4.1.d Composition of Enteral Nutrition: Immune Enhancing Diets: Ornithine Ketoglutarate (OKG)

There were no new randomized controlled trials since the 2015 update and hence there are no changes to the following summary of evidence.

Question: Does supplementation of enteral nutrition with ornithine ketoglutarate (OKG) result in better outcomes in the critically ill adult patient?

Summary of evidence: There were three level 2 studies that compared OKG supplementation to placebo in burn patients.

Mortality: All three studies reported on mortality and found no differences between the groups (RR 0.92, 95% CI 0.39, 2.19, p=0.9; figure 1).

Infections: Not reported.

LOS: Not reported.

Other complications: Wound healing times were significantly shorter (Coudray-Lucas p<0.05) and wound healing scores were significantly higher (Donati) in the groups receiving OKG. Improved nutritional indices were seen in the groups receiving OKG in all three studies [a higher increase in serum transthreytin levels from day 4-21 (Coudray-Lucas) and improved nitrogen balance, serum transthyretin and retinol binding protein was also observed in the groups receiving OKG (Donati, DeBandt)].

Conclusions:

- 1) EN supplementation of OKG has no effect on mortality in critically ill burn patients.
- 2) EN supplementation of OKG may be associated with improved nutritional indices and may be associated with improved wound healing in burn 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

Study	Population	Methods (score)	Intervention	Mortality # (%) Experimental Control		RR (CI)**	Infections # (%) Experimental Control	
1)De Bandt 1998	Severe Burns ≥ 20 % - 50 % TSBA N = 54	C.Random: not sure ITT: no Blinding: no (5)	OKG 10, 20, 30 gms bolus and continuous vs. soy protein 10, 20, 30 gms* Isonitrogenous, isocaloric	5/32 (16)	2/16 (13)	1.25 (0.27,5.75)	NR	NR
2) Donati 1999	Severe Burns 20-60 % TSBA N = 60	C.Random: not sure ITT: yes Blinding: double (8)	OKG 10 gms BID via boluses for 21 days vs. placebo (20 gm maltodextrine) Non-isonitrogenous ,isocaloric	0/31 (0)	0/29 (0)	0.94 (0.02,45.8)	NR	NR
3) Coudray-Lucas 2000	Severe burns ≥ 25 % TSBA N= 49	C.Random: yes ITT: yes*** Blinding: double (8)	OKG 10 gms BID via enteral route vs. Soy protein mixture 10 gms BID for 3 weeks Isonitrogenous, isocaolric	5/25 (20)	6/24 (25)	0.08 (0.28, 2.28)	NR	NR

Table 1. Randomized Studies Evaluating Supplementation Of Enteral Nutrition With OKG In Critically ill Patients

C.Random: Concealed randomization

ITT: Intent to treat

NR: Not reported

TSBA: total surface burn area

* De Bandt et al: data from the combined OKG group (i.e. continuous and bolus and all doses) is compared to the combined control group. ** RR= Relative risk, CI= Confidence intervals

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Figure 1. Mortality

Comparison: 01 OKG vs. Placebo Outcome: 01 Mortality

Study	OKG n/N	Placebo n/N	RR (95%Cl Random)	Weight %	RR (95%Cl Random)	Year	
Coudray-Lucas	5/25	6/24		68.0	0.80[0.28,2.28]	2000	
DeBandt	5/32	2/16		32.0	1.25[0.27,5.75]	1998	
x Donati	0/31	0/29		0.0	Not Estimable	1999	
Fotal(95%Cl)	10/88	8/69	-	100.0	0.92[0.39,2.19]		
Fest for heterogeneity chi-s	quare=0.22 df=1 p=0.0	64					
Test for overall effect z=-0	.18 p=0.9						
		.01	.1 1 10	100			
		Fav	ours OKG Favours p	lacebo			

Table 2. Excluded Articles

#	Reason excluded	Reference
1	Elective surgery pts	Hammarqvist F, Wernerman J, von der Decken A, Vinnars E. Alpha-ketoglutarate preserves protein synthesis and free glutamine in skeletal muscle after surgery. Surgery 1991;109:28-36.
2	No clinical outcomes	Le Bricon T, Coudray-Lucas C, Lioret N, Lim SK, Plassart F, Schlegel L, De Bandt JP, Saizy R, Giboudeau J, Cynober L. Ornithine alpha-ketoglutarate metabolism after enteral administration in burn patients: bolus compared with continuous infusion. Am J Clin Nutr. 1997 Feb; 65(2): 512-8.