Selected Summaries

Partial Liquid Ventilation in Neonates

[Leach CL, Greenspan JS, Rubenstein SD, et al. Partial liquid ventilation with perflubron in premature infants with severe respirator]/ distress syndrome. N Ehgl J Med 1996; 335: 761-767]

Experimental evidence has suggested that instillation of perfluorocarbon liquid into the lungs during continuous positive pressure gas ventilation [partial liquid ventilation (PLV)] improves lung function in animals with surfactant deficiency(l). The present uncontrolled clinical trial assessed the efficacy of PLV in 13 premature infants (gestational age, 24 to 34 weeks; birth weight, 600 to 2000 g) with severe respiratory distress syndrome who were less than 5 days old and were considered to have a high risk of death on the basis of lack of sustained response to surfactant therapy and the continued requirement for a high level of supplemental oxygen and ventilator support. All 13 infants had PaO_2 values < 60 mm Hg or $PaCO_2$ > 60 mm Hg on two consecutive determinations and required oxygen therapy with a fraction of inspired oxygen of 1.0 and a mean airway pressure of more than 10, 12 and 14 cm water for birth weights 600 to 1000 g, 1001 to 1500 g and 1501 to 2000 g, respectively. PLV was initiated by instilling perflubron at a rate of 1 ml per kilogram of body weight per minute, through the side port of endotracheal tube without interrupting mechanical gas ventilation, maintaining a positive and expiratory pressure of 4 cm of water until a column of fluid welted up in the endotracheal tube during momentary disconnection from the ventilator. The volume of liquid thus required represented the infant's functional residual capacity (FRC). Ten infants received PLV for 42±5 h (range 24-76h). Three infants who had received high frequency ventilation prior to enrollment were withdrawn from the trial within four hours due to continued refractory hypercapnia and were put back on high frequency ventilation. The initial volume of perflubron instilled was 15±4 ml/kg. Within one hour of instillation of perflubron, thearterial PaO_2 rose from a baseline of 60±34 mmHg to 143±99 mmHg (p=.O2), the dynamic compliance from 0.18±0.12 ml/cm H_2O/kg to 0.29±0.12 ml/cm H_2O/kg. During the first 24 h there was a significant reduction in oxygen index and mean airway pressure, arterial pCO_2 value and an increase in tidal volume. In most infants chest skiagrams revealed scant traces of perflubron 48 h after return to gas ventilation. No adverse effects clearly attributable to PLV were observed. Infants were weaned from PLV without complications. Eight of 10 infants survived.

Comments

Perfluorocarbon liquids have low surface tension and high density and at atmospheric pressure large amount of oxygen and carbon dioxide dissolve in them. Replacement of the gas functional residual capacity by perfluorocarbon liquid eliminates the alveolar membrane air liquid interface, reduces surface tension in the surfactant deficient lung and physically keeps the alveoli opn(2). Perflubron is not absorbed from the lungs into the systemic circulation. Further, perflubron is not inact ivated

by protein an d thus will reduce sur face ten-sion in a proteinaceous alveolar environment less responsive to surfactant. This is perhaps the reason why the infants in the present s tudy did not respond to surfac tant therapy and PLV may prove an effective alternat ive.

However, several questions still rema in unanswered . The discontinuation of PLV after 24 to 72 hours leaves the optimum duration for partial liquid ventilation unanswered. All the infants had received prior surfactant therapy and the possible benefits of PLV as an alternative to surfactant therapy rema in unkn own, as also it's ab ility to prevent chronic lung disease in pret erms ventila ted for RDS. The uncontrolled design and small sample size precludes at the present drawi ng firm conclusions on the efficacy and safety of this new ventilatory technique. While PLV may appear a promising alternative to avai lable ventil atory modalites, it is still to be considere d investigational and one w ould have to a wait the result of more ran domized trials.

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Withdrawal of Antiepileptic Drugs After One Year?

