CONFERENCE PROCEEDING

Nutrition in neuro-intensive care and outcomes

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INTRODUCTION

The aim of nutrition is to supply nutritional needs of the critically ill patients. The patients who are seriously ill are prone to malnutrition owing to nausea, vomiting, dysphagia, poor mentation and mechanical ventilation. Patients with the head injury, stroke, brain tumours, acute spinal cord injury, and neurologic and neuromuscular disorders are the typical group of patients admitted to Neuro-Intensive Care Units (ICUs). These patients often require non-enteral nutrition owing to dysphagia, poor neurological status and mechanical ventilation. These patients are at risk for malnutrition due to hypercatabolism owing to the disease process, reduced oral intake, visceral protein loss and wasting of muscles due to immobility. A good nutrition supplementation can improve immunity, morbidity and mortality and length of hospital stay.[1]

Over the past several years, there is increasing emphasis on early nutritional therapy to all critically ill patients.[2,3] Early enteral feeding has been shown to reduce catabolism and reduce complications and hence can reduce the length of hospital stay and morbidity and mortality in critically ill neurological patients. The benefits of early enteral feeding are more when the therapy initiated within 48–72 h of neurological insult.[3,4] However, many neuro physicians and surgeons hesitate to start early nutrition therapy in these patients. Even the patients with silent abdomen can tolerate low jejunal feeds when initiated as early as 36 h post-injury.[5] However, many questions remain unanswered in neurologically ill patients, due to lack of precise clinical trials.

- Timing of intervention: Early versus delayed initiation of nutritional therapy and their effect on poor outcome and mortality
- Enteral versus parenteral nutrition and their effect on poor outcome and mortality
- Enteral nutrition: Jejunal versus gastric feeding and their effect on poor outcome and mortality
- Use of immunomodulating agents and effect on the outcome.

The present article focuses on the nutrition in traumatic brain injury (TBI) patients and its effect on outcomes in Neuro-ICUs and a small note on nutrition in patients with stroke.

EFFECT OF CRITICAL ILLNESS ON DIFFERENT ORGAN SYSTEMS IN THE BODY

Almost all organs are affected during critical illness. The severity of the organs affected depends on the severity of the disease. The hypercatabolism and subsequent inappropriate nutritional supplementation can rapidly worsen the functioning of different organ systems in the body [Table 1].

NUTRITIONAL SCREENING AND ASSESSMENT OF NUTRITIONAL STATUS

Nutritional screening is the identification of the patient who is at risk of malnutrition based on the available basic data. Many nutritional tools such as malnutrition universal screening tool, nutrition risk index, mini nutritional assessment and subjective global assessment. Any nutritional screening tool can be adopted based on the institution, the infrastructure and available resources. A detailed discussion on these tools is out of the purview of this article and can be found elsewhere in the literature.

At present, there is no universally accepted gold standard for nutritional assessment of TBI patients. For

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adequate nutritional assessment, assessment of both medical condition of the patient and nutritional status is important. The diagnosis of the illness, comorbidities (coronary artery disease, diabetes, hypertension, etc.,) and assessment of each organ function should be considered. The anthropometric measurements and blood chemistry are used for assessing the nutritional status. The anthropometric measurements such as weight, height and body mass index are difficult to measure most of the times as patients are critically ill. The estimated measurements can also be inaccurate, due to disturbed fluid balance. The biochemical measurements include calculation of nitrogen balance, albumin, haemoglobin, magnesium, phosphorous, transferrin and pre-albumin.

CALCULATION OF CALORIC REQUIREMENT

The traditionally used Harris-Benedict's equation or weight-based formulas (25–30 kcal/kg/day) are used for calculation of basal energy expenditure (BEE). These static formulas may not accurately predict the amount of replacement required considering the dynamic nature of the disease and hypercatabolism in patients with TBI. Repeated measurements of indirect calorimetry can be used for accurately assessing the energy expenditure. An amount of 140% of BEE is advocated in patients with TBI with the protein replacements of 1–2 g/kg/day. Considering the hypercatabolism state in patients with TBI, proteins can constitute 20% of the energy of the total daily intake.

