

SURFACTANT IMPROVES BLOOD GASES BUT NOT DYNAMIC LUNG COMPLIANCE IN ARDS LUNGS - WHAT ARE THE MECHANISMS INVOLVED?

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Introduction Despite improvements in oxygenation there was no improvement in dynamic compliance directly after surfactant instillation in several clinical studies in neonates with respiratory distress syndrome (RDS). Therefore, it is unclear whether the immediate improvement in oxygenation is caused by, or followed by improvements in lung mechanics and/or lung volumes. That is why we investigated the immediate effects of exogenous surfactant therapy on blood gases, lung volumes and lung mechanics in adult rabbits with acute RDS.

Methods The studies were performed in 12 adult New Zealand White rabbits (bodyweight: 2.7 ± 0.3 kg). The animals were anesthetized, tracheotomized, paralyzed and ventilated by a Siemens Servo ventilator 900C at the following ventilator settings: pressure-controlled ventilation, $FiO_2=1.0$, frequency=20/min, I/E ratio=1:2, peak inspiration pressure (PIP)=9-12 cm H₂O and zero end-expiratory pressure (ZEEP). After reaching steady state respiratory failure was induced by repeated lung lavage as described by Lachmann et al. After PaO_2 decreased < 80 torr (10.6 kPa), the animals were divided into 2 groups: Group I (n=6) received surfactant 120 mg/kg which was suspended in a 0.6% NaCl solution; Group II (n=6) received comparable volumes of the same hypotonic solution (0.6% NaCl) and served as controls. Data were collected before lavage at ZEEP and at PEEP of 4, 6 and 8 cm H₂O; 5 min after lavage; 5, 15 and 30 min after surfactant or hypotonic solution instillation; and every 30 min for 3 h. At each data collection point PaO_2 , $PaCO_2$, base excess (BE), pH, FRC and dynamic compliance (C_{dyn}) measurements were obtained. P-V curves were recorded before and after lavage and at 15 min, 1, 2, 3 and 3 h after surfactant or hypotonic solution instillation. A computerized technique with sulfur hexafluoride (S₆) as tracer gas was used for measurement of functional residual capacity (FRC) together with recordings of static pressure-volume (P-V) curves. C_{dyn} was calculated as $VU/(PIP-PEEP)$, where V_t is the tidal volume. PaO_2 , $PaCO_2$, pH and BE of the samples were measured by conventional methods (ABL 330).

Results Within 60 min after surfactant instillation there was a dramatic improvement in arterial oxygen pressure (61 ± 7 torr (8.2 \pm 0.9 kPa) to 470 ± 47 torr (62.6 \pm 6.2 kPa)) and FRC (7.6 ± 1.4 to 17.7 ± 1.6 mL/kg bodyweight) at unchanged ventilator settings. There was no significant change in dynamic compliance, but maximum compliance calculated from the P-V curves increased by 92%. After intratracheal surfactant instillation the P-V curve became steeper and the P-V curves for total lung volume restored to an almost normal state. In the control group no improvements in any measured or calculated lung parameters were seen.

Conclusion The findings indicate that during mechanical ventilation the effects of surfactant therapy on lung mechanics are best characterized by FRC and maximum compliance obtained from static P-V curves and not by dynamic compliance.

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Nutritional therapy

SHOULD PROTEIN ENERGY BE INCLUDED IN THE CALCULATION OF ENERGY INTAKE IN CRITICALLY ILL PATIENTS?