[Dooley J, Gordon K, Camfield P, Camfield C, Smith E. Discontinu ation of antico nvulsan t therapy in children free of seizures for 1 year: A prospective study. Neurology 1996; 46: 969-974]

In an attempt to study whether anticonvulsant can be withdraw n after one year of seizure free period, authors included 97 children who had two or more afebril e seizures, and subsequently were seizure free for 12 to 13 mon ths on antiepi leptic drug (AED) monotherapy. At the time of inclusion, all patients were subjected to detailed neurologica l history and examination. Info rmation recorded includ-ed details of seizures and neuro-development status of child. Medication was discontinued gradually over 4 to 6 weeks. Before discontinuation of drug, every patient had electroencephalography (EEG); however, results of EEG did not influence the decision to withdraw. The primary end point of the study was the recurrence of a clinical seizure. All children were followed at 6,12,18 and 20 months after AED withdrawal, or a seizure relapse occur red.

Out of total 97 patients, 50 were boys and 47 were girls. The age at seizure onset was from 1 to 198 months (mean 65.9±43.89 month). The mean age at attaining seizure control (date of last seizure) was 86.95 ±49.2 months. The patients were followed for 12 to 57 months (32.4±13.1 months), or until seizure recurrence. The overall probability of remaining seizure free was 78% at 3

months, 71% at 6 months, 66% at 12 months, and 61% at 24 months. Four important factors were noted to be important for predicting seizure recurrence; These factors were female sex, age at seizure onset over 120 months, seizure type, and clinical evidence of neurological abnormalities. Of those over age 10 years, 72% had further seizures, whereas only 33% of younger children had recurrences. Girls did less well than boys. Patients with 'non-rolandic' partial seizures did poorly when compared with children who had generalized seizures. Authors concluded that treatment for only 1 year after last seizure is sufficient for many children with a recurrence risk similar to studies that have required 2 or more years before withdrawal was attempted. It is possible to select the children who are at least risk and to identify those whose chance of recurrence is high-Comments

In patients with epilepsy who have been seizure free for sometime while taking antiepileptic medications, the question of 'when to discontinue medications' invariably arises. There is general agreement that most children who are seizure free for several years on antiepileptic drug therapy will remain so when medications are withdrawn(1). Children who have benign epilepsy with rolandic spikes or benign familial neonatal convulsions usually do well after drug withdrawal whereas those with juvenile myoclonic epilepsy often have relapses(2,3). Children with idiopathic generalized seizures whether 'absence' or 'tonic-clonic seizures' are least likely to have a recurrence after control has been achieved and medication withdrawn. Even, complex partial seizures can disappear after a long period of seizure control. The patients with the highest probability of remaining seizure free after the medication has been withdrawn are those who have had no seizures for a long period, those who had few seizures before control was achieved, and those with a normal neurological examination and no structural brain lesion(4). The observations of present study also suggest that in these similar groups of patients, the withdrawal of antiepileptic drugs may be considered even after 1 year of seizure free period. Consideration of the earliest withdrawal is worthwhile because of the potential of antiepileptic drugs to adversely affect cognition and behavior in children who are already at risk for disability.

Another important issue of withdrawal of antiepileptic medications is the optimal regimen for tapering of antiepileptic medications in children with epilepsy. Recommendations for tapering the antiepileptic drugs have ranged from abrupt discontinuation of therapy to gradual tapering over a period of two years. In most studies, the taper period was three to six months reflecting the usual practice in various epilepsy centers. A recent study(5) observed that the risk of seizure recurrence during drug tapering and after discontinuation of antiepileptic drug therapy in children with epilepsy is not different whether the medications are tapered over a six-week of nine-month period. In the study under discussion, the authors have demonstrated that a tapering period of even 4 to 6 weeks for children who have no risk factors predictive of seizure recurrence, is sufficient.

However, one should be cautious while considering early withdrawal of antiepileptic drugs in patients with clinical evidence of neurological abnormalities. Delgado *et al.(6)* in a similarly designed "antiepileptic drug withdrawal study" observed that epileptics among patients of cerebral palsy could also have long term seizure remission. However, they needed a

minimum of two years of seizure free period. In such patients of cerebral palsy spastic hemiparesis significantly increases the risk of relapse.

Symptomatic epilepsies are inherently difficult to treat and frequently seizures recur on attempted withdrawal of drugs. In India, single enhancing (ring/disc) CT lesions are the commonest cause of epilepsy in children and adolescents. In such cases seizures are easily controllable as CT lesions usually disappear in 12-20 weeks time. There is feeling from different Indian Neurological Centers(7,8) that a short term (6 months to 1 year) antiepileptic drug therapy is sufficient for long term remission of seizures. However, there is need to study the long term course of epilepsy in these patients before recommending short course of antiepileptic treatment.

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