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Titrated prostaglandin E₂ tablets for induction of labour

We report here a study on the use of orally administered prostaglandin E₂ to induce labour in 100 women (41 primiparae and 59 multiparae).

Patients, methods, and results

All the patients were at 38 to 41 weeks' gestation and had a recognised indication for induction. Their inducibility rating was assessed by Bishop's method¹, 28 patients (13 multiparae and 15 primiparae) having a score below 6 and the remaining 72 patients (46 multiparae and 26 primiparae) having a score of 6-11. Patients who had had previous spontaneous onset of labour or rupture of membranes and patients of parity 5 or more were excluded from the trial.

Starting with a minimum dose of one tablet (0.5 mg), the tablets (prostin E₂) were given 30 minutes after low amniotomy was performed and then at every hour, vaginal assessment being made every four hours. If the cervix was dilating and the uterus contracting satisfactorily on examination the original dose was continued. If not the dose was increased by one tablet (0.5 mg) up to a maximum of three tablets (1.5 mg) for a maximum of 12 hours, after which the treatment was changed to intravenous oxytocin. Doses were changed only after the four-hourly vaginal and abdominal examination. Intrauterine monitoring, using the Sonicaid FM2 with an intrauterine catheter, was undertaken on all patients receiving the maximum dose of 1.5 mg.

Labour was successfully induced and vaginal delivery achieved in 94 patients, including 13 who required forceps delivery. The mean amniotomy-delivery interval in multiparous patients was 6 h 56 min and in the primiparous patients 8 h 51 min. The doses used in each group are shown in the table.

Dose required to induce labour in 94 women in whom induction was successful

Maximum dose:	1.5 mg	1.0 mg	0.5 mg	Mean total dose
Multiparous (n = 57) ..	6	28	23	4.9
Primiparous (n = 37) ..	10	16	11	6.3

Six patients were excluded from the study, one because of persistent vomiting after the first dose of 1.5 mg prostaglandin E₂. Two patients were delivered by caesarean section because of fetal distress (2 h 15 min and 8 h 10 min after amniotomy). Three primiparous patients did not progress satisfactorily after 12 hours of prostaglandin treatment: two required caesarean section, one after 8 and the other after 12 hours of oxytocin infusion, and the third had only achieved 3 cm dilatation after 12 hours but had a normal vaginal delivery after oxytocin infusion for a further 9 h 40 min. No serious maternal side effects could be attributed to oral prostaglandin. There was no uterine hypertonus or significant alteration in maternal blood pressure or heart rate. Eight patients developed mild fever, which subsided without treatment. Vomiting occurred in 18 patients and one patient developed diarrhoea. The fetal heart rate was not affected in the 94 successful cases, and the mean Apgar score after one minute was 8.6. Third stage complications included four retained placentae and five cases of post-partum haemorrhage of more than 500 ml.

Discussion

The use of prostaglandin E₂ tablets is a further refinement of oral administration, which overcomes the bitter taste of the solution¹

and the occasional nausea and vomiting it produces.² Oral administration also has advantages over intravenous infusions in ease of administration, convenience for medical and nursing staff, and increased acceptability to the patient.³ The absence of overstimulation and adverse effects on fetomaternal wellbeing was noteworthy.

The incidence of maternal gastrointestinal side effects appears to be related to dose, as suggested by Craft,⁴ who found an incidence of side effects 36% in women using oral prostaglandin E₂ solution. The low incidence of vomiting and diarrhoea in our series (19%) may therefore have been due to the low titrated dose administered or the use of prostaglandin E₂ tablets rather than solution.

The short induction-delivery interval, especially in multigravidae, together with the safety of prostaglandin E₂ tablets, the ease of administration, and acceptability to the patient with such a titrated dose commend this method of induction for routine clinical use in suitable patients.

We thank the patients who participated in this study, the consultant staff of St Mary's Hospital for permission to use their patients, the midwifery staff for their enthusiastic help, and the Upjohn Company for the supply of prostaglandin E₂ tablets.

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Heerfordt's syndrome in two sisters

Two middle-aged sisters, living separately, developed sarcoidosis with bilateral uveoparotitis and cranial palsies within six months of each other.

