Early enteral nutrition of the critically ill –
advantages and pitfalls

Monday 2nd September 2002 18:15hrs-19:45hrs

ABSTRACTS

Pharmaconutrition:
A new concept in critical care

Fresenius Kabi

Caring for Life

Introduction

Peter Fürst, MD, PhD

Institute of Nutrition Science, University of Bonn, Germany

Professor Peter Fürst is Professor Emeritus of Biochemistry of Nutrition and Director Curatorium for Clinical Dietetics at the Institute for Nutrition Science, University of Bonn, Germany. Having studied music for seven years in his birth place of Budapest, Hungary, Professor Fürst then initiated his study of medicine, which he continued at the Karolinska Institute in Stockholm, having emigrated to Sweden in 1957. In addition to his medical training, Professor Fürst also studied chemistry and biochemistry at the University of Stockholm, obtaining a PhD in biochemistry in 1967. Since obtaining his MD, he has worked and taught at various hospitals in Sweden and also in Germany, where he was Professor and Chairman of the Institute for Biological Chemistry and Nutrition at the University of Hohenheim in Stuttgart. He has extensive research experience, including many aspects of clinical nutrition, and the development of methods to study the metabolism of substances such as carnitine, phospholipids and eicosanoids. Professor Fürst has published approximately 500 titles and has given more than 500 lectures all over the world. In addition to his current posts in Bonn, he has extensive responsibilities as adviser or member of various national and international nutrition bodies.

The supply of adequate nutrients is important for optimal recovery from illness. Nutrients may be supplied via the parenteral or enteral routes, the composition and types of nutrients that can be delivered via each route being different. It has been repeatedly claimed that enteral feeding is superior to parenteral nutrition and that it is important to use enteral nutrition whenever possible. However, it is neither easier to apply nor to monitor, and is not even feasible in some critically ill patients. Others are at risk of being harmed by too much enteral feed, and so great caution and vigilance should be exercised. Poor delivery and partial feeding are also problems to be considered. In his lecture, Professor Robert Martindale will look at both sides of the coin and consider the advantages and limitations of early enteral nutrition.

Early provision of specific nutrients facilitates organ and system functions. Provision of antioxidants and related compounds, such as selenium, zinc and glutamine, is of the utmost importance during critical illness. Their use in pharmacological doses should be carefully controlled. In the second lecture, Professor Hans Biesalski will scrutinise the indications for antioxidant therapy in various clinical conditions. Finally, in the third lecture, Dr Ulrich Suchner will present a novel therapeutic system that allows early combined enteral/parenteral nutrition in critically ill patients with adequate content and composition of nutrients.

Any future interventions to alter the pathological processes in critically ill patients – i.e. to modify the metabolic response to stress – must be undertaken with caution. Maximisation of the benefit to risk ratio and improvement of outcome with nutritional interventions is most likely due to correction of nutrient deficiencies and the use of specific nutrients in order to achieve favourable metabolic effects.

Early enteral nutrition of the critically ill – advantages and pitfalls

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Early enteral nutrition: two sides of the coin

Robert G Martindale, MD, PhD

Gastrointestinal Surgery Section and Surgical Nutrition Service,
Medical College of Georgia, Augusta, Georgia, USA

Professor Robert Martindale is Associate Professor of Surgery, Chief of the Gastrointestinal Surgery Section, and Director of the Surgical Nutrition Service at the Medical College of Georgia, Augusta, Georgia, USA. He obtained a PhD in nutrition, in the area of gastrointestinal physiology, at the University of California, Los Angeles, and then went on to qualify in Medicine at George Washington University, Washington, DC in 1984. He undertook his Surgical Residency at the Madigan Army Medical Center in Tacoma, Washington, where he became Director of the Nutrition Support Service until 1989. Between 1989 and 1993, Professor Martindale was initially Director of Surgical Research and then Director of Surgical Critical Care at the Eisenhower Army Medical Center at Fort Gordon, Georgia. In 1993, Professor Martindale became, and remains, Chief of the General Surgery Service at the Department of Veterans Affairs Medical Center in Augusta, Georgia, in addition to his posts at the Medical College of Georgia. He is a member of many societies, including the American Society for Parenteral and Enteral Nutrition and the Society for Surgery of the Alimentary Tract, and is a Fellow of the American College of Surgeons. He has published extensively on a wide range of surgical and nutrition-related subjects, in peer-reviewed journals, textbooks and audiovisual media, and has presented papers at meetings throughout the USA.

Nutritional support and care of the intensive care unit (ICU) patient has evolved substantially since its inception over 50 years ago. It should be borne in mind that nutrition is just one of the many treatment variables altering outcome. Variables such as the quantity and timing of resuscitation, wound care, respiratory support, and medications all must be considered when making a nutrition plan. Nutrition plans should include not only the quantity of nutrient but the composition of nutrient, the timing and the route of nutrient delivery.

