

Title: RANDOMISED TRIAL OF HIGH-DOSE SUFENTANIL ANESTHESIA IN NEONATES UNDERGOING CARDIAC SURGERY: HORMONAL AND HEMODYNAMIC STRESS RESPONSES

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**Introduction.** Little is known about the stress responses of neonates undergoing cardiac surgery<sup>1</sup> or about the effects of anesthesia on such responses. We have found that neonatal stress responses are greater in magnitude than those of adult patients and can be suppressed by fentanyl anesthesia<sup>2</sup>. A double-blind randomised trial with 80% power (for  $\alpha < 0.05$ ) was designed to investigate whether: 1) cardiac surgery and CPB<sup>3</sup> stimulate a greater stress response as compared to conventional surgery, 2) this response is suppressed by high-dose opiate anesthesia; and 3) the stress suppression can be maintained by a continuous infusion of opiates.

**Methods.** Approval of the Clinical Investigation Committee and informed parental consent were obtained to study 45 neonates undergoing cardiac surgery with CPB and DHCA<sup>3</sup>. 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 (morphine 0.1 mg/kg or fentanyl 10 ug/kg) (SC group) after surgery. Plasma beta-endorphin immunoreactivity (PBE) and hemodynamic variables were measured 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 19 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 three groups were similar with regard to age and weight; the dextrose infusion rates before, during and after surgery; the anesthetic management; and the durations of CPB and DHCA were similar in the three randomised groups.

**Results.** PBE values decreased below preoperative concentrations in the SS and SC groups and remained near or below baseline values during and after surgery. In the CC group a marked PBE response was observed during surgery; with

significant differences between the three groups before the start of CPB ( $p < 0.01$ ), at 5 min after DHCA ( $p < 0.02$ ) and at the end of surgery ( $p < 0.05$ ) (Table 1). Apart from a decrease in the heart rate in neonates given sufentanil ( $p < 0.025$ ), no significant differences were found in the systolic, diastolic or mean blood pressures in neonates of the three randomised groups.

**Discussion.** Marked changes in PBE concentrations have been documented in adults undergoing cardiac or non-cardiac surgery<sup>4</sup>. This study shows that similar responses are also mounted by neonates undergoing cardiac surgery, which can be inhibited by high-dose opiate anesthesia. Further studies on modification of the pathological stress responses of neonates to severe surgical stress may lead to an improvement in clinical outcome.

#### References.

1. Anand KJS: Hormonal and metabolic functions of neonates and infants undergoing surgery. *Curr Opin Cardiol* 1:681-689, 1986.
2. Anand KJS, Sippell WG, Aynsley-Green A: Randomised trial of fentanyl anesthesia in preterm babies undergoing surgery: Effects on the stress response. *Lancet* 1:243-248, 1987.
3. Abbreviations used: CPB = cardiopulmonary bypass, DHCA = deep hypothermic circulatory arrest, PBE = plasma beta-endorphin immunoreactivity.
4. Anand KJS: The stress response to surgery: From physiological basis to therapeutic implications. *Prog Food Nutr Sci* 10:67-132, 1986.

Table 1: Changes in PBE immunoreactivity from preoperative values

	Group SS	Group SC	Group CC
Pre-CPB	-11 ± 8	-2 ± 1	45 ± 21
5' after DHCA	-23 ± 14	-13 ± 10	34 ± 12
End-op	-19 ± 16	3 ± 17	21 ± 9
6 h postop	-12 ± 9	1 ± 18	11 ± 7
12 h postop	-16 ± 8	-14 ± 18	13 ± 11
24 h postop	-16 ± 9	-5 ± 16	10 ± 13

All PBE values in pg/ml; Mean ± SEM.