TYPES OF NUTRITIONAL SUPPORT: ENTERAL AND PARENTERAL NUTRITION

There are essentially two types of dietary methods available: Enteral and parenteral nutrition. Enteral feeding is considered as the first choice, where a functioning gastrointestinal (GI) tract is a prerequisite. It has been found to reduce GI bacterial translocation and improves the mucosal integrity and enzymatic activity.[8] The main contraindications to enteral feeding include complete mechanical bowel obstruction, high draining enterocutaneous fistula (>500 ml) and intolerance to enteral feeding. The parenteral route of nutrition is employed, when there is a failure of enteral feeding or enteral feeding alone is not sufficient to meet all nutritional demands. Table 2 compares the advantages and disadvantages of both types of nutrition.

Table 1: Involvement of various organ systems in critically ill patients[6,7]

Organ involvement	Pathophysiology	Manifestation
Cardiovascular system	Depression of cardiac function by cytokines Increased oxygen requirement High cardiac output Reduced systemic vascular resistance	Myocardial injury Cardiac failure
Neurologic involvement	Altered catecholamines levels Altered metabolites and amino acid metabolism Decrease in forebrain b-receptor density	Confusion, agitation Altered level of consciousness encephalopathy
Gastrointestinal and hepatobiliary	Reduced endogenous mucosal protection (due to lack of feeding) Reduced gastric acid secretion Release of pro-inflammatory mediators by liver	Gastric (stress) ulcers Acalculous cholecystitis Altered liver function (reduced albumin production and increased production of acute phase reactants)
Pulmonary	Neutrophil migration Impaired surfactant function Atelectasis of lung Ventilator-associated infections	Acute lung injury Adult respiratory distress syndrome
Renal	Changes in renal blood flow (vasoconstrictor mediated) Tubular dysfunction (endotoxin-related)	Acute kidney injury
Fluid and electrolytes	Deranged electrolyte balance due to increased extracellular water, reduced intracellular water, altered excretion of electrolytes by kidneys	All electrolyte imbalance including hypo/hypernatremia, hypo/hyperkalaemia Hypomagnesaemia, hypophosphatemia
Endocrine	Increased acute phase hormones (catecholamines, cortisol, glucagon) Reduced thyroxine levels	Stress-induced hyperglycaemia Critical thyroidal illness
Immunologic	Suppressed cell mediated immunity	Increased risk of infections

TIMING OF NUTRITION: EARLY VERSUS DELAYED NUTRITION

The current trend is to start early nutritional replacement to all critically ill patients. Brain trauma Foundation guidelines recommend attaining full caloric requirement by 7 days.[9] For this, the nutrient replacement needs to be started within 72 h and gradually increased to achieve the complete caloric requirement. Studies in the past have tried to compare the early versus delayed nutritional replacement and outcomes in patients with TBI [Table 3].[4,10-17] One of the prerequisites for the enteral feeding is the functioning bowel (presence of bowel sounds). In two of these studies, enteral feeding was started even in the absence of bowel sounds and the patients tolerated the enteral feeding well.[12,13] One of the studies demonstrated reduced infective and overall complications with early jejunal/gastric feeding.[13] This study also demonstrated that the patients who were fed early had a higher percentage of energy and nitrogen requirement by the end of 1 week.[13] A Cochrane meta-analysis[18] which included five studies[4,10-14] concluded that there is a trend towards improved outcome and reduced complications with early enteral feeding.

As a part of New York State quality improvement programme, Brain trauma foundation collects data of 22 trauma centres in New York State.[14] The analysis of data collected from 2000 to 2006 revealed that there was 2–4-fold increased the risk of death in patients who were not fed within 5–7 days. Every 10 kcal/kg decrease in caloric intake during the first 5 days was associated with 30–40% increase in mortality rates. Similarly, the other two trials published recently concluded that early nutrition is associated with better outcomes.[15,16] Chourdakis *et al*.[17] studied the effect of early versus delayed enteral feeding on endocrine functions of the patients with TBI. The hormonal levels of thyroid stimulating hormone, free T4 and free T3 were reduced in patients with delayed enteral feeding. A recent meta-analysis of available studies on nutritional supplementation in patients with TBI included 4 randomised controlled trials[4,10,11,17] and three non-randomised prospective observational trials.[14-16] The pooled data indicated early nutrition is associated with significant reduction in mortality as compared to delayed initiation of nutrition.[19] Furthermore, analysis of 4 trials[10,11,15,16] revealed the risk of poor outcome is significantly decreased with early nutrition. In summary, early feeding is associated with positive nitrogen balance, better hormonal profile, lower risk of infectious complications, with a reduction in mortality and risk of poor outcomes.