Case reports

A previously healthy 41-year-old housewife developed bilateral anterior uveitis in June 1972; there was no lacrimal gland enlargement or xerophthalmia. In August the parotid and submandibular glands were bilaterally enlarged and painful. There was no palpable lymphadenopathy or hepatosplenomegaly. Investigations showed Hb 12.9 g/dl; WBC $7.4 \times 10^9/l$; ESR 4 mm h; protein electrophoresis normal; serum calcium 2.4 mmol/l (9.6 mg/100 ml); urinary calcium 8.75 mmol (350 mg)/24 h; Mantoux test negative at 1/1000 and 1/100 dilutions; diffusing capacity (DCO) marginally reduced at $5.7 \text{ mmol min}^{-1} \text{ kPa}^{-1}$; chest radiographs and ECG within normal limits; Kveim test gave positive sarcoid histology. While being investigated the patient developed a left facial palsy. She was admitted to hospital and started on systemic corticosteroids. Her urinary calcium fell to 4.75 mmol/24 h, and she was discharged. By November 1972 chest radiographs showed bilateral hilar adenopathy. Reduction of the steroid dose resulted in a flare-up of the anterior uveitis and the development of peripheral lung mottling. She remained well on prednisolone 10 mg daily.

A previously healthy 35-year-old housewife, younger sister of the above patient, developed erythema nodosum in December 1972. Two months later her parotid and submandibular glands were bilaterally enlarged and painful, her mouth was dry, and her eyes felt gritty. She had enlarged lymph nodes in the right supraclavicular fossa and right epitrochlear region, bilateral anterior uveitis, and bilateral lacrimal gland enlargement with complete absence of tears. Investigations showed Hb 12 g/dl; WBC $4.3 \times 10^9/l$; ESR 10 mm h; protein electrophoresis normal; serum calcium 1.9 mmol/l (7.6 mg/100 ml); urinary calcium 3.25 mmol (130 mg)/24 h; pulmonary function, ECG, and chest radiographs within normal limits. Biopsy of a supraclavicular node and parotid gland showed sarcoid tubercles and a Kveim test was positive.

In March 1973 she developed a complete bilateral facial nerve palsy. She was started on systemic corticosteroids. By the end of June her facial weakness had fully recovered and tear production was normal but she had bilateral

choroidal lesions with blurred vision in the right eye due to macular oedema. This gradually improved, though visual acuity remained somewhat reduced due to chronic posterior uveitis. In August 1974 chest radiographs showed peripheral lung mottling and her maintenance dose of corticosteroid was increased to 10 mg daily.

Discussion

Heerfordt's syndrome is an unusual manifestation of sarcoidosis consisting of parotitis with chronic or subacute uveitis and often complicated by cranial nerve pareses, usually of the facial nerve. Originally described in 1909,¹ it was not recognised as a manifestation of sarcoidosis until 1937. The complete picture is rare. Scadding² had no cases of the complete syndrome in his series, and Greenberg *et al.*,³ reviewing 388 cases of sarcoidosis, reported only 8 with uveo-parotitis and only one with a facial palsy. Familial association in sarcoidosis is well recognised.⁴ In 13 instances of sarcoidosis affecting identical twins the manifestations of the disease in each twin pair tended to be similar.⁵ This seems to be true of less closely related subjects. Interestingly, both our cases presented almost simultaneously with a most uncommon form of sarcoidosis and followed very similar courses.

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Tear fluid lysozyme concentration: guide to practolol toxicity

By the end of 1974 the Committee on Safety of Medicines had reported 187 cases of diminished tear secretion and conjunctivitis or corneal damage associated with long-term practolol therapy.¹ Wright, reporting toxic effects of practolol, stated that several out of 27 patients had low levels of tear lysozyme.² We report here the tear fluid lysozyme concentrations in 30 patients who had been taking practolol over a long period.