Enteral and parenteral nutrition each have their own benefits and drawbacks, with advantages clearly outweighing the disadvantages when enteral nutrition is used. These advantages include, but are not limited to, attenuation of the metabolic response to stress, better nitrogen balance, better glycaemic control, maintenance of the mucosal barrier and gut associated lymphoid tissue (GALT), enhanced visceral blood flow and greater variety of potential nutrient sources. Enteral nutrition has also remained cost effective.

Despite all these advantages, enteral nutrition must be used with caution in the severely ill, as GI dysmotility, aspiration, diarrhoea and gut ischaemia are all potential and fairly common problems. Frequent arguments against enteral feeding include 'ileus', medications altering GI function, inadequate resuscitation, access difficulties and haemodynamic instability. Enteral feeding associated jejunal necrosis has been reported and is usually associated with overly aggressive feeding during states of haemodynamic instability and the use of adrenergic agents for blood pressure or cardiac support.

Many ICU patients require combinations of enteral and parenteral nutrition, the former being given at a quantity sufficient to yield mucosal protection and enhanced visceral blood flow, with the energy deficit made up parenterally.

Nutrition support continues to evolve with our growing knowledge of metabolism. New concepts should continually be critically tested and evaluated so that this evolution of critical care nutrition will continue to yield optimal patient care.

Has the Pendulum For Enteral Feeding Swung Too Far?

- 15-39% intolerant
- Respiratory compromise
- Aspiration (pneumonia)
- Access complications
- Jejunal necrosis

Enteral Nutrition

Advantages	Disadvantages
↓ Metabolic Response	GI Dysmotility
↑ Nitrogen Balance	Aspiration
Better Glycaemic Control	Distention
Mucosal Barrier Function	Diarrhoea
↑ GALT	Gut Ischaemia
↑ Variety of Nutrients	Access Problems
↑ Visceral Blood Flow	
Cost Effective	

Treatment Variables Altering Outcome

- Resuscitation
- Operative Procedures
- Wound Care
- Respiratory Support
- Medications
- Nutrition
  - Quantity
  - Composition
  - Timing
  - Route

Enteral supply of antioxidants: too little of a good thing?

Hans K Biesalski, MD

Institute of Biological Chemistry and Nutrition,
University of Hohenheim, Germany

Professor Hans Biesalski is currently based at the Institute of Biological Chemistry and Nutrition at the University of Hohenheim, Germany, where he was appointed C4-professor in 1993 and became Executive Director in 1995. He undertook his medical training at the University of Bonn and the University of Mainz, where he qualified as MD in 1981 and also held a C1 position within the Institute of Physiological Chemistry from 1985 to 1987. Professor Biesalski is a member of many societies and advisory boards, including ESPEN, the International Vitamin A Consultative Group, the Managing Board of the German Academy of Nutrition and the New York Academy of Science. He is also a Member of the Advisory Board of the International Journal of Vitamin and Nutrition Research, and the Scientific Advisory Board of the European Journal of Nutrition, and has published extensively in his own right. The focus of his own scientific research projects has been on the mode of action of antioxidant vitamins, retinoid metabolism and therapeutic possibilities and, in cooperation with various European groups, the development of novel feeds.

Conditions leading to oxidative stress in the hospitalised patient

Attack by reactive oxygen species (ROS) and activation of neutrophils, including the increased adherence of leucocytes and monocytes to vascular endothelial cells, lead to increased microvascular permeability and thrombosis. These events, which involve tissue damage, leukocyte and endothelial cell activation, and a systemic immune response with activated PMNs damaging remote vascular beds, are currently thought to be fundamental to post-trauma complications such as pulmonary dysfunction, acute respiratory distress syndrome (ARDS) and multiple organ failure.

In particular, high concentrations of nitric oxide (NO°) (formed during oxidative stress) increase epithelial permeability, affect cellular proliferation and lead to the endothelial damage that occurs during sepsis. NO° rapidly reacts with superoxide ($^{\circ}O_2^-$) to form peroxynitrite ($OONO^-$), which oxidises essential sulfhydryl groups on proteins. Peroxynitrite rapidly decays and leads to lipid peroxidation and nitrosylation of aromatic amino acids, one result of which is alteration of membrane protein (Fig. 1) and endothelial barrier function. Moreover, excessive generation of NO° contributes to hypotension in septic shock. A sufficient concentration of antioxidants might decrease oxidative damage by reducing the excess of superoxides and NO°, followed by attenuation of peroxinitrate formation.