METHOD OF FEEDING: ENTERAL VERSUS PARENTERAL NUTRITION

The neurologically ill patients can be fed via enteral or parenteral route [Table 4]. The enteral nutrition can be provided either via gastric or jejunal routes. Some studies indicate that nitrogen balance is better with early jejunal or parenteral nutrition.[11,12,20] Unfortunately, none of the studies comparing parenteral nutrition with enteral nutrition are large enough to draw a conclusion, about which of the route is better. A recent meta-analysis that included five trials[10,11,20-22] concluded that there is a trend towards improved outcome with early parenteral nutrition. However, no statistical significance was achieved. In summary, both enteral and parenteral nutrition can be used for nutritional supplementation in patients with TBI. More emphasis should be given to nitrogen intake, nitrogen loss due to the hypercatabolism in these groups of patients.

Table 2: Comparison of enteral and parenteral feeding

Enteral feeding	Parenteral feeding
Through	
Gastric tube Jejunal tube PEG catheters	Peripheral intravenous Central venous catheters
Advantages	
Simpler Cheaper Fewer complications Maintains GI mucosal barrier Stimulates intestinal blood flow Prevents disuse atrophy Improved healing Reduced catabolism of muscles Avoids TPN-induced immunosuppression	Simpler Can be started early No dependence on gastric/intestinal function Better muscle mass (ANZICS trial) Less need for interruptions
Disadvantages	
Nasogastric tube induced sinusitis Risk of pneumonia (microaspirations, vomiting) Metabolic derangement like hyperglycaemia, re-feeding syndrome Intolerance (large volume aspirations)	Cather-related complications – sepsis, occlusion Hyperglycaemia Hypercholesterolemia (TPN solutions) Hyperchloremic metabolic acidosis Abnormalities in liver function tests

TPN = Total parenteral nutrition, PEG = Percutaneous endoscopic gastrostomy, GI = Gastrointestinal, ANZICS = Australian and New Zealand Intensive Care Society

NASOGASTRIC VERSUS NON-NASOGASTRIC FEEDING

The enteral feeding can be provided through a naso-gastric, naso-pyloric, naso-intestinal or with percutaneous gastrostomy routes [Table 5]. The nasogastric feeding can be associated with more risk of microaspirations, thus increasing the risk of pneumonia. One study showed

Table 3: Studies with early enteral/parenteral nutrition in patients with traumatic brain injury

Trial (year)	Number of patients	EN/PN	Outcome measures studied	Trial design	Trial results/conclusion
Rapp *et al.* (1983)[10]	38	Early parenteral versus delayed enteral	Survival and functional recovery at the end of 1 year	RCT	Higher survival with early nutrition, more positive nitrogen balance and higher serum albumin levels
Young *et al.* (1987)[11]	96	Early TPN/EN	Effect on intracranial pressure	RCT	No effect on intracranial pressure on both the groups
Grahm *et al.* (1989)[12]	32	Early jejunal versus conventional feeding	Tolerance of feeds, risk of infections, days of ICU hospitalizations	Prospective observational trial	Tolerated early jejunal feeding despite silent abdomen, reduced infections and ICU stay
Taylor *et al.* (1999)[13]	82	Early enhanced EN versus standard EN	Glasgow outcome scale at 3 and 6 months, infective and total complications	RCT	No difference in neurologic outcome in two groups, fewer infectious complications in patients with early enhanced enteral feeding
Minard *et al.* (2000)[4]	30	Early versus delayed enteral feeding	Comparing length of hospital stay and infectious complications	RCT	No difference in length of hospital stays and infectious complications
Härtl *et al.* (2008)[14]	797	Feeding practices with adjusted poor outcomes	Mortality and risk of poor outcome	Analysis of prospectively collected database of 22 trauma centres	Patients no fed within 5 days had 2-4 fold increased likelihood of death
Dhandapani *et al.* (2012)[15]	67	Attaining full nutrition replacement by 3 days, 4-7 days and after 7 days	Various nutritional markers	Prospective observational trial	Favorable outcome in patients with early nutrition (<3 days)
Chiang *et al.* (2012)[16]	297	Early EN versus non-enteral controls	Survival at 1 week and better outcome at 1 month	Multicentre cohort trial	Better outcome with early EN, better GCS recovery
Chourdakis *et al.* (2012)[17]	59	Early versus delayed enteral feeding	Effect on endocrine functions	RCT	Decreased levels of TSH, free T4 and T3 in delayed EN group

