

Surfactant replacement therapy in high-risk congenital diaphragmatic hernia

SIR,—Clinical trials of surfactant replacement therapy have shown a reduction in the frequency and severity of respiratory distress syndrome (RDS) in premature newborn babies,¹ and first clinical trials in adults have also shown the beneficial effect of this therapy.^{2,3}

Does surfactant have a role in the treatment of more mature infants with pneumonia and meconium aspiration syndrome, or in infants with hypoplastic lungs, as seen in congenital diaphragmatic hernia? Congenital diaphragmatic hernia presents in 1 in 3000 liveborn babies. Although new treatments, such as delayed surgery and extracorporeal membrane oxygenation (ECMO), have been advocated, the case fatality rate for this malformation still remains 30–50% worldwide because of pulmonary hypoplasia and persistent pulmonary hypertension.⁴ The hypoplastic lung in these patients is probably biochemically immature, and low lecithin/sphingomyelin ratios in amniotic fluid have been recorded.⁵ We investigated the effect of surfactant replacement therapy in 4 newborn babies with a congenital diaphragmatic defect. Their mean gestational age was 37 (range 36–40) weeks and their mean birthweight 2880 g (range 2560–3400). All 4 patients had respiratory insufficiency within 6 h after birth. They were ventilated with a time-cycled pressure controlled ventilator ('Servo 900C', Siemens Elema, Sweden) with high inflation pressures and 100% O₂. We did not use surfactant prophylactically, but as rescue therapy within 24 h of birth to improve oxygenation and to diminish further damage to the hypoplastic lung. The surfactant used was a natural substance isolated from minced bovine lungs. It consists of about 83% phospholipids, 1% hydrophobic proteins (SP-B and SP-C), and other lipids such as cholesterol, glyceride, and free fatty acids, but does not contain SP-A. The freeze-dried preparation was resuspended in a 0.9% NaCl solution resulting in a total concentration of 40 mg phospholipids per ml. We gave 150 mg/kg of the surfactant extract endotracheally, and recorded the alveolar-arterial oxygen tension difference (A-a)DO₂, which indicates gas exchange by the lungs, immediately before and after administration and after 6 h. In patients 1 and 2 (figure), (A-a)DO₂ fell strikingly and led to a decrease in FiO₂ and inspiratory peak pressures. The effect was most pronounced immediately after administration. Repeated doses had only a short-term effect. The diaphragmatic defect was closed afterwards and both patients survived. In the other two patients no effect was noted; both had had ECMO treatment. Patient 3 died on ECMO with uncorrectable coagulation disorders and a massive intracranial haemorrhage. After being weaned from ECMO successfully at age 12 days, patient 4 died at six weeks because of relapsing episodes of persistent pulmonary hypertension.

Our preliminary conclusion is that in some newborn infants with congenital diaphragmatic hernia, surfactant therapy may induce a transient but important improvement of oxygenation. This

improvement may lead, especially when used as a prophylactic measure, to a reduction of barotrauma to the hypoplastic lung and a reduction of risk factors for persistent pulmonary hypertension (ie, hypoxia) as well as to the possibility of gaining time to introduce other treatments such as ECMO. The best dosing schedule and the optimum preparation of surfactant for these patients needs to be established. We have lately treated a fifth baby born at term (patient 5 in figure) with congenital cystic adenomatoid malformation of the lung who responded well to treatment and who survived without chronic lung disease.

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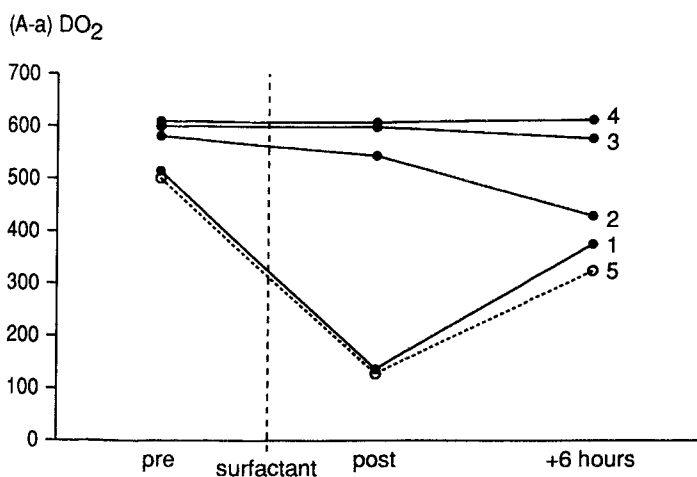
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Breastfeeding anaphylaxis

SIR,—We describe here a 29-year-old woman who had generalised urticaria 30 min after the first breastfeeding of her first-born baby in 1986, concurrent with the use of aspirin for episiotomy pain. The symptoms gradually resolved but recurred within minutes of the second feed 4 h later, this time accompanied by upper airway angioedema, and which happened at every feed for 3 days until aspirin was stopped because of possible hypersensitivity. Breastfeeding was uneventful after that and the patient was discharged.