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In clinical studies on the effects of an increased protein intake on nitrogen balance, some authors count protein as part of metabolizable energy, while others do not. As a consequence the energy intake varies depending on the method of calculation. A questionnaire was sent to 37 leading researchers from all over the world to ascertain the authors' motives for including or excluding protein energy in the energy requirements. Protein was counted as energy by 17 of the 26 respondents based on the assumption that after deamination of amino acids the carbon skeleton will be oxidized. The other 9 did not include protein energy because they assume amino acids are used for protein synthesis only and not for energy supply. Studying the effects of increasing nitrogen supply, 13 respondents substituted carbohydrate or fat by protein to maintain the amount of total energy. Another 11 just supplied an additional amount of protein, in particular to maintain the amount of nonprotein energy. Since both methods of calculation have pros and cons, the ambivalence concerning protein energy remains. Clinically, the difference between the methods of calculation might be irrelevant. However, since both protein and energy intake may affect the nitrogen balance, energy intake in research needs to be controlled by providing all diets with equal amounts of total energy, thus including protein energy. Since it is also important to prevent marginal energy intake, a compromise, obtained from the results of the questionnaire, might be to provide both diets with an equal amount of total energy which is slightly higher than the calculated energy requirements. A possible lack of non protein energy on a high protein diet is thus prevented.

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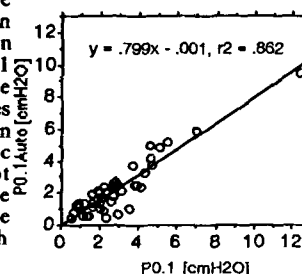
AUTOMATIC METHOD FOR CONTINUOUS EVALUATION OF P0.1 ON AN OCCLUSION PHASE SHORTER THAN 100 MSEC.

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The short occlusion phase necessarily imposed by demand valves can theoretically be used in order to evaluate P0.1, making unnecessary a longer occlusion phase and allowing cycle-by-cycle measurements. Modern demand valves, however, apply an occlusion that is generally shorter than 100 msec, so that the conventional measurement cannot be performed, unless the trigger sensitivity is intentionally reduced. We can, otherwise, identify the straight line describing the airway pressure (Paw) drop during occluded inspiratory effort even using an interval shorter than 100 msec, and compute P0.1 by extrapolation. On this basis works our method for automatic cycle-by-cycle computation (Auto-P0.1). This method requires Paw and airflow (V_{aw}) to be sampled at 60 Hz. After identification of the onset of the occluded effort by the reversal of V_{aw}, the straight line of the pressure drop is identified on the first 4 points (66 msec) and finally the pressure drop is extrapolated to 100 msec.

Methods. The study included 12 patients in pressure support ventilation (PSV) for ARF, each of them in four different times. For each test, Paw and V_{aw} were sampled at 60 Hz and Auto-P0.1 data were the mean over of 160 consecutive cycles. The reference values for P0.1 were obtained from the mean of 3 manual measurements, the only difference from the conventional method being the use of the ventilator valves as a shutter.

Results and conclusions. The figure shows the relationship between Auto-P0.1 and reference P0.1. Mean errors \pm SD are 0.564 ± 0.743 . Auto-P0.1 correlates well with reference P0.1. The underestimation observed in some cases is probably due to an effective occlusion phase even shorter than the 66 msec required. This kind of error does not compromise the validity of the principle on which Auto-P0.1 is based and can be reduced by technical improvements such as increased sampling rate.



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THE EFFECT OF INCREASED PROTEIN INTAKE ON NITROGEN BALANCE IN MECHANICALLY VENTILATED CRITICALLY ILL PATIENTS RECEIVING TOTAL PARENTERAL NUTRITION

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The amount of protein required to minimize nitrogen loss in critically ill patients receiving total parenteral nutrition (TPN) varies in literature. Therefore, we studied the effect of increased protein intake on the N balance, administering TPN with either a low (1.2 g/kg/day) or a high (1.8 g/kg/day) protein content. Twenty-one mechanically ventilated critically ill patients were studied. After at least two days of standard TPN, patients were randomly assigned to either the low or the high protein diet. Ten patients were studied on the low protein diet and 11 on the high protein diet. Nonprotein energy was supplied according to estimated energy requirements. During five consecutive days the N balance was measured daily. Total urinary nitrogen (TUN) was analysed using the Kjeldahl method. This method was compared to calculation of TUN from urinary urea nitrogen. Unpaired Student's t test showed no difference in N balance between the groups. On the low protein diet nitrogen balance was -0.113 ± 0.088 g N/kg/day and on the high protein diet -0.113 ± 0.109 g N/kg/day. Results of a previous pilot study show that in 20 similar patients the nitrogen balance became 80% less negative when protein intake increased from 0.9 to 1.5 g/kg/day. Since these results are consistent with other studies, we conclude that there seems to be an optimal range of protein supply in this type of critically ill patients of approximately 1.2 - 1.5 g protein/kg/day. Estimation of TUN from urinary urea underestimated TUN measured with the Kjeldahl method with $11.9 \pm 15.5\%$, indicating that urea cannot be used for estimating TUN in nitrogen balance studies, in this type of patients.