RCT = Randomised controlled trials, ICU = Intensive Care Unit, EN = Enteral nutrition, PN = Parenteral nutrition, TPN = Total parenteral nutrition, GCS = Glasgow Coma Scale, TSH = Thyroid stimulating hormone

that early nasojejunal feeding is well-tolerated despite the absence of bowel sounds.[12] The likelihood of incidence of pneumonia can be reduced by feeding via gastrostomy or transpyloric enteral feeding.[23,24] A recently concluded meta-analysis of the available studies concluded small bowel feeding is associated with lower incidence of pneumonia and ventilator-assisted pneumonia. However, there was no difference in the length of ICU stay, the length of hospital stay and mortality in patients with either intestinal or gastric feeding.[25]

CONSTITUENTS OF NUTRITION: STANDARD DIET VERSUS IMMUNE ENHANCING DIET

Immunity enhancing agents such as arginine, glutamine, probiotics and omega 3 fatty acids can be used in addition to the standard diet used for supplementation of nutrition. The results of pooled data from trials using these agents show that used of these agents is associated with lesser risk of infection, reduction in the cytokine levels and inflammatory markers.[26-28]

NUTRITION IN PATIENTS WITH STROKE

The principles of nutrition are essentially same in stroke patients as that of TBI. However, 30–50% of stroke patients suffer from dysphagia during acute illness. This dysphagia gradually resolves over next 6 months, but still nearly 10% of patients experiencing persistent dysphagia.[29] Hence, these patients are at increased risk of malnutrition and dehydration due to poor oral intake. Not only this but also the patients are also at risk of infectious complications such as aspiration

Table 4: Comparison of enteral and parenteral nutrition in patients with severe traumatic brain injury

Trial (year)	Number of patients	EN/PN	Outcome measures studied	Trial design	Trial results/conclusion
Rapp *et al*. (1983)[10]	38	Early parenteral versus delayed enteral	survival and functional recovery at the end of 1 year	RCT	Higher survival with early nutrition, more positive nitrogen balance and higher serum albumin levels
Hadley *et al*. (1986)[20]	45	Early parenteral versus early enteral	Daily nitrogen intake, nitrogen loss, albumin levels and outcome after severe TBI	RCT	TPN group had higher daily nitrogen intake, less nitrogen loss and no difference in albumin levels or patient outcomes
Young *et al*. (1987)[11]	96	Early TPN/EN	Effect on intracranial pressure	RCT	No effect on intracranial pressure on both the groups
Borzotta *et al*. (1994)[21]	48	Early parenteral versus early jejunal feeding	Attaining nutritional goals through two different routes	RCT	Both routes were equally effective in achieving nutritional goals
Justo Meirelles and de Aguilar-Nascimento (2011)[22]	22	Parenteral versus EN	Nitrogen intake, nitrogen balance, serum glucose level, acute phase reactants, length of hospital stay and outcome	RCT	Higher glucose level in parenteral group, no difference in nitrogen balance, length of hospital stay and clinical outcome

RCT = Randomised controlled trials, EN = Enteral nutrition, PN = Parenteral nutrition, TBI = Traumatic brain injury, TPN = Total parenteral nutrition

