REFERENCES


To the Editor:

Although there was no history of exposure to tocolytic agents in the case recently presented, Dr. Van Dyke calls attention to a subject little known in cardiopulmonary circles and, in the process, may stimulate the readers of CHEST to consider some interesting concepts both within and beyond the world of obstetrics.

One method to suppress uterine contractions associated with premature labor is through the use of tocolytic drugs, i.e., β-adrenergic agonists such as terbutaline, isofoxsuprine, ritodrine, and albuterol. These drugs apparently retard uterine contraction by increasing intracellular cyclic adenosine monophosphate, in the process decreasing the activity of myosin light-chain kinase, an agent which plays a role in promoting uterine contraction. As is well known, commonly encountered side effects of β-adrenergic drugs include tachycardia, hyperglycemia, hypokalemia, and antidiuresis. Although the mechanism is poorly understood, these drugs may induce pulmonary edema in pregnant women, even though this effect has not been observed with the treatment of asthma in the nonpregnant state. This pulmonary effect has been reported to occur in association with the short-term use of these drugs (average 54 h) in late pregnancy with an incidence of approximately 0 to 4.4%. It appears to represent a form of noncardiac pulmonary edema, possibly caused by drug-induced fluid retention superimposed on that normally occurring in the gravid state. This syndrome is unassociated with evidence of myocardial dysfunction and responds readily to diuretics and oxygen.

In contrast to the above mentioned syndrome of acute pulmonary edema, one group has postulated, through the retrospective analysis of a small number of cases of cardiomyopathy associated with late pregnancy, that the prolonged administration (4 to 11 weeks) of β-agonist drugs could actually induce a syndrome closely mimicking peripartum cardiomyopathy, featuring evidence of dilatation of one or both ventricles combined with various objective indices denoting reduced systolic function. Although the numbers were too small to be statistically valid, their report does warn us that this may be another situation in which prolonged use of sympathomimetics might produce or aggravate myocardial dysfunction, possibly through incessant tachycardia associated with down regulation of β-adrenergic receptors or through a direct toxic effect of these drugs. Consistent with this hypothesis is the reported occurrence of left-ventricular failure and myocarditis in association with catecholamine therapy for pulmonary disease. Moreover, a form of reversible cardiomyopathy may be induced by chronic tachycardia alone, providing another potential mechanism for catecholamines to create an adverse effect. It is possible that pregnancy might render the heart more susceptible to the toxic effects of catecholamines, creating a potentially reversible form of cardiomyopathy. In the study cited above, the four cases of cardiomyopathy associated with β-agonists showed complete recovery of cardiac function after these drugs were withdrawn. Although spontaneous recovery is not unusual in peripartum cardiomyopathy, this latter observation would tend to support the hypothesis, mentioned in our report, that, rather than a single disease entity, pregnancy related heart failure may be the end result of any one of a number of potential factors noxious to the myocardium. In a given case, reversibility of cardiac dysfunction might depend, at least partially, on which underlying factors were responsible. Increasing awareness of the possible general association between β-agonists and myocardial dysfunction might lead to further observations in patients receiving such drugs, whether or not they are pregnant. We hope that the information provided by this exchange might spark some thought and additional investigation into this matter.

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The Reduced Sensation of Dyspnea During Exercise by Inhaled Oxitropium Bromide in Severe COPD Patients

To the Editor:

We read, with great interest, the article by Ikeda and coworkers published in the December 1994 issue (CHEST 1994; 106:1740-45) concerning the effects of oxitropium bromide (OTB) on exercise capacity in severe COPD patients.

The authors showed that the OTB increased the exercise capacity in severe COPD patients. However, the improvement of exercise capacity was obviously small as previously reported. The exercise capacity can be expressed by several parameters including maximal work load, maximal minute ventilation (Ve), and maximal oxygen uptake (Vo2). Theoretically, there are linear relationships between these parameters. However, in the current study, the maximal work rate may not be an appropriate indicator of the exercise capacity. The coefficient of variation of the mean value of work rateVo2 is 3 to 4 fold greater than that of the ventilatory ratio (Ve/Vo2) (Table 1).

Another problem is that an increase rate of work load (20 W/min) is too hard to perform especially in patients with severe COPD. The placebo data suggest that the first exercise testing cannot be adapted to the patients. In our experience, the maximal VeO2 in patients with severe COPD (FEV1<0.8 L) could not reach the same level of first exercise testing in the second testing 90 min after the first exercise. Compared with the changes in Vo2 after placebo administration (about 54 mL/min), the absolute value of the venous blood was 800 mEq/L, the arterial blood was 300 mEq/L.