NEW TOPIC: Vitamin C Supplementation May 2015

NEW SECTION in 2015

2015 Recommendation: *There are insufficient data to make recommendation on Vitamin C supplementation in critically ill patients*

2015 Discussion: The committee noted the one new small study that evaluated the safety of high dose IV vitamin C (200 mg/kg/day) vs low dose vitamin C (50 mg/kg/day) vs placebo (5% dextrose) in septic patients as assessed by biomarkers(Fowler 2014). The supplementation by Vit C was shown to be safe in the study as demonstrated by improved biomarkers of inflammation and endothelial injury. The committee agreed that there were not enough information on clinical outcomes from this small dosing study to make a recommendation on the use of Vitamin C.

For studies that used Vit C supplementation in addition to other antioxidants, refer to section 11.1 Supplemental Antioxidant Nutrients: Combined Vitamins and Trace Elements

Semi Quantitative Scoring

Values	Definition	2015 Score (0,1,2,3)
Effect size	Magnitude of the absolute risk reduction attributable to the intervention listed--a higher score indicates a larger effect size	0
Confidence interval	95% confidence interval around the point estimate of the absolute risk reduction, or the pooled estimate (if more than one trial)--a higher score indicates a smaller confidence interval	0
Validity	Refers to internal validity of the study (or studies) as measured by the presence of concealed randomization, blinded outcome adjudication, an intention to treat analysis, and an explicit definition of outcomes--a higher score indicates presence of more of these features in the trials appraised	2
Homogeneity or Reproducibility	Similar direction of findings among trials--a higher score indicates greater similarity of direction of findings among trials	0
Adequacy of control group	Extent to which the control group presented standard of care (large dissimilarities=1, minor dissimilarities=2, usual care=3)	2
Biological Plausibility	Consistent with understanding of mechanistic and previous clinical work (large inconsistencies=1, minimal consistencies=2, very consistent=3)	2
Generalizability	Likelihood of trial findings being replicated in other settings (low likelihood i.e. single centre=1, moderate likelihood i.e. multicentre with limited patient population or practice setting=2, high likelihood i.e. multicentre, heterogenous patients, diverse practice settings=3)	0
Low cost	Estimated cost of implementing the intervention listed--a higher score indicates a lower cost to implement the intervention in an average ICU	2
Feasible	Ease of implementing the intervention listed--a higher score indicates greater ease of implementing the intervention in an average ICU	2
Safety	Estimated probability of avoiding any significant harm that may be associated with the intervention listed--a higher score indicates a lower probability of harm	2

NEW TOPIC: Vitamin C Supplementation

Question: Does Vitamin C supplementation result in improved clinical outcomes in critically ill patients?

Summary of evidence: There was one level 2 RCT of IV vitamin C supplementation that examined high dose IV vitamin C ($200\ \mathrm{mg/kg/day}$) vs low dose vitamin C (50 mg/kg/day) vs placebo (5% dextrose) (Fowler 2014).

Mortality: There was a signal for reduced 28 day mortality in the patients randomized to the lower Vit C group (38.1%) vs the higher Vit C group (50.6%) vs the control group (62.5%) and these differences were/were not statistically significant.

Infections: none reported

Length of Stay: There were no differences in ICU length of stay between the 3 groups.

Duration of ventilation: There were no differences in ventilator free days between the 3 groups

Other: Ascorbic acid infusion rapidly and significantly increased plasma ascorbic acid levels. No adverse safety events were observed in ascorbic acid-infused patients. Patients receiving ascorbic acid exhibited prompt reductions in SOFA scores while placebo patients exhibited no such reduction. Ascorbic acid significantly reduced the proinflammatory biomarkers C-reactive protein and procalcitonin.

Conclusions:
1, Vit C supplementation has no effect on 28 day mortality in critically ill patients
2. Vit C supplementation has no effect on ICU LOS or ventilator free days in critically ill patients

Level 1 study: if all of the following are fulfilled: concealed randomization, blinded outcome adjudication and an intention to treat analysis.
Level 2 study: If any one of the above characteristics are unfulfilled.

Table 1. Randomized studies evaluating glutamine (PN + EN) in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)*	Infections # (%)†
1) Fowler 2014	Septic patients N=26	C.Random: yes ITT: no Blinding: double (7)	IV low dose ascorbic acid (50 mg/kg/day) vs IV high dose ascorbic acid (200 mg/kg/day) vs placebo (5% dextrose in water).	Low dose / High dose / Control 28-day 3/8 (38.1) / 4/8 (50.6) / 5/8 (62.5) Denominator unknown p-value not specified	NR

Table 1. Randomized studies evaluating glutamine (PN + EN) in critically ill patients (continued)

Study	LOS days	Ventilator free days ‡	Other Outcomes
1) Fowler 2014	Low dose / High dose / Control ICU 8.1 (1-19) / 9.1 (2-25) / 11 (2-25) p-value not available	Low dose / High dose / Control 8.4 (0-22) / 4.8 (0-19) / 7.6 (0-23) p-value not available	Low dose / High dose / Control Days on Pressors 2.1 (1-6) / 3.6 (2-8) / 3.9 (1-10) p-value not available

* presumed hospital mortality unless otherwise specified
† refers to the # of patients with infections unless specified