Effect of Intralipid infusion on transcutaneous oxygen and carbon dioxide tension in sick neonates

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Summary
We evaluated the change in transcutaneous oxygen (tcPO₂) and carbon dioxide (tcPCO₂) tension in response to 60 minutes' infusion of Intralipid (Kabi Vitrum (Saphar)) (mean dose (0.16 ± 0.07 g/kg/h) in neonates with lung disease (hyaline membrane disease or bronchopulmonary dysplasia). The tcPO₂ was 10% lower following Intralipid infusion (P < 0.05), whereas no significant change occurred in tcPCO₂ measurements. The data confirm the need for limited use of Intralipid in this category of patients.

Transcutaneous oxygen (tcPO₂) and carbon dioxide (tcPCO₂) tension measurements are often used to monitor the oxygen requirements and ventilatory status of infants with respiratory distress. The provision of adequate nutrition, although difficult to achieve, is fundamental for resolution of and recovery from the lung disease. This has led to the frequent use of parenteral nutrition in the supportive management of these infants. Various undesirable metabolic, mechanical and immunological complications have been reported with intravenous nutrition solutions used in the newborn. Recently Intralipid-induced hypoxia has been emphasised, particularly in the presence of pre-existing pulmonary or vascular damage. We used a combined O₂ and CO₂ surface electrode to investigate the influence of Intralipid on tcPO₂ and tcPCO₂ in infants with pulmonary disease.

Patients and methods
The patients were 7 sick infants from the intensive care unit, studied on 13 different occasions. The protocol was reviewed and approved by the Committee for Research on Human Subjects and consent was obtained from the parents. The mean age at entry into the study was 19 days (range 6 - 34 days); the mean body weight at entry was 1402 g (range 740 - 3110 g). All infants were considered on clinical and radiological criteria to have respiratory difficulty related to hyaline membrane disease or bronchopulmonary dysplasia. They all required endotracheal intubation and were treated with intermittent positive-pressure ventilation and continuous positive airway pressure. Fractional inspired oxygen (FiO₂) concentrations averaged 0.44 (range 0.24 - 1). No change in ventilator settings or FiO₂ was made during the study. It was not possible to feed the infants orally because of their respiratory illness or because of proven or suspected necrotising enterocolitis. All infants were receiving parenteral nutrition comprising 10% dextrose, amino acids, multivitamins and varying amounts of electrolytes via a peripheral vein. The volume of infusion was not determined by a study protocol but was based on each infant's estimated fluid requirements. Their total energy intake was approximately 272 kJ/kg/d (range 176 - 329 kJ/kg/d).

Using a constant-rate syringe pump we infused the soybean fat emulsion (Intralipid 20%; Kabi Vitrum (Saphar)) simultaneously with the parenteral nutrition solution. The mean rate of fat administration was 0.16 g/kg/h (range 0.05 - 0.27 g/kg/h). The day's fat dose was infused continuously over at least 10 hours. During the experimental infusion studies with Intralipid, the infants' serum was inspected for lipaemia and none was noted.

We used the Radiometer TCM2/MCN20 monitor and dual-channel recorder to monitor tcPO₂ and tcPCO₂, during the experimental infusion studies. The skin sensor utilises Clark and Severinghaus-type electrodes housed in a single 15 mm diameter capsule. The O₂ and CO₂ transducers were calibrated with room air and standard CO₂/N₂ gas mixtures immediately before and at the end of each study. After calibration the sensor was attached to the skin of the anterior abdominal wall with an adhesive ring and contact solution, and allowed to stabilise for approximately 1 hour. The sensor temperature was 44°C and the chart speed 0.5 cm/min for all measurements.

The tcPO₂ and tcPCO₂ recordings were digitised with a laboratory microcomputer and plotter (HP 9816; HP 7475A). The differences between paired values obtained after equal times into the baseline hour (normal parenteral nutrition) and Intralipid hour were determined every 30 seconds and averaged over 5 and 10 minutes for tcPO₂ and tcPCO₂ respectively. Missing data included periods of endotracheal suctioning and abnormal activity determined by clinical observation. The response to Intralipid infusion lasting 60 minutes was evaluated by plotting the mean % tcPO₂ and tcPCO₂ differences against time. Because the tcPO₂ and tcPCO₂ did not change significantly from baseline immediately Intralipid administration was started, the data were analysed by linear regression to determine if there was a gradual shift over the 1-hour study period. If linear regression showed a significant correlation, any appropriate higher-order model could only improve that significance. If the changes in blood gases are mediated via the accumulation of any substance which has a half-life greater than 1 hour, then a linear model can be expected to fit well. We also tested the significance of differences between time intervals using analysis of variance.

Data analysis
When digitising an analogue signal it is necessary to sample the signal at a rate greater than the Nyquist rate if no information is to be lost. Since the frequency spectra of the transcutaneous blood gas signals were not known, the signals were manually digitised at the maximum rate possible in the time available. It was not the intention to reproduce the original curves from the digital records, but merely to perform statistical analysis.
Results

Using the calibrating gas at a high flow rate and with the sensor mounted in the calibration post, we determined that the tcPo2 and tcPCO2 digitised readings were calculated. It was found that there was a strong periodic component of approximately 9 minutes in the O2 autocorrelation function indicating that data points separated by more than 4.5 minutes were uncorrelated.

