Title: RANDOMISED TRIAL OF HIGH-DOSE SUFENTANIL ANESTHESIA IN NEONATES UNDERGOING CARDIAC SURGERY: EFFECTS ON THE METABOLIC STRESS RESPONSE

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Introduction. Newborn infants undergoing cardiac or non-cardiac surgery mount a metabolic stress response characterised by catabolism and substrate mobilization. Such changes may be detrimental in critically ill neonates due to their precarious metabolic balance, poor metabolic reserves, and the metabolic cost of rapid growth in the neonatal period. A randomised trial with 80% power (for $\alpha<0.05$) was designed to investigate whether severe metabolic changes are precipitated by cardiac surgery and CPB[1], and whether these changes can be prevented by high-dose opiate anesthesia.

Methods. Approval of the Clinical Investigation Committee and informed parental consent were obtained to study 45 neonates undergoing cardiac surgery with CPB and DHCA[1]. Neonates were randomised in a ratio of 2:1 to receive either sufentanil (35-40 ug/kg) or conventional anesthesia (CC group) (halothane 0.5-2%, morphine 0.5 mg/kg, ketamine 1-2 mg/kg) respectively; neonates in the sufentanil group were randomised further to receive either a continuous sufentanil infusion (2 ug/kg/hr) (SS group) or routine analgesia (SC group) after surgery. Blood concentrations of glucose, lactate pyruvate, acetoacetate, 3-hydroxybutyrate, alanine and glycerol were measured by specific enzymatic methods before induction of anesthesia, just before CPB, 5 min after DHCA, at the end of surgery and at 6, 12 and 24 hours postoperatively. A preliminary analysis of data from 18 neonates is included in this abstract; data on all neonates will be presented at the meeting. The response of each neonate was characterised by the change in each variable from its preoperative value and analysed with Kruskal-Wallis ANOVA and Mann-Whitney U tests. Patients in the 3 groups were similar with regard to diagnosis, age and weight at the time of surgery; there were no significant differences in dextrose infusion rates, anesthetic management, or durations of CPB and DHCA between the randomised groups.

Results. Neonates in group CC mounted a greater metabolic response as compared to groups SS and SC (Tables I and II), with significant differences in the hyperglycemic responses before the start of CPB ($p<0.05$), at the end of surgery ($p<0.05$) and at 6 hours postop ($p<0.05$). Changes in blood lactate and pyruvate were significantly different at the end of surgery ($p<0.02$) and at 6 hours post op ($p<0.05$). Postop alanine responses were also greater in group CC neonates, with significant differences between the 3 groups at 6, 12 and 24 hours after surgery ($p<0.025$). No differences were observed in the ketone bodies or glycerol responses during or after surgery.

Discussion. Severe catabolism following surgery may lead to major detrimental effects and postop complications[2], and there is preliminary evidence that prevention of catabolic responses in neonates may provide greater clinical stability during and after surgery[3]. Thus, it is proposed that suppression of stress responses in vulnerable newborn infants may lead to further improvement in their postoperative outcome.

References.

1. Abbreviations used: CPB= cardiopulmonary bypass, DHCA= deep hypothermic circulatory arrest, PBE= plasma beta-endorphin immunoreactivity.
2. Moyer E, Cerra F, et al: Multiple systems organ failure: IV. Death predictors in the trauma septic state - the most critical determinants. J Trauma 21:862-869, 1981.
3. Anand KJS, Sippell WG, Aynsley-Green A: Randomised trial of fentanyl anestheia in preterm babies undergoing surgery: Effects on the stress response. Lancet 1:243-248, 1987.

Table I: Changes in blood glucose and lactate from preoperative values

	Group SS	Group SC	Group CC	Group SS	Group SC	Group CC
	Blood Glucose			Blood Lactate		
Pre-CPB	3.4±3.7	5.7±2.7	8.4±3.1	0.4±0.3	0.4±0.2	1.6±1.0
5' after DHCA	5.1±1.2	6.5±1.0	6.7±2.3	3.7±0.6	3.5±0.8	4.7±0.5
End-op	8.4±1.4	7.2±1.3	11.6±2.0	4.4±0.8	5.7±2.3	10.6±2.8
6 h postop	1.7±2.2	-2.4±1.8	5.2±2.1	1.9±1.1	2.9±2.1	8.2±2.2
12 h postop	-2.2±1.8	-0.5±1.3	0.9±0.3	0.2±0.3	-0.1±1.4	1.9±1.8
24 h postop	-4.4±1.5	-1.2±2.3	1.4±1.5	0.2±0.5	-0.6±0.9	2.6±2.5

Table II: Changes in pyruvate and alanine from preoperative values

	Group SS	Group SC	Group CC	Group SS	Group SC	Group CC
	Blood Pyruvate			Blood Alanine		
Pre-CPB	.01±.02	.03±.05	.06±.03	.05±.05	-.02±.05	.01±.04
5' after DHCA	.06±.02	.01±.06	.12±.04	.09±.05	-.05±.05	.08±.04
End-op	.06±.03	.09±.07	.20±.04	.11±.03	-.03±.05	.00±.03
6 h postop	.04±.01	.03±.05	.21±.10	.06±.05	.-3±.08	.36±.05
12 h postop	.00±.01	-.02±.05	.07±.05	.09±.07	.00±.09	.19±.07
24 h postop	.02±.03	-.07±.05	.10±.04	.01±.02	-.08±.08	.43±.16