Influence of trauma and injury on antioxidant levels

A couple of reports exist describing a substantial antioxidant deficiency in critically ill patients. Patients with septic shock showed significantly reduced levels of α-tocopherol, ß-carotene and lycopene (Figs. 2 and 3), while antioxidant co-factors (selenium and zinc) were depleted in burns injuries. Thiobarbituric acid reactive substances (TBARS) as markers of oxidative stress are usually increased in patients with sepsis or ARDS. Decreased α-tocopherol and ascorbic acid concentrations are described in critically ill patients and increased markers of oxidative stress (TBARS, exhaled pentane, etc) were detected. A decrease in α-tocopherol was documented within the ischaemic period during aortic aneurysm repair.

Conclusion

There is a good evidence from experimental and clinical studies that trauma and injury result in an imbalance of the antioxidative system due to an increase in ROS formation and a decrease in exogenous antioxidants. Clinical studies indicate that loss of antioxidants is accompanied by an increased risk for sepsis and MOF. Consequently, supplementation with antioxidants should have a beneficial effect. To avoid problems with peri- and post-traumatic exhaustion of antioxidants, which might be accelerated in cases with inadequate nutrition, antioxidants should be supplied as early as possible.

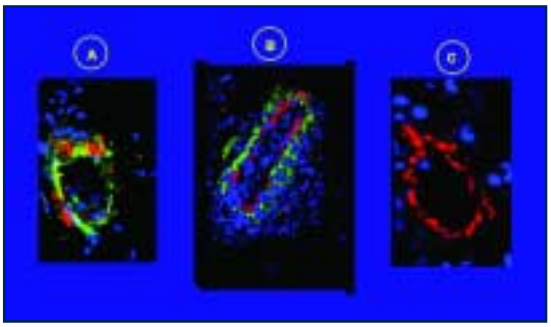

Fig. 1. Nitrosylated proteins were demonstrated in the endothelium of burns patients (see A and B). Either partial or total reduction of protein nitrosylation could be demonstrated when parenteral vitamin C was administered (see C).

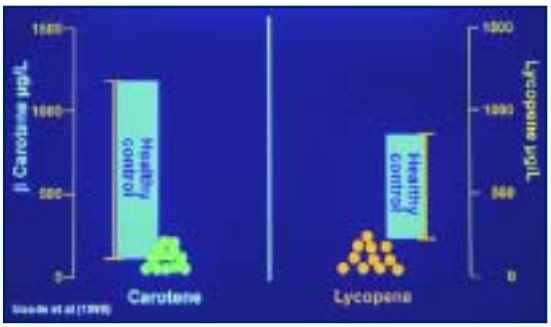

Fig. 2. Plasma β carotene and lycopene concentrations in patients with sepsis and healthy controls.

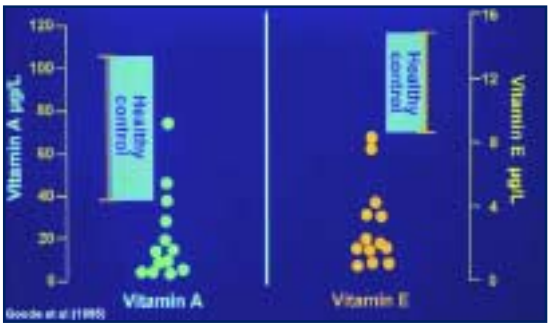

Fig. 3. Plasma vitamin A and E concentrations in patients with sepsis and healthy controls.

A step forward: novel concepts in early enteral nutrition

Ulrich Suchner, MD

Medical Director, Fresenius Kabi Deutschland GmbH, Bad Homburg, Germany

Dr Ulrich Suchner is currently Medical Director at Fresenius Kabi Deutschland GmbH at Bad Homburg in Germany. He qualified as a doctor at the Medical School of the Technical University in Munich and subsequently specialised in anaesthesiology. Following several years as Resident in Anaesthesiology at the Ludwig-Maximilian-University, Munich, Dr Suchner spent a year as a Visiting Research Fellow in Anaesthesiology (Critical Care) at the Montefiore Medical Center in New York, USA, where he investigated the metabolic effects of recombinant human growth hormone in patients receiving parenteral nutrition. He then returned to Germany where he spent six years as a staff member of the interdisciplinary ICU in the Department of Anaesthesiology at the University of Munich, carrying out research into immunonutrition and early enteral nutrition. He then spent a further six years as Resident in Anaesthesiology at the Ludwig-Maximilian-University, Munich where, until 2001, he also held a teaching position in the Department of Anaesthesiology of the Klinikum Großhadern. Since then, Dr Suchner has continued with unremunerated teaching in the same department, specialising in nutrition therapy in the critically ill.