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CHANGING NUTRITIONAL THERAPY IN A GENERAL ICU.
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Parenteral nutrition (TPN) is usually prescribed when enteral nutrition (EN) is contra-indicated by conventional criteria (aspirate, diarrhoea or absent bowel sounds). We tested the hypothesis that most ICU patients could be fed enterally. **METHOD.** Data was collected on all patients over a 20 month period and analyzed using a computerised audit system (Riyadh Intensive Care Programme V4.0). Patients were fed enterally with undiluted Nutrison (Cow and Gate Ltd, Trowbridge, UK) via a nasogastric tube. Feeding was commenced at 30 ml/hour and increased every four hours until the patient's requirements were met. EN was only stopped and TPN prescribed if the volume of aspirate exceeded the feed despite a 12 hour rest period and prokinetic agents (metoclopramide and cisapride). **RESULTS.** Data from 1686 consecutive patients were analyzed in 4 month cohorts. The proportion of patients requiring feeding (mean 15.96%, SD 1.14) and the risk of death of the fed patients (ROD, mean 30.32%, SD 4.17) calculated from the APACHE II scores remained constant. The proportion receiving EN alone increased significantly from 48% in the first 4 months to 91% in the last 4 months ($p < 0.01$). In consecutive cohorts the proportions were: 48%, 67%, 85%, 92%, 91%. The standardized mortality ratio (SMR) for the fed group improved from 2.0 to 1.1 [consecutive cohorts 2.0, 1.3, 1.3, 1.1, 1.1]. **CONCLUSION.** We have shown a dramatic increase in the proportion of patients receiving EN, within the same number of patients receiving feeding. The change in SMR suggests that such a change in practice is not detrimental, and may even be beneficial.

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THE EFFECTS OF THE PARENTERAL ADMINISTRATION OF OMEGA-3-FATTY ACIDS (n-3-FA) ON THE LEUKOTRIENE PRODUCTION OF HUMAN LEUKOCYTES. H. Lessire, E. Torwesten, B. Morlion, N.M. Nguyen, B. Miele, G. Sturm, P. Fürst, B.M. Peskar, C. Puchstein. Eicosapentaenoic acid (EPA) competes with arachidonic acid in the lipoxygenase pathway, thereby resulting in reduced formation of n-6-FA derived eicosanoids and less pro-inflammatory activity. In this study, the influence of the parenteral administration of EPA and n-3-FA on the leukotriene C₄ and C₅ (LTC₄ and LTC₅) synthesizing capacity in stimulated leukocytes was assessed. 20 patients (40-75 y) were studied following major elective abdominal surgery. They received TPN over 5 days comprising 3 g/kg/day of glucose, 1.5 g/kg/day of aminoacids and 1 g/kg/day of fat. Fat emulsion was composed either of 100% Soybean emulsion (SO, Lipovenös 20% Fresenius) or of 85% Lipovenös and 15% Fish oil emulsion (FO, Omegavenös 10%, Fresenius). At day 0, 6 and 14, a suspension of leukocytes was prepared from heparinized venous blood samples and stimulated with Ca-ionophor A23187. LTC₄ and LTC₅ were separated by chromatography (HPLC) and measured by RIA.

		day 0	day 6	day 14
SO	LTC ₄	1946 ± 462	2373 ± 425	2463 ± 429
	LTC ₅	77 ± 40	155 ± 96	94 ± 36
FO	LTC ₄	2575 ± 733	3560 ± 631	2077 ± 476
	LTC ₅	98 ± 48	645 ± 250*	209 ± 106

Mean ± SEM expressed as pg/10⁶ WBC; * $p < 0.05$

An significant increase in LTC₅ production was observed after only 5 days of parenteral n-3-FA supply but was not associated with the expected reduced LTC₄ synthesis.

