

ISOXSUPRINE IN PREMATURE LABOUR

by

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Abortions and premature labours, directly or indirectly, account for colossal wastage of human lives every year. Prematurity resulting from premature labour is responsible for 50 to 60 per cent of all neonatal deaths (McNeil, 1942). In a large number of premature births, 50% (Joint Committee of Royal College of Obstetricians and Gynaecologists and the British Paediatric Association, 1949) to 60% (Eastman, 1950),—the underlying causes are unknown and, therefore, the treatment is unsatisfactory. As a matter of fact, in most of the cases of premature onset of labour, the clinicians are mere helpless passive onlookers and can do little to arrest the process of labour except prescribe rest, sedatives, analgesics or antispasmodics. None of the drugs at our disposal today is effective in suppressing or postponing premature labour. Morphine is perhaps most commonly used. But in safe doses, it has little effect on the amplitude of the uterine contractions, although the intervals between contractions may be prolonged (Bickers, 1942; Bourne and Burn, 1930). One or two initial doses of morphine may rather help in improving the quality of labour pains instead of inhibiting them. So is the

case with pethidine. The need for a drug which could safely and effectively postpone premature labour, allowing valuable time for the foetus to attain reasonable maturity, has long been felt by the obstetricians. However, in recent years, several authors (Bishop and Woutersz, 1961; Whitelaw *et al*, 1961; Hendricks *et al*, 1961; Prakash and Mehrotra, 1966) have reported encouraging results from the use of Isoxsuprine.

Isoxsuprine hydrochloride (duvadilan—Duphar, Crookes Interfran, Limited) is a derivative of phenethanolamine group of drugs and is related to epinephrine. The benzyl ring in its side chain is connected with the alkyl group by means of an oxygen atom. There are two chains on both sides of the nitrogen atom.

Besides its vasodilant, neurotropic (beta—mimetic and alpha—lytic) and smooth muscles relaxant actions, isoxsuprine has a highly selective and strongly musculotropic (papavarine like) and spasmolytic effect on the uterine musculature. According to the recent reports (*vide supra*), it is effective in suppressing or postponing premature labour in 40 to 80 per cent of the cases. It was, therefore, considered worthwhile to undertake a clinical trial of the drug. Our experience with isoxsuprine in premature labour is reported here.

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Material and methods

Twenty-five pregnant women who were in labour between 28th and 37th weeks of pregnancy were selected at random for study. In addition to the usual conservative measures, each patient was given initially 30 mg. of isoxsuprine in 500 ml of 5 per cent dextrose solution by intravenous drip. The rate of flow was about 20 to 30 drops per minute, but was adjusted according to the response of the uterus, its effects on pulse rate, blood pressure and foetal heart beats. The dose was, however, never allowed to exceed 0.5 mg. per minute. This was followed by 20 to 30 mg. of isox-

A control group of 25 cases of premature labour were subjected to the same study, but treated with only rest, sedatives, analgesics and anti-spasmodics. Cases with premature rupture of membranes received an antibiotic in addition.

Observations

The patients under study in the treated and the control groups were comparable so far as their age and parity status were concerned. There was also no significant difference in the incidence of complications of pregnancy amongst the women of the two groups. (Table I).

TABLE I
Showing the complications of pregnancy

	Pre-eclampsia	Ante-partum haemorrhage	Anaemia	Twin pregnancy	Malpresentation	Fibromyoma of uterus
No. of cases						
A. Treated	7	2	14	2	3	1
B. Control group	8	2	15	2	2	—

suprine administered daily in divided doses by intramuscular injections or orally. Six cases had no intravenous drips and three received only oral tablets of isoxsuprine. The treatment was continued till the patient went to term or delivered. All the patients were kept under close observation and the effects of the drug on the uterine activity, pulse rate, blood pressure, foetal heart beats, etc. were carefully recorded. All the cases were followed up through pregnancy, labour and puerperium, and the time and mode of delivery, complications, if any, and condition of the new-born babies were noted.

Pre-eclampsia, anaemia and malnutrition were quite common in both the groups, but none had any evidence of essential hypertension, chronic nephritis, diabetes mellitus, syphilis, Rh iso-immunisation or cervical incompetency. Five patients in the control group and four in the treated group gave a history of previous premature labours. Table II shows the condition of the cervix and membranes at the beginning of the treatment, and Tables III and IV show the results of treatment with isoxsuprine as compared with that in the control group.

It will be noticed that in the treated

TABLE II
Showing the condition of cervix and membranes at the beginning of treatment

	Condition of cervix			Condition of membranes	
	Closed	1 finger	2 fingers	Intact	Ruptured
No. of cases					
A. Treated group	3	16	6	21	4
B. Control group	2	15	8	22	3

TABLE III
Showing the period for which labour could be postponed

	Less than 24 hrs.	1 to 3 days	4 to 7 days	8 to 14 days	15 to 21 days	22 to 28 days	5 to 8 wks.	9 to 12 wks.
No. of patients								
A. Treated group	2	2	3	5	6	1	2	4
B. Control group	19	3	3	—	—	—	—	—

TABLE IV
Showing foetal survival rate

	Mature and alive	Premature and alive	Mature and dead	Premature and dead	Total survival
No. of babies					
A. Treated group	11	10	1	3	21
B. Control group	—	15	—	10	15

group, the labour could be postponed by one week to twelve weeks in 18 of 25 women (72%), and 21 out of 25 babies (84%) could be salvaged. In the control group, 19 of 25 women (76%) delivered within 24 hours, and only in 6 patients (24%) labour could be postponed by 1 to 7 days; and 10 out of 25 babies (40%) were lost. No increase in the incidence of complications of labour, e.g. uterine inertia, postpartum haemorrhage, etc. was observed.

