropriate study design for nutritional intervention studies are still in debate. Fortunately these problems have also been extensively studied. Within the last 6 years, e.g. 91 Cochrane reviews on enteral nutrition have been published. Therefore the guidelines can provide clear responses to most of these questions.

Study design

It is important do distinguish between the approach to evaluate some pharmacological innovation and that to study physiological issues which are so obvious that no trials are necessary. Nobody ever would doubt that a patient on complete starvation will die eventually. This may be termed a parachute issue on the basis that no trial on the use of parachutes is necessary to prove that jumping out of an aeroplane without one is likely to be fatal. In the same sense acute and worsening respiratory failure is likely to be fatal in minutes without artificial ventilation, cessation of fluid intake is fatal in days, acute renal failure without dialysis may be fatal in weeks and complete starvation without nutritional support leads to impaired function within days or weeks and death in 2–3

months even in a healthy person.⁴ No controlled trial of artificial ventilation, dialysis or fluids has been undertaken for obvious reasons in patients with respiratory failure or renal failure respectively and it therefore seems rather silly to expect a treatment of prolonged starvation to be tested in this way. It is inherently obvious for example, that the alternative to tube feeding in complete dysphagia or to parenteral nutrition in prolonged gastrointestinal failure is death within a finite time.

Besides the fact, that the consequences of starvation are obvious as outlined above, it is almost impossible to perform blinded studies of nutritional support versus no nutritional support due to obvious reasons. It is therefore not a scientific question if nutritional support is necessary in starvation but rather to which degree may a patient be starved without increasing his risk or what is an adequate balance between the risks of artificial nutrition and the risks of starvation.

Relevant endpoints for nutritional support

The choice of appropriate endpoints by which to judge the efficacy of nutritional support needs to be considered carefully and separately for each clinical condition, for example: in a condition with a low mortality, such as colorectal surgery or one with a high mortality in which 95% of the mortality risk relates to the disease and other coincident pathology, the use of mortality as the sole endpoint of nutritional support may be unhelpful or misleading. It may be more appropriate to use other parameters such as complication rates, use of antibiotics, time on the ventilator, length of stay or time to rehabilitation, in other words—does the patient get better more quickly with less consumption of resources. For most therapies this is well accepted, e.g. quality of life or reduction of fatigue is an accepted endpoint for chemotherapy and lower cost with similar efficacy is an important endpoint for many drug studies. For nutritional support the validity of these endpoints was long dismissed as soft or surrogate endpoints. This may be due to the fact, that everybody considered it logical, that a well-nourished person feels better than a starving person. However to achieve this in disease states needs the therapeutic intervention of nutritional support.

Relevant question and endpoints are therefore:

- How can clinically relevant undernutrition be diagnosed?
- Does nutritional support improve nutritional status in a specific situation?
- Does nutritional support affect prognosis in a specific situation?
- Do short periods of starvation (i.e. <7 days) matter in terms of outcome?
- What is the preferred feeding method in a given situation?
- What is the most appropriate enteral or parental formula, composition and amount for each condition?
- Does feeding beneficially affect or alternatively exacerbate the underlying pathological process?

Evidence-based benefits of nutritional support

While the authors of each section have examined the evidence in their respective specialties, the general evidence concerning the benefits of oral nutritional supplements (ONS) and enteral tube feeding have been comprehensively and systematically reviewed by Stratton, Green, and Elia in a recent publication.² In 7–11 RCTs of ONS reviewed, they found a reduction in mortality (26% vs. 17%), reduced complications (27% vs. 12%), and reduced length of stay (28 vs. 19 days). In patient groups without significant prior undernutrition, i.e. with a BMI > 20 kg/m², mortality was not significantly reduced (20% vs. 19%), but complications were reduced in three trials (27% vs. 12%), and length of stay was reduced (16 vs. 12 days).

In 12 RCT's (600 patients) of enteral tube feeding, mortality was reduced (23% vs. 11%), in 17 RCT's (749 patients) total complication rates were reduced (48% vs. 33%) and in 9 RCTS (442 patients) infective complications were reduced (46% vs. 23%). Improved outcome was correlated with adequate nutritional intake and weight gain.

The general indication and effectiveness of ONS and enteral tube feeding in patients who cannot fulfil their substrate needs adequately is therefore well established and the whole consensus group strongly agreed on this.

Although, as the authors of the various sections conclude, results may vary according to diagnosis, prior nutritional status, age, the technical adequacy of treatment, and patient selection.

In some areas, evidence for specific questions like timing and composition of enteral nutrition is still lacking upon which to make level A recommendations and much practice, as in other areas of medicine, is guided by level C evidence. Further studies are clearly required in these areas.

Integration of nutritional support in the therapeutic strategy

Although nutritional support is therapy in most cases it is exactly what it says—supportive rather than specific treatment of the underlying disease. It prevents the deleterious effects of starvation while the underlying condition resolves naturally or in response to treatment. It is therefore, only one facet of overall management and needs to be integrated properly into it. Shortcomings in other aspects of care may negate any benefits of nutritional support, similarly inappropriate, unbalanced, unskilled, or excessive feeding may interfere with other aspects of treatment and render them less effective. Similarly the technical interventions associated with enteral tube feeding have their own risks, which must be weighed, in each case, against the expected benefits. Such risks are minimised when treatment is carried out by expert staff. Conversely other treatments e.g. drugs may impair appetite, G.I. function and nutritional status.

Conclusion

It should therefore be clear, that nutritional support is indispensable for patients not fulfilling their energy and substrate needs. These guidelines do provide evidence-based information about specific problems like timing, dosing, composition and route of application. They also show where additional studies are needed and under which conditions limitation or withdrawal of nutritional support like other therapies might be adequate.

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References

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