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EARLY ENTERAL NUTRITION IN ISOLATED SEVERE CRANIOENCEPHALIC TRAUMA (CET).
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OBJECTIVES:

The aims of this study were: 1.-To determine the metabolic evolution pattern by indirect calorimetry in patients with isolated severe (CET) and early enteral nutrition and 2.- To clarify the usefulness of early enteral nutrition (EN) to control the metabolic response and morbidity produced by the duration of intensive care.

METHODS

40 Patients, mean age 33±9 years, 32 males and 8 females with isolated severe CET were divided in a prospective study, into two groups, with similar characteristics in respect to anthropometrics, initial apache II score, ISS and GCS.

Group A n=24, with gastric hyperproteic feeding 0.21 gr.prot/kg. body weight with total caloric supply of 1700 Kcal/24 h, started 24 hours after injury an group B, n=14, with equivalent caloric supply but intravenously provided. All patients were under controlled mechanical ventilation (EE with a metabolic monitor and a capnograph), without PEEP, similar therapy and clinically stable and did not present septic syndrome. Five determinations of VO₂I, VCO₂I, RQ, REE/BMR were done at 24 hours intervals.

The t-Student test was used to do the statistical analysis.

RESULTS:

Are shown in the following (Table I).

	24 H. Post-CET	48 H. Post-CET	72 H. Post-CET	96 H. Post-CET	120 H. Post-CET
VO ₂ I	183±33	183±36	182±37	188±28	189±36
VCO ₂ I	126±21	138±24	140±25	142±28	144±24
RQ	0.68±0.1	0.74±0.1	0.75±0.1	0.73±0.1	0.74±0.1
REE/BMR	1.28	1.31	1.29	1.33	1.36

REE: resting Energy expenditure; BEE:Basal metabolic rate.

There were no significant differences in the mortality rate of the two groups, but the mean stay in intensive care in group A (924 VS 1426 days) and the relation REE/BEE were lower than in group B.

CONCLUSIONS:

The metabolic performance rules out the need of high important caloric supply in severe CET. Early enteral nutrition could reduce the traslocation of bacteria preventing sepsis, hypermetabolism and, therefore morbidity, showing clear worse results, in this patients, the utilization of parenteral nutrition.

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EFFECT OF TWO DIFFERENT LIPID EMULSIONS ON PLATELETS.

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OBJECTIVE. The aim of the present study was to compare the effects on platelet function of two lipid emulsions, containing different quantities of essential fatty acids (linoleic and linolenic) in critically ill patients receiving total parenteral nutrition (TPN).

METHODS. 33 critically ill patients admitted to the Intensive Care Unit were randomised into 2 groups. Group A (n=12) received a 50% MCT/50% LCT and group B (n=11) received a 100% LCT emulsion. The TPN composition administered to both groups was 0.25 g N/kg.d, 5 g glucose/kg.d and 1.7 g lipid/kg.d. The lipid emulsions were infused over 12 hours. Blood samples were collected without a tourniquet, before TPN was started (control) and 12 hours after the end of lipid infusion on the 4th and 7th days of TPN. Platelet aggregation was examined "in vitro" using ADP, collagen, araquidonic acid and adrenaline at different concentrations. Platelet activation was analyzed for beta-thromboglobulin and platelet factor 4 levels in plasma, by RIA. 6-keto-PGF_{1α} in urine and TXB₂ in plasma were also determined by RIA.

Analysis of variance (ANOVA) was performed using the SPSS procedure.

RESULTS. Before TPN was started, an increase in platelet activation and a decrease in platelet aggregation against ADP (2 μM) and collagen (2 μg/ml), were found in both groups, with no significant differences between the groups. After 4 and 7 days of TPN, no significant changes were noted in the different parameters studied.

In conclusion, the critically ill patients studied showed an alteration in platelet function which was not modified by the two lipid emulsions administered. Although further studies are necessary, our data indicate that neither of the lipid emulsions administered over a short period modified platelet function.

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