Table 5: Nasogastric versus non-nasogastric feeding

Trial (year)	Number of patients	EN/PN	Outcome measures studied	Trial design	Trial results/ conclusion
Grahm *et al*. (1989)[12]	32	Early jejunal versus conventional feeding	Tolerance of feeds, risk of infections, days of ICU hospitalizations	Prospective observational trial	Tolerated early jejunal feeding despite silent abdomen, reduced infections and ICU stay
Minard *et al*. (2000)[4]	30	Early nasoenteric versus delayed gastric feeding	Comparing length of hospital stay and infectious complications	RCT	No difference in length of hospital stays and infectious complications
Kostadima *et al*. (2005)[23]	41	Early gastrostomy versus conventional nasogastric feeding	To check for infectious complications like ventilator-associated pneumonia	RCT	Lower incidence of ventilator-associated pneumonia but no difference in length of hospital stay or mortality
Acosta-Escribano *et al*. (2010)[24]	104	Transpyloric versus gastric feeding	Early ventilator-associated pneumonia, days of mechanical ventilation, length of ICU stay and hospital stay	RCT	Transpyloric group had lower incidence of pneumonia Nitrogen difference in other parameters

RCT = Randomized controlled trials, ICU = Intensive Care Unit, EN = Enteral nutrition, PN = Parenteral nutrition

pneumonia.[30,31] Hence, the outcome is worse in patients with dysphagia as compared to non-dysphagic stroke patients.

It is necessary to conduct a screening test for dysphagia in all acute stroke patients. The three most commonly performed tests are (1) water swallowing test,[32] (2) multiple consistency test[33] and (3) swallowing provocation test.[34] The low sensitivities or specificities of these tests preclude their routine use as a screening tool in patients with acute stroke.[35] Videofluoroscopic swallowing study (VFSS) and fibreoptic endoscopic evaluation of swallowing (FEES) are used for dysphagia screening. These tests have shown better predictive accuracy compared with the three clinical tests.[35] In VFSS, a non-ionic contrast agent is given to swallow, and all oral, pharyngeal and oesophageal structures can be visualised using fluoroscopy. In FEES, a fibreoptic bronchoscope is passed through the nose near pharynx and direct visualisation of the swallowing can be done. The FEES has advantages as it can be done bed-side, no radiation exposure and saliva of patients can be directly

visualised.[36] Initially, in the acute stages, dysphagia screening can be done on daily basis and in later stages twice weekly. If dysphagia persists at the time of discharge, then once month evaluation is indicated for next 6 months.

Then incidence of malnutrition ranges from 24% to 48% in acute stroke patients.[37] This may be due to reduced oral intake due to dysphagia, poor level of consciousness and varying grades of cognitive dysfunction. Hence, any of the nutritional screening tools (stated earlier in the article) can be used for nutritional screening in these groups of patients. In the acute phases, a nasogastric feeding is beneficial due to the presence of dysphagia or poor Glasgow Coma Scale (GCS). Early tube feeding within 7 days showed a trend towards improved outcomes in stroke patients.[38,39] Patients with poor GCS and on mechanical ventilation may benefit from early tube feeding. There are no trials comparing enteral or parenteral nutrition in these settings. The tube feeding should be initiated as early as possible, once the patient is stabilised. A nasogastric tube is sufficient for tube feeding in most of the patients. However, in patients with anticipated prolonged enteral feeding (>28 days), early feeding can be initiated through gastrostomy tubes.[23] Additional oral intake may be allowed in stroke patients depending on the severity of dysphagia. Parenteral nutrition is indicated when there is a contraindication for enteral nutrition, or the enteral nutrition fails to meet the demand for nutritional supplementation.

CONCLUSION

Patients with severe TBI and stroke are at risk of malnutrition due to the dysphagia, poor GCS, mechanical ventilation and hypercatabolism. Nutrition supplementation should be initiated as early as possible, and by 5–7 days should attain the full caloric requirement. Enteral or parenteral or combination of both can be considered for nutritional replacement. Intestinal feeding reduced the risk of pneumonia as compared to gastric feeding. Immune-enhancement diet can reduce the infectious complications in these patients.