Patients, methods, and results

Of the 30 patients examined four had taken practolol for 6 months, the remaining 26 had taken it for at least a year. Ten showed signs of ocular toxicity and 20 showed no signs. Eight of the 10 toxic patients had been off practolol for periods varying from 1 to 12 weeks (average 6.4 weeks). We assayed the lysozyme concentration in the tear fluid of both eyes of all the patients by our quantitative method with calibrated standards,³ the measurements being in units of activity/ μ l.

All the 10 toxic patients had tear lysozyme concentrations below normal in one or both eyes (see table). In one patient (case 2) lysozyme was absent. In 3 of the 10 patients (cases 1, 3, 7) the concentration in one eye was about three times that of the other, and in one patient (case 4) it was 9 times. These differences are outside normal limits of variation between the two eyes.³

Of the 20 patients with no signs of toxicity 15 had normal tear lysozyme concentrations (see table). One (case 19) had low concentrations in both eyes. Three (cases 11, 14, 26) had low concentrations in one eye, but the differences in concentrations between the two eyes were within normal limits. In one patient (case 17) the initial concentrations were 201 U/ μ l right and 57 U/ μ l left. A month later they were 16 U/ μ l and 25 U/ μ l respectively—a striking fall. A month after that (in January) the patient developed signs of toxicity and practolol was stopped. In May the concentrations had risen to 40 U/ μ l and 45 U/ μ l, and in July to 120 U/ μ l and 60 U/ μ l.

We also examined two patients with sclerosing peritonitis due to practolol but with no signs of ocular toxicity. Both had abnormally low levels of tear lysozyme (45 U/ μ l and 55 U/ μ l, and 30 U/ μ l and 36 U/ μ l respectively). One, in whom lysozyme levels fell further, later developed signs of ocular toxicity.

Lysozyme concentrations in tear fluid in 30 patients on long-term practolol treatment

Case No	Age	Sex	Lysozyme concentrations (U/ μ l)		
			Right eye	Left eye	Lowest normal for age
<i>Toxic patients</i>					
1	47	F	{45* 63†	{18* 21†	59
2	52	F	—	—	56
3	54	M	81	33	55
4	57	F	54	6	54
5	58	F	12	9	54
6	62	F	12	24	51
7	64	M	78	24	50
8	67	F	33	10	49
9	68	M	{48† 21‡	{42† 27‡	48
10	75	F	15	6	45
<i>Non-toxic patients</i>					
11	16	M	91	57	72
12	41	F	93	75	61
13	43	M	68	98	60
14	48	F	57	48	58
15	48	M	114	153	58
16	48	F	66	57	58
17	50	F	201	57	56
18	52	M	243	177	56
19	56	F	42	45	54
20	57	F	70	65	54
21	59	F	116	118	53
22	61	F	123	96	52
23	63	F	57	62	51
24	65	M	108	213	50
25	66	F	87	60	49
26	72	M	39	63	46
27	74	F	93	141	45
28	75	F	102	108	45
29	77	F	234	168	43
30	79	M	99	51	42

*Three weeks after practolol stopped.

†Seven weeks after practolol stopped.

‡One week after practolol stopped.

§Seven weeks after practolol stopped.

Comment

The tear lysozyme concentration could be useful as a screening test for toxicity in patients taking practolol, since the level may fall before signs of ocular toxicity appear. We are continuing this work.

We thank Mr P Wright for his advice and help, Dr D G Fleck for his continued support, and Mr J D Pescod for his technical help.

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Guillain-Barré syndrome in acute HBs Ag-positive hepatitis

In acute viral hepatitis (AVH) several neurological complications have been described. The central¹ and the peripheral² nervous systems may be affected, but the Guillain-Barré syndrome (GBS), characterised by progressive symmetrical pareses, sensory loss, and a raised spinal fluid protein level with normal cell count, is extremely rare in the course of AVH.³ We report here on a patient who developed hepatitis B and GBS and in whom we were able to define accurately the relation between the onset of hepatitis B and the onset of GBS.

Case report

The patient was a 21-year-old nurse seronegative for hepatitis B surface antigen (HBsAg) in a haemodialysis unit with HBsAg (subtype adw)-positive patients. The clinical course of her disease is summarised in the figure. On