12.0 Vitamin D

March 2013

NEW SECTION in 2012

Recommendation: *There are insufficient data to make a recommendation for the use of Vitamin D in critically ill patients.*

Discussion: Although there are several observational studies describing low levels of Vit D and its association with worse clinical outcomes in critically ill patients (Nair NEJM 2009, Braun Critical Care Medicine 2011, Am J Surgery 2012, Higgins JPEN 2012, etc), the committee noted that there was only on small pilot RCT focused on biochemical outcomes only. The committee decided to await the results of ongoing randomized trial in ICU patients before making a recommendation and decided to forgo the scoring of values.

Semi Quantitative Scoring

Values	Definition	2013 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	n/a
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)	1
Low cost	Estimated cost of implementing the intervention listed--a higher score indicates a lower cost to implement the intervention in an average ICU	3
Feasible	Ease of implementing the intervention listed--a higher score indicates greater ease of implementing the intervention in an average ICU	3
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

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Question: Does supplementation with Vitamin D result in better outcomes in critically ill vitamin D deficient adult patients?

Summary of evidence: There was one level 2 study that compared the use of a single oral high dose Vitamin D3 to placebo in critically ill patients that were deficient in Vitamin D.

Mortality: No differences in hospital mortality (RR 1.08, 95% CI 0.48, 2.45, p=0.85) were found between the two groups.

Infections: Data on infectious complications were not reported.

LOS and ventilator days: No differences in ICU length of stay (p=0.54), hospital length of stay (p=0.97), or duration of ventilation (p=0.88) was found between the two groups

Other: Serum levels of 1,25(OH)D showed a transient significant increase in the Vitamin D group only. No adverse effects such as hypercalcemia or hypercalciuria were observed.

Conclusions:

1) Vitamin D3 supplementation in critically ill vitamin D deficient adult patients has no effect on hospital mortality, length of stay, or duration of ventilation.

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 vitamin D supplementation in critically ill patients

Study	Population	Methods (score)	Intervention (both interventions started at same time)	Mortality # (%)†		Infections # (%)‡	
1) Amrein 2011	ICU patients with Vit D deficiency Expected LOS > 48 hrs N=25	C.Random: yes ITT: no Blinding: double (9)	Single dose D3 (540 000 IU) via NG vs placebo	Vit D Hospital 6/12 (50)	Placebo Hospital 6/13 (46)	NR	NR

Table 1. Randomized studies evaluating vitamin D supplementation in critically ill patients (continued)

Study	LOS days		Ventilator days		Other
1) Amrein 2011	Vit D ICU 10 (5-21) Hospital 16 (8-32)	Placebo ICU 6 (3-23) Hospital 15 (8-38)	Vit D 229 hours (82-366)	Placebo 163 hours (91-541)	Serum 1,25OH-D levels Vit D group: significant increase in 8/10 patients

C.Random: concealed randomization
† presumed hospital mortality unless otherwise specified
± ( ) : mean ± Standard deviation (number)

ITT: intent to treat; NA: not available
‡ refers to the # of patients with infections unless specified