Enlargement of the salivary gland after ritodrine treatment in pregnant women

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Preterm labour continues to complicate a substantial number of pregnancies, and preterm delivery accounts for most early neonatal deaths not due to congenital abnormalities.¹ Ritodrine hydrochloride, a β sympathomimetic agent with predominant effects on β receptors such as those of the uterus,² is effective in suppressing premature uterine contractions.² We describe six pregnant women given ritodrine hydrochloride who developed swelling of the salivary glands with hypersecretion of amylase.

Patients and results

From May 1990 to October 1991 we treated 150 pregnant women with premature uterine contractions with ritodrine hydrochloride. The drug was administered intravenously in a solution containing 50 mg of ritodrine hydrochloride in 500 ml of 5% glucose. The solution was administered at a rate of 50 μ g/min, increased by 50 μ g/min every 20-30 minutes in response to continued uterine activity until tocolysis or toxicity occurred or a dose of 350 μ g/min was reached.

Of the 150 patients six developed symptoms of parotitis after the administration of ritodrine (table). Each of the women complained of swelling of the cheeks in the first 24 hours after treatment; some also had swelling of the submandibular area. These swellings were easily felt by palpation. Four patients (cases 1 to 4) had a low grade fever (37.2-38.0°C) which lasted for up to two days. The total dose used in these six patients varied from 184-2900 mg, given over 11 hours to 26 days. The swelling resolved within five days in all cases. Since the women were suspected of having parotitis their serum amylase concentration

was determined. An abnormally high serum amylase level (>215 U/l) was observed within the first 12 hours in all cases. The highest amylase concentration occurred at 12 to 36 hours in all but one patient (case 4). The raised amylase concentration was shown to be exclusively derived from the salivary glands by the analysis of isozyme pattern (table). Serological tests for mumps infection (enzyme linked immunosorbent assay kits provided by Behring, Germany, for measuring immunoglobulin G and M antibodies to mumps virus, and mumps microneutralisation assay conducted by SRL, Japan), performed in paired serum samples from five patients, ruled out mumps. Although follow up amylase concentrations were not determined in three patients, in the other three (cases 1, 5, and 6) they returned to normal within 14 days. All six women had healthy babies, and neither mothers nor children had any other abnormalities.

Comment

Six pregnant women developed symptoms of parotitis several hours after the administration of ritodrine hydrochloride. Serological tests performed in five of them excluded the possibility of mumps infection.

The clinical side effects of ritodrine reflect its β mimetic activity.² To our knowledge, however, β mimetics have not been reported to have an effect on the salivary gland in humans, though Selye observed that another β mimetic agent, isoprenaline, induced hypertrophy of the salivary gland in rats.³ Following this observation the relation between adrenergic agents and salivary gland function was investigated in rats since hypertrophy of the salivary gland and hypersecretion of amylase occur via the stimulation of β adrenoceptors.⁴ In vitro experiments showed that human salivary gland tissues also secrete amylase in response to isoprenaline.⁵ The hypersecretion of amylase and the swelling of the salivary glands in our six patients therefore probably resulted from the administration of ritodrine hydrochloride. Clinicians should be aware of this adverse effect of ritodrine, which might also occur in women receiving other β_2 agonists for the treatment of premature labour.

Clinical profiles of six pregnant women who developed enlarged salivary glands

Case No	Age (years)	Parity	Ritodrine treatment			Peak serum amylase (U/l) (salivary: pancreas isoenzymes)
			Gestational week of administration	Average rate during first 12 h (μ g/min)	Duration	
1	26	0	20	76	23 days	300 (7.5:2.5)
2	28	1	35	270	11 hours	510 (8.3:1.7)
3	31	1	34	167	53 hours	2572 (9.6:0.4)
4	28	0	12	83	8 days	1560 (8.6:1.4)
5	30	1	34	100	62 hours	4049 (9.6:0.4)
6	43	0	30	67	26 days	3143 (9.6:0.4)

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- 4 McPherson MA, Hales CN. Control of amylase biosynthesis and release in the parotid gland of the rat. *Biochem J* 1978;176:855-63.
- 5 McPherson MA, Dormer RL, Bradbury NA, Dodge JA, Goodchild MC. Defective β -adrenergic secretory responses in submandibular acinar cells from cystic fibrosis patients. *Lancet* 1986;ii:1007-8.

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Regular balloon inflation for patients with chronic bronchitis: a randomised controlled trial

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Patients with severe airways obstruction due to chronic bronchitis and emphysema are disabled by their symptoms, particularly breathlessness. Regular lung exercises can reduce the severity of their symptoms,¹⁻³ but these are expensive and demand resources from a

multidisciplinary team. We had observed that even patients with severe airways limitation could blow up ordinary rubber balloons so we investigated whether the simple exercise of regularly inflating a balloon could improve exercise tolerance and reduce the severity of breathlessness experienced by such patients.

Patients, methods, and results

The study was approved by the local medical ethics committee. Twenty eight patients were randomly recruited (by random numbers sampling from full clinic list) from an outpatient respiratory clinic over six months with the following inclusion criteria: (a) spirometrically proved airways obstruction (a ratio of forced expiratory volume in one second (FEV₁) to