Numerous trials evaluating immune-modulating diets (IMD) have suggested that they are associated with a number of beneficial clinical effects, including reductions in infectious complications, fewer days on antibiotics and respirator, and shortened ICU and hospital stay. These effects, in turn, have been shown to be associated with cost benefits. There has been concern, however, that better outcome is observed only in patients who tolerate significant amounts of formula. Thus, the claimed benefit cannot be extrapolated to all patients. In fact, critically ill patients with severe sepsis, shock and organ failure not only do not benefit but may actually be harmed by treatment with IMD, since current diets are unsuitable for this type of patient (Fig. 1). Major problems are:

1) Inadequate provision of 'key nutrients' via the enteral route due to feeding intolerance.
2) Lack of short chain fatty acids (SCFA) due to reduced enteral tolerance of fibre.
3) Insufficient capacity to counteract free radical induced damage of the intestinal barrier.
4) Administration of pro-inflammatory and radical generating substrates.

In order to facilitate adequate nutrition as far as essential nutrients – but not energy or nitrogen – are concerned, a ready-to-use supplement for enteral nutrition (EN) was developed (Intestamin®, Fresenius Kabi, 250kcal in 500ml/d). This supplement contains glycerol esters of SCFAs (1g tributyrin as a substitute for fibre), a high glutamine content (30 g) as dipeptides and an ample load of antioxidants (selenium 300µg, zinc 20mg, vitamin C 1.5g, vitamin E 500mg, ß-carotene 10mg). Since there is a functional overlap of the antioxidant substrates, their simultaneous administration is relevant (Fig. 2). Arginine is not included to avoid undesirable formation of NO, which is especially detrimental during critical illness. Adequate energy and nitrogen have to be provided by means of conventional parenteral/enteral regimens (Fig. 3).
Intestamin® is designed for use in severely stressed patients receiving TPN, presenting with severe intolerance to conventional EN (i.e. in SIRS, sepsis, organ failure, or burns), but without strong contraindications for EN, in order to support maintenance of gut barrier integrity. Clinical studies have confirmed the safety and tolerability of this new enteral supplement, while efficacy has yet to be demonstrated.

In conclusion, Intestamin® is positioned as an 'interface' between enteral and parenteral nutrition, facilitating new areas of application for enteral feeds and complementing parenteral feeding, thereby initiating innovative strategies in clinical nutrition.

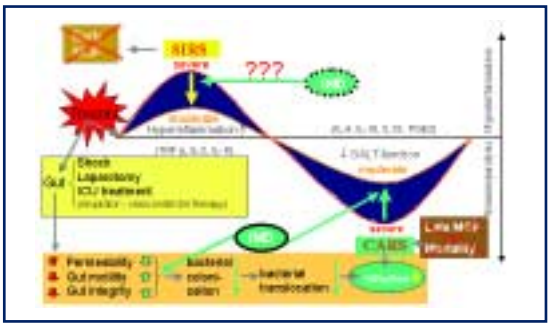

Fig. 1. Scientific rationale of currently available immune-modulating enteral diets (IMD) and their limitations affecting immune response and outcome in critical illness.*

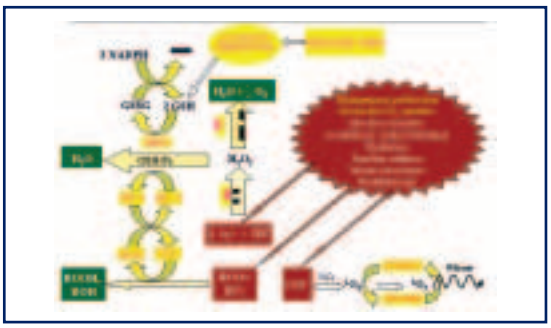

Fig. 2. Functional overlap of zinc, selenium, Vitamin E, Vitamin C, glutamine and ß-carotene to maintain antioxidant defences.*

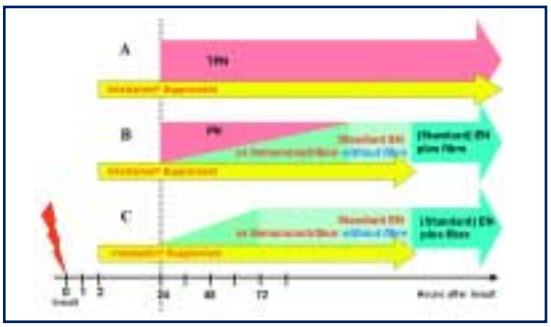

Fig. 3. Options for clinical application of Intestamin® with TPN, combined PN/EN or EN only.

*Modified with permission from Suchner U. Enterale Immunonutrition: wann, für wen, welche Zukunftsperspektiven gibtes? Aktuel Emaehr Med 2002; **27**: 205-215. ©Georg Thieme Verlag Stuttgart, New York.

Notes

Fresenius Kabi

Caring for Life

Fresenius Kabi Deutschland GmbH
Else-Kröner-Straße 1
61352 Bad Homburg v.d.H.
Germany
Tel: +49(0) 6172-686-0
Fax: +49(0) 6172-686-2613