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REFERENCES

1. Young B, Ott L, Twyman D, Norton J, Rapp R, Tibbs P, *et al.* The effect of nutritional support on outcome from severe head injury. J Neurosurg 1987;67:668-76.
2. Minard G, Kudsk KA. Is early feeding beneficial? How early is early? New Horiz 1994;2:156-63.
3. Nyswonger GD, Helmchen RH. Early enteral nutrition and length of stay in stroke patients. J Neurosci Nurs 1992;24:220-3.
4. Minard G, Kudsk KA, Melton S, Patton JH, Tolley EA. Early versus delayed feeding with an immune-enhancing diet in patients with severe head injuries. JPEN J Parenter Enteral Nutr 2000;24:145-9.
5. Kirby DF, Clifton GL, Turner H, Marion DW, Barrett J, Gruemer HD. Early enteral nutrition after brain injury by percutaneous endoscopic gastrojejunostomy. JPEN J Parenter Enteral Nutr 1991;15:298-302.
6. Brealey D, Singer M. Multi-organ dysfunction in the critically ill: Effects on different organs. J R Coll Physicians Lond 2000;34:428-31.
7. Tripathy S. Nutrition in the neurocritical care unit. J Neuroanaesth Crit Care 2015;2:88-96.
8. Hillhouse JH, Neiger R. Pregnancy and lactation. In: Gottschlich MM, Fuhrman MP, Hammond KA, Holcombe BJ, Seidner DL, editors. The Science and Practice of Nutrition Support: A Case-Based Core Curriculum. Dubuque, IA: Kendall/Hunt Publishing Company; 2001. p. 302-19.
9. Brain Trauma Foundation; American Association of Neurological Surgeons; Congress of Neurological Surgeons; Joint Section on Neurotrauma and Critical Care, AANS/CNS, Bratton SL, Chestnut RM, Ghajar J, McConnell Hammond FF, *et al.* Guidelines for the management of severe traumatic brain injury. XII. Nutrition. J Neurotrauma 2007;24 Suppl 1:S77-82.
10. Rapp RP, Young B, Twyman D, Bivins BA, Haack D, Tibbs PA, *et al.* The favorable effect of early parenteral feeding on survival in head-injured patients. J Neurosurg 1983;58:906-12.
11. Young B, Ott L, Haack D, Twyman D, Combs D, Oexmann JB, *et al.* Effect of total parenteral nutrition upon intracranial pressure in severe head injury. J Neurosurg 1987;67:76-80.
12. Grahm TW, Zadrozny DB, Harrington T. The benefits of early jejunal hyperalimentation in the head-injured patient. Neurosurgery 1989;25:729-35.
13. Taylor SJ, Fettes SB, Jewkes C, Nelson RJ. Prospective, randomized, controlled trial to determine the effect of early enhanced enteral nutrition on clinical outcome in mechanically ventilated patients suffering head injury. Crit Care Med 1999;27:2525-31.
14. Härtl R, Gerber LM, Ni Q, Ghajar J. Effect of early nutrition on deaths due to severe traumatic brain injury. J Neurosurg 2008;109:50-6.
15. Dhandapani S, Dhandapani M, Agarwal M, Chutani AM, Subbiah V, Sharma BS, *et al.* The prognostic significance of the timing of total enteral feeding in traumatic brain injury. Surg Neurol Int 2012;3:31.
16. Chiang YH, Chao DP, Chu SF, Lin HW, Huang SY, Yeh YS, *et al.* Early enteral nutrition and clinical outcomes of severe traumatic brain injury patients in acute stage: A multi-center cohort study. J Neurotrauma 2012;29:75-80.
17. Chourdakis M, Kraus MM, Tzellos T, Sardeli C, Peftoulidou M, Vassilakos D, *et al.* Effect of early compared with delayed enteral nutrition on endocrine function in patients with traumatic brain injury: An open-labeled randomized trial. JPEN J Parenter Enteral Nutr 2012;36:108-16.
18. Perel P, Yanagawa T, Bunn F, Roberts I, Wentz R, Pierro A. Nutritional support for head-injured patients. Cochrane Database Syst Rev 2006:CD001530.
19. Wang X, Dong Y, Han X, Qi XQ, Huang CG, Hou LJ. Nutritional support for patients sustaining traumatic brain injury: A systematic review and meta-analysis of prospective studies. PLoS One 2013;8:e58838.
20. Hadley MN, Grahm TW, Harrington T, Schiller WR, McDermott MK, Posillico DB. Nutritional support and neurotrauma: A critical review of early nutrition in forty-five

