Timing of Parenteral Nutrition:

General or Parent(er)al Guidance required?

Nepean WTET summary 15/12/20

Background and Rationale

- Critical illness is associated with a hypermetabolic state, once glycogen stores deplete proteolysis occurs
- Nutritional deficits in critically ill predispose to muscle wasting, infection, delayed recovery
- Enteral nutrition (EN) fewer complications than parenteral nutrition (PN) but may often not achieve calorie (or protein) targets / needs
- TPN established benefit in patients with chronic non-functioning gastrointestinal systems, but is this translatable to the critically ill who may be only transiently intolerant to EN?

Advantages and Disadvantages

- Advantages
  - Good physiological rationale – ensure calorie and protein delivery in hypermetabolic states
  - Able to administer irrespective of gut function– less issues with high gastric residual volumes → aspiration / VAP, less hypoglycaemia
  - Does not increase gut perfusion (undesirable during severely shocked states)
  - Can be made to order – specific needs catered for with individual formulations
- Disadvantages
  - Increased hyperglycaemia and infection, in particular blood stream infections (also PN is a candidaemia risk factor)
  - Unlike EN does not protect against stress ulceration and bacterial translocation
  - Requires dedicated central access (and associated complications)
  - More hyperammonaemia and hypertriglyceridaemia
  - Financial (EPaNIC); more expensive than EN
  - When supplemental (in combination with EN) risk overfeeding → harmful
  - Is underfeeding actually harmful? Starvation a physiological response to illness…

Key studies

- EPaNIC 2001 NEJM
  - MC (7) RCT; Intensive care patients with a nutritional risk screening score =/>3 (of 1-7) randomised to early PN (20% dextrose at 400kcal/d d1, 80kcal/d d2, then PN d3 targeting 100% nutritional requirements alongside other intakes) vs late PN (5% dextrose in volumes to achieve hydration in addition to enteral nutrition; if insufficient enteral nutrition by d7, PN was commenced to achieve goal), stratified by diagnosis (broad inclusion). N=4640
  - Primary outcome; number of ICU days (by time identified as ready for ICU discharge); 4d vs 3d (P=0.02) being shorter in the late initiation group
  - No difference in mortality. Significantly higher rates of hypoglycaemia in late PN initiation group but higher rates of new ICU infection (26.2% vs 22.8%, P=0.008) with early initiation

- Doig 2013 JAMA
    - MC RCT; <24h ICU admission, expected to remain >2d, ineligible for EN by attending clinician due to a short-term relative contraindication (expected no enteral nutrition <2d) and CVC in situ. Randomised to early PN (start PN < 24h achieve target by d3) vs standard care (based on local practice, they describe in AU/NZ dextrose infusion would be atypical). N=1372
    - Primary outcome; death by 60d; 21.5% vs 22.8% no difference, even when adjusted for co-variates
    - Statistically significant improvement in quality of life (RAND 36 General Health Status) with early PN but did not correlated to (predetermined) clinically significant difference. No difference in rates of new infections between groups but greater muscle wasting with standard care. Fewer invasive ventilation days (but not ICU or hospital LOS) with early PN
- Heidegger 2013 Lancet
    - MC (2) RCT; Medical/surgical ICU patients with a functional GI tract who received <60% energy target from EN by d3 (and expected to be in ICU >5d and survive >7d) randomised to receive supplemental PN (SPN) vs EN alone. N=305
    - Primary outcome; occurrence of nosocomial infections d9-d28 (adjusted); significantly lower in SPN group; 27% vs 38%, HR 0.65, 95% CI 0.43-0.97, P=0.0338 (…and less Abx use)
    - Good separation of energy and protein intake between groups
- Calories 2014 NEJM
    - MC (33) RCT; Patients <36h expected to be in ICU =/>3d and require nutritional support =/>2. Randomised to 5d (or until oral feeding, d/c from ICU or death) of either EN (NG/NJ) or PN aiming to reach target within 48-72h. N=2388
    - Primary outcome; all-cause mortality at d30; 34.2% vs 33.1%; no difference even after risk adjustment
    - Less hypoglycaemia with PN, no difference in infectious complications. Both groups did not meet their calorie target

Summary (my practice)

- Much like fluid, perhaps more important than choice of agent is timing and dose (specific targets will be covered in subsequent WTET). TPN has a place and may not be as harmful as often advertised. However rarely is it beneficial to initiate PN early. A number of benefits of enteral nutrition are lost with PN and so unless severely malnourished or established gut failure, methods to optimise enteral nutrition should be pursued first if appropriate to do so (overfeeding more harmful than underfeeding)
- I do not use supplemental PN; the only time I may concurrently use both EN and PN is whilst commencing / attempting to re-establish EN in a patient established on PN (for a strong indication). When doing this I am highly vigilant for harmful effects of over-feeding and take advise from dietetics colleagues on how best to facilitate this