In preterm infants, does the supplementation of carnitine to parenteral nutrition improve the following clinical outcomes: Growth, lipid metabolism and apneic spells?

Part A: Evidence-based answer and summary

Tim Van Aerde BMSc

Carnitine is involved in fatty acid oxidation, and it has been hypothesized that a deficiency of carnitine, as is often found in preterm infants, would decrease available energy stores. Current literature, however, does not support the routine supplementation of carnitine to parenterally fed neonates for improvement of clinical outcomes. The addition of carnitine showed no effect on growth, lipid metabolism, or the amount and severity of apnea (Grade of Recommendation: A, based on a systematic review and a single randomized control trial).

To determine if carnitine would have an effect on weight gain for preterm infants, Cairns et al (1) conducted a systematic review comparing carnitine supplementation with placebo for parenterally fed neonates. The review included only randomized controlled trials, the highest level of evidence for assessing efficacy of an intervention. Six trials met the criteria for inclusion in the review. The results of three of the trials demonstrated no significant difference in weight gain between supplemented neonates and control group neonates after two weeks (weighted mean difference [WMD] 0.74 g/day, 95% CI –1.88 to 3.35). One study noted a difference in growth in the second week, but this was accounted for by the fact that the rate of weight gain halved in the control group between week 1 and 2 (ie, there was no difference between the groups when analyzed over the entire study period). Also, one study reported a weight gain with carnitine supplementation, but only in a larger infant group (1001 g to 1500 g). Unlike the weight gain results found in the large infant group, no weight gain was noted in the smaller birth weight group (750 g to 1000 g). Finally, a single study examined growth rate for longer than two weeks but found no difference at one month and three months post-term.

Similarly, in a more recent randomized controlled trial, Whitfield et al (2) found that carnitine did not have an effect on the growth of 64 randomized preterm infants. The study was conducted with good methodological quality, with a Jadad score of five (a score of less than three indicates a poor quality study; a score of five indicates maximum quality) (3). The study's analysis had a power of 80%, and indicated that infants weighing less than 1500 g had low carnitine levels. Despite this, the study was unable to find an effect of routine supplementation with carnitine on growth.

The secondary outcome of the Cairns et al (1) review was the effect of carnitine on lipid metabolism. This was evaluated by measuring plasma free fatty acids, plasma triglycerides, amount of lipid tolerated and ketogenesis. For the first three parameters, there were no differences between the supplemented group and the placebo group (WMD –0.16 mmol/L, 95% CI –0.37 to 0.05; WMD –0.69 mmol/L, 95% CI –1.84 to 0.45; and WMD 0.09 g/kg/day, 95% CI –0.20 to 0.38, respectively). Yet, the studies showed a statistically significant increase in ketogenesis in the carnitine-supplemented group (WMD 0.05 mmol/L, 95% CI 0.03 to 0.06). This supported the results of a study by Labadaridis et al (4), which illustrated an increase in ketone production by neonates receiving medium-chain triglycerides and carnitine. However, the results were not found to be clinically significant. That is, despite an increase in ketogenesis in carnitine-supplemented infants, the authors did not find evidence of clinical effect on fat metabolism.

Division of Neonatology, Department of Pediatrics, University of Alberta, Edmonton, Alberta
Correspondence and reprints: Ms Michelle Tubman, Department of Pediatrics, Alberta Research Centre for Child Health Evidence, Aberhart Centre One, Room 9429, 11402 University Avenue, Edmonton, Alberta T6G 2J3. Telephone 780-492-0550, fax 780-407-6435, e-mail mtubman@ualberta.ca

The secondary outcome for the Whitfield et al (2) study was the length and severity of apnea of prematurity. Both the placebo group and carnitine-supplemented group demonstrated similar results and had an equal incidence of apneic spells. The number of apneic episodes, percentage of periodic breathing and length of ventilation were similar between the supplemented and placebo groups. The authors noted that the concurrent use of xanthines to facilitate extubation may have masked the effects of carnitine.

The evidence from these studies does not support the practice of routine supplementation of carnitine to parenterally fed neonates. The Cairns et al (1) review had several limitations. First, the studies in the review evaluated mainly short-term effects on weight gain. The study of short-term effects may be justified given that there is usually a diminishing role for parenteral nutrition after a few weeks (5). Because of the lack of long-term research in this area, future studies should focus on the effect of carnitine for those infants requiring long-term parenteral nutrition, particularly those who are receiving home parenteral nutrition. Second, it is necessary to note that there were only six studies included in the systematic review. This raises the question of whether there was enough power to detect a clinically significant effect of supplementing. Despite these shortcomings, current research does not support the use of carnitine supplementation for improvement of growth, lipid metabolism and apnea of prematurity in the parenterally fed preterm infant.

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