Five women of the treated group complained of giddiness, nausea,

weakness and palpitation and had tachycardia and a moderate fall in blood pressure, but only in one the side-effects were severe enough to require discontinuation of the drug. This patient had a fainting attack with quick feeble pulse and her systolic blood pressure fell to 70 mm. of Hg. and diastolic pressure to 30 mm. of Hg. within 15 minutes of starting the intravenous drip of isoxsuprine. She, however, recovered promptly on stopping the drip and could continue the drug orally. No ill effects could be observed on the foetus or the newborn baby.

Discussion

Although the birth weight and the period of gestation are not always correlated, a baby born before the 37th week of pregnancy is usually premature or immature and has less chance of survival. Despite the modern advances in paediatrics, prematurity still remains the most important single factor in perinatal or neonatal deaths. Crosse (1949) also observed that 43 per cent of 2,189 stillbirths and 58 per cent of 1,907 neo-natal deaths were amongst premature babies. The incidence of prematurity varies from 6.9 per cent (Crosse, 1949) to 9.9 per cent (Baird 1942) of all births. In our country, the incidence is still higher. Unfortunately, premature onset of labour which is due to a wide range of underlying causes—maternal, foetal, placental and idiopathic—cannot always be prevented, even by a high standard of antenatal care. Hence, any drug which claims to be useful in postponing premature labour and thus gives the foetus valuable time for maturity should receive due importance. This clinical study supports the view held by some authors that isoxsuprine hydrochloride is a valuable drug in the treatment of premature onset of labour. It was found effective in postponing premature labours by one to 12 weeks in 72 per cent of cases, and 84 per cent of the babies could be saved in the treated group, whereas in the control group of patients, all but six women (76%) delivered within 24 hours, and in none could the labour be postponed for more than 7 days, and only 15 babies could be salvaged. Our results compare well with those of

Whitelaw *et al* (1961) who reported a success rate of 73 per cent amongst 22 cases of premature labour treated with isoxsuprine. Suzuki, *et al* (1960) used isoxsuprine in premature labour and obtained a higher success rate of 82 per cent amongst 11 cases, and Prakash and Mehrotra (1966) were successful in postponing labour in 80 per cent of 25 cases of premature labour treated with isoxsuprine. On the other hand, Bishop and Woutersz (1961) were able to postpone labour with isoxsuprine only in 40 per cent of 120 cases of premature labour. For correct assessment of results, it should be ensured that no case with false pains is included in the series. Where premature labour is anticipated, as in women with multiple pregnancy, hydramnios, toxaeemias of pregnancy, habitual premature labours, or with surgical interventions during pregnancy, prophylactic use of isoxsuprine is likely to be helpful. It is interesting and gratifying to note that the two unfortunate mothers, who had lost all their children (five and six in number) due to premature labour and prematurity, could get healthy live babies this time after treatment with isoxsuprine. A young primigravida with twin pregnancy had rupture of the membranes at 30th week and came to the hospital with labour pains. With isoxsuprine, her labour could be postponed for 16 days and both the babies could be saved. Another patient, an elderly primigravida, had multiple fibromyomas of the uterus which were mistaken for ovarian tumours and a laparotomy was performed at 28th week of pregnancy. She started

labour pains on the second post-operative day, but the labour could be suppressed with isoxsuprine, and a healthy, mature male baby was delivered at term by caesarean section. As an effective vasodilator, isoxsuprine is expected to be of particular value in pre-eclampsia and eclampsia. Apart from preventing a premature onset of labour, it may lower the blood pressure and prevent placental, uterine and renal ischaemia and cerebral anoxia by improving the circulation through these organs. We intend to undertake soon a large scale clinical trial of isoxsuprine in toxaeemias of pregnancy.

Side-effects are rare and not of serious nature, but occasionally the patient may suffer from syncope with marked fall of blood pressure soon after an intravenous or intramuscular injection or isoxsuprine.

Summary

1. Twenty-five cases of premature onset of labour were treated with isoxsuprine hydrochloride, and the results were compared with those of a control group of 25 similar cases treated with the usual rest, sedatives and antispasmodics.

2. Isoxsuprine hydrochloride was found to be effective in postponing premature labour by one week to 12 weeks in 72 per cent of the women in the treated group; whereas, all but six women of the control group delivered within 24 hours, and in none could the labour be postponed for more than 7 days.

3. Foetal salvage rate in the treated group was 84 per cent against 60 per cent in the control group.

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