Based on the results of the ensemble-averaged autocorrelation function the O2 data were reduced by averaging each subject's tcPo2 over 12 equal periods of 5 minutes; tcPCO2 data were averaged over 10 minutes, producing 6 data points per patient.

Discussion

The results of the present study demonstrate that there was a mean decrease of 10% (-1.0 kPa) in tcPo2 values 1 hour after Intralipid infusion. There was no change in tcPCO2 in response to the infusion. The fall in tcPo2 induced by the Intralipid may be potentially harmful to infants with lung disease associated with severely compromised gas exchange. Our findings are in accord with those of a previous report of the effects of Intralipid on blood gases and pulmonary function in infants. Pereira et al. used intermittent blood gas sampling to assess arterial oxygenation in sick newborn infants given an infusion of Intralipid 1 g/kg over a 4-hour period. In infants less than 1 week old the infusion was followed by elevated levels of triglyceride with a concomitant fall in the partial arterial oxygen pressure (PaO2). The findings were similar but less pronounced than our study. 4 Recently Flaggeman et al. have suggested a prostaglandin-mediated effect on pulmonary vasculature in response to Intralipid infusion in rabbits with damaged lungs. McKeen et al. concluded from studies in sheep that Intralipid at a maximum rate of 0.25 g/kg/h causes pulmonary hypertension, increased lung microvascular pressure and arterial hypoxaemia. Indomethacin prevented and reversed these effects, suggesting strongly that prostaglandin cyclic endoperoxides are the most likely mediators. A disadvantage common to any form of transcutaneous gas monitoring is the inherent variability of the signal which makes data acquisition, storage, analysis and interpretation difficult. Although it cannot be proved that the analogue data from our study were sampled above the Nyquist rate, it is of interest to compare the dynamic performance of the O2 and CO2 measurement systems as observed in the step response and autocorrelation functions. If it is assumed that the dynamic characteristics of the measurement systems were predominantly first-order, then their approximate bandwidths (BW) can be calculated from the 90% rise times (Tr) of the instruments. The signal BW was also estimated from the autocorrelation according to Betts:

\[ Tr(90\%) = \frac{BW}{2} \]

FIG. 1. Linear regression between the average % difference of tcPo2 and tcPCO2 in response to 60 minutes of Intralipid infusion. % Difference = transcutaneous measurement during glucose, amino acid, Intralipid infusion - transcutaneous measurement during glucose, amino acid infusion. A broken line indicates 95% confidence limits for regression. Slope of % tcPo2 difference line is significantly different from zero at \( P = 0.05 \).
A more detailed analysis of the dynamic performance of transcutaneous blood gas instruments should include Fourier (spectral) analysis of the analogue signals and digital sampling at a rate above that required by the Nyquist sampling theorem.

In summary, this study shows that the infusion of Intralipid contributes towards the hypoxia of respiratory distress in neonates. It is therefore recommended that Intralipid should be administered to this category of patients only in limited quantities and with extreme caution. Prolonged routine use of high-dose Intralipid is not recommended in infants with pulmonary disease, and alternative energy sources need to be considered.

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REFERENCES


Kliniese ondervinding met atrakurium  — 'n aanhoudende infusie-tekniek

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Summary

A continuous infusion technique for atracurium was investigated. It provided a stable neuromuscular block, with a mean infusion rate of 0,008 mg/kg/min after an initial bolus of 0,5 mg/kg. A wide individual response was found and an arbitrary infusion rate based on mass alone is therefore not possible. The above rate is thus a starting point and should be adjusted according to individual requirements, preferably by using a peripheral nerve stimulator. The technique obviates the need for repeated increments of atracurium during lengthy surgical procedures.

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Atrakurium is een van die nuwer kort- tot mediumwerkende nie-depolariserende spierverslappers. Van sy voordelige eien- skappe is o.a.: (i) kort werkingsduur met vinnige spontane herstel van neuromuskulêre funksie binne 20 - 30 minute (eliminasiehalfleyfye = 20 minute); (ii) metabolisme wat onalhanklik is van lever- en nierfunksie weens hoofsaaklik nie-ensiimatisie chemiese degradering (Hoffmann-eliminasie) en in 'n mindere mate esterhidrolise van sy estergroep; en (iii) nie-kumulatiewe aard; en (iv) minimale kardiovaskulêre neweeffekte weens sy wye ontonge veiligheidsgrens. Hypotensie mag egter soms voorkom, veral na groot bolusdosierings wat vinnig toegedien is en wat verband hou met histaminenvrystel­ling. Sporadiese bradikardie is al gerapporteer tydens die gebruik van atrakurium, 'n Moontlike verklaring hiervoor is dat weens die minimale kardiovaskulêre aktiwiteit van atrakurium, die cholinere effekte van ander narkosemiddels of stimuuli ongeopponere is sodat bradikardie makliker kan ont­wikkel.

Weens sy kort werkingsduur en gevolglik die herhaalde inkre­mente wat tydens lang operasies nodig is, is 'n aanhoudende infusie-tekniek ondersoek om vas te stel of dit 'n prakties uitvoerbare tegniek is, wat die optimale infusiedosering sou wees, gegrond op pasientmassa alleen, en wat die duur van spontane herstel van neuromuskulêre aktiwiteit sou wees na staking van atrakurium-infusie.