acute head injury patients. Neurosurgery 1986;19:367-73.
21. Borzotta AP, Pennings J, Papasadero B, Paxton J, Mardesic S, Borzotta R, *et al.* Enteral versus parenteral nutrition after severe closed head injury. J Trauma 1994;37:459-68.
22. Justo Meirelles CM, de Aguilar-Nascimento JE. Enteral or parenteral nutrition in traumatic brain injury: A prospective randomised trial. Nutr Hosp 2011;26:1120-4.
23. Kostadima E, Kaditis AG, Alexopoulos EI, Zakynthinos E, Sfyras D. Early gastrostomy reduces the rate of ventilator-associated pneumonia in stroke or head injury patients. Eur Respir J 2005;26:106-11.
24. Acosta-Escribano J, Fernández-Vivas M, Grau Carmona T, Caturla-Such J, Garcia-Martinez M, Menendez-Mainer A, *et al.* Gastric versus transpyloric feeding in severe traumatic brain injury: A prospective, randomized trial. Intensive Care Med 2010;36:1532-9.
25. Wang D, Zheng SQ, Chen XC, Jiang SW, Chen HB, *et al.* Comparisons between small intestinal and gastric feeding in severe traumatic brain injury: A systematic review and meta-analysis of randomized controlled trials. J Neurosurg 2015:1-8.
26. Falcão de Arruda IS, de Aguilar-Nascimento JE. Benefits of early enteral nutrition with glutamine and probiotics in brain injury patients. Clin Sci (Lond) 2004;106:287-92.
27. Briassoulis G, Filippou O, Kanariou M, Papassotiriou I, Hatzis T. Temporal nutritional and inflammatory changes in children with severe head injury fed a regular or an immune-enhancing diet: A randomized, controlled trial. Pediatr Crit Care Med 2006;7:56-62.
28. Khorana J, Rerkasem K, Apichartpiyakul C, Sakonwasun C, Watcharasakslip W, Waniyapong T, *et al.* Immunonutrition and cytokine response in patients with head injury. J Med Assoc Thai 2009;92:188-94.
29. Mann G, Hankey GJ, Cameron D. Swallowing function after stroke: Prognosis and prognostic factors at 6 months. Stroke 1999;30:744-8.
30. Hilker R, Poetter C, Findeisen N, Sobesky J, Jacobs A, Neveling M, *et al.* Nosocomial pneumonia after acute stroke: Implications for neurological intensive care medicine. Stroke 2003;34:975-81.
31. Holas MA, DePippo KL, Reding MJ. Aspiration and relative risk of medical complications following stroke. Arch Neurol 1994;51:1051-3.
32. DePippo KL, Holas MA, Reding MJ. Validation of the 3-oz water swallow test for aspiration following stroke. Arch Neurol 1992;49:1259-61.
33. Trapl M, Enderle P, Nowotny M, Teuschl Y, Matz K, Dachenhausen A, *et al.* Dysphagia bedside screening for acute-stroke patients: The Gugging Swallowing Screen. Stroke 2007;38:2948-52.
34. Warnecke T, Teismann I, Meimann W, Olenberg S, Zimmermann J, Krämer C, *et al.* Assessment of aspiration risk in acute ischaemic stroke – Evaluation of the simple swallowing provocation test. J Neurol Neurosurg Psychiatry 2008;79:312-4.
35. Bours GJ, Speyer R, Lemmens J, Limburg M, de Wit R. Bedside screening tests vs. videofluoroscopy or fibreoptic endoscopic evaluation of swallowing to detect dysphagia in patients with neurological disorders: Systematic review. J Adv Nurs 2009;65:477-93.
36. Warnecke T, Teismann I, Oelenberg S, Hamacher C, Ringelstein EB, Schäbitz WR, *et al.* The safety of fiberoptic endoscopic evaluation of swallowing in acute stroke patients. Stroke 2009;40:482-6.
37. Stratton R, Green CJ, Elia M. Disease-related Malnutrition. An Evidence Based Approach to Treatment. CABI Publishing; 2003.
38. Dennis MS, Lewis SC, Warlow C. Effect of timing and method of enteraltube feeding for dysphagic stroke patients (FOOD): A multicenter randomised controlled trial. Lancet 2005;365:764-72.
39. Dennis M, Lewis S, Cranswick G, Forbes J. FOOD: A multicentre randomized trial evaluating feeding policies in patients admitted to hospital with arecent stroke. Health Technol Assess 2006;10:1-120.