30 days later she was readmitted after two closely spaced episodes of urticaria and upper-airway angioedema immediately after breast feeds, the second while taking paracetamol because of breast engorgement. She manually expressed milk without further difficulty. The patient had intercurrent urticarial reactions to seafood, dermatographism, and mild bronchial asthma treated with salbutamol. Physical examination between attacks was unremarkable. Laboratory investigations were either normal or negative. No episodes ensued when the patient was placed on an elimination diet of rice, peeled pears, and steamed lamb and chicken. One week later, blinded placebo-controlled oral capsule challenges were given, followed 1 h later by breastfeeding. While mild bronchospasm developed 12 h after monosodium glutamate, no reaction followed tartrazine, sodium benzoate, or sodium metabisulphite. 300 mg aspirin was given and within minutes of breastfeeding an hour later she had bronchospasm and generalised urticaria. Reports of hypersensitivity to exogenous oxytocin^{1,2} raised the possibility of sensitisation to endogenous oxytocin during milk letdown, so skin prick and intradermal injections of oxytocin were done but failed to elicit a wheal and flare in either the patient or three healthy controls. Over the next 24 h, manual expression of milk (twice) and spontaneous milk letdown (once) was followed immediately by urticaria, laryngeal oedema, and hypotension, and it was decided to stop lactation with oral bromocriptine. She declined further challenges with aspirin or paracetamol and was discharged on a low salicylate diet with instructions to avoid aspirin. She was advised that lactation might need to be suppressed should this reaction recur with subsequent pregnancies.

The patient remained symptom-free for 5 years (despite occasional paracetamol) until the birth of a second child in 1991. The post-partum period was uneventful for 48 h until she again experienced generalised urticaria, upper airway angioedema, and



Effect of surfactant therapy on (A-a)DO₂ values in newborn babies with congenital diaphragmatic hernia (1–4) and cystic adenomatoid malformation of the lung (5).

hypotension within a few minutes of every breastfeed. Between episodes there were no signs of systemic mastocytosis or carcinoid syndrome, and 24 h urinary histamine, noradrenaline, serotonin, and 5-hydroxyindoleacetic acid were normal. Lactation was suppressed with bromocriptine and the episodes resolved.

Urticaria and angioedema may be triggered by several factors including physical stimuli, hormones, cyclo-oxygenase inhibitors, CI esterase deficiency (excluded in this case), collagen vascular disease, and malignancy.^{3,4} This patient's anaphylactoid episodes were triggered by breastfeeding or milk letdown and, at least in the first instance, by aspirin and paracetamol. The restriction of episodes to the post-partum period suggests that hormonal changes after childbirth, such as the disappearance of progesterone over the first 24-48 h, may have had an influence. A protective effect of progesterone in recurrent urticaria and angioedema⁵ remains controversial⁶⁻⁸ but awareness of the potential influence of sex hormones has led to resolution of symptoms by inhibition of ovulation^{7,8} or, as in this case, suppression of lactation.

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Testing for carpal tunnel syndrome

SIR,—In your Aug 24 editorial you discuss several provocative tests for carpal tunnel syndrome (CTS), including a new test with direct pressure on the median nerve in the carpal tunnel. You conclude that: "none of these tests is entirely satisfactory; with the possible exception of the direct pressure test..." We have reviewed in *The Lancet* the value of twelve provocative tests for CTS,¹ and concluded that none of these tests alone, nor the three best in combination, should be used in the diagnosis of CTS.

A new test has now been proposed by Durkan.² This carpal compression test was applied only in selected patients with CTS (in whom referral bias and disease severity bias may have played a part) and symptom-free controls (of whom no further details are given). Sensitivity and specificity were as high as 87% and 90%, respectively. We feel that the value of this test in patients with symptoms has not yet been established. The likelihood ratio of certain tests should be studied in a population with CTS-like complaints for it to be more applicable to medical practice. Additionally, these sensitivity and specificity values are too low for a reliable diagnosis of CTS. Neurophysiological confirmation therefore remains necessary to avoid misdiagnosis and needless surgery.

Your discussion about the value of electrophysiological testing is based on rather dated studies. In Semple and Cargill's investigation³ no nerve conduction tests were done. Because of disappointing surgical results, due to incorrect diagnosis, they suggested that accurate diagnosis of CTS would be improved by wider use of nerve conduction studies.³ In the two studies cited that support surgical therapy despite normal electrophysiological findings,^{4,5} ulnar and median nerve distal sensory latencies were not compared. These tests are much more sensitive than others, especially if the ring finger is used for recording or as the stimulation site for both nerves.^{1,6} They are quick to do and surface electrodes can be used, and are easily tolerated by most patients. Undoubtedly, there are patients with signs and symptoms suggestive of, or even typical of CTS, who have normal electrophysiological findings. We feel that in such patients one should search for other causes, refrain from early surgery, and repeat distal sensory latency measurements after several months in those with persistent symptoms. Damaging median nerve compression is unlikely if there is no increased distal sensory latency.

Thus, there is no reason to do provocative tests in the diagnostic workup of CTS. We believe that this is also true for Durkan's carpal compression test.

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Lactose intolerance

SIR,—I read with interest your Sept 14 editorial on lactose intolerance. To assist people with lactase-phlorizin hydrolase deficiency (LPH) several approaches were mentioned. I would like to draw attention to yoghurt, a milk product low in lactose. Since absolute deficiency of LPH is rare, yoghurt could easily be substituted as a milk product for those people with hereditary (or acquired) LPH deficiency. It has been used for centuries in Turkey. Most people tolerate yoghurt well even if they cannot consume milk because of LPH deficiency.

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SIR,—Another symptom of lactose intolerance, apparently unrecognised yet far more serious than the intestinal signs, may be anal fissure. For years I had tolerated gastrointestinal discomfort until new and agonising pain made me seek medical help. I was told that the trouble was an anal fissure and haemorrhoids, and surgery was advised. My sister told me that she had had a similar experience, and that her condition had been cured by using a commercial lactase product with dairy foods. I did the same and felt better almost immediately; in several months the fissure and haemorrhoids eventually disappeared and for five years I have been free of intestinal and anal symptoms. What might have happened if I had accepted surgery and continued to take untreated milk, ice cream, and so on? Perhaps, physicians should consider the possibility that lactose intolerance causes some cases of anal fissure and haemorrhoids and tell their patients that a simple remedy might allow them to avoid surgery.

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