# A CLINICAL EVALUATION OF ISOXSUPRINE (DUVADILAN) IN PREMATURE LABOUR

by

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Premature birth is by far the most common cause of neonatal mortality. Prematurity resulting from premature labour is responsible for 50 to 60 per cent of all neonatal deaths (McNeil, 1942). The usual conservative line of treatment consisting of bed rest, sedation, analgesics and hormones may have some beneficial effect in a few cases but is not effective in postponing the premature labour and so a drug which can postpone labour to any extent is of great clinical value. Recently, some encouraging reports have appeared in the literature regarding the use of duvadilan in premature labour (Bishop and Wautersz, 1961; Whitelaw *et al* 1961; Prakash and Mehrotra, 1966, and Das (1969).

Isoxsuprine is related to naturally occurring substance epinephrine and is marketed by M/s. Crookes Laboratories Ltd. as duvadilan. It is a vasodilator and has got a marked relaxant action on smooth muscles. It has been found to reduce the frequency and also the intensity of uterine contractions. This effect is produced chiefly by the inhibition of beta-adrenergic receptors which are abundant in the uterine muscles.

*Material and Methods*

In the present study 50 cases of premature labour, between 26th to 37th weeks of gestation, were selected. Cases of premature labour with ruptured membranes, or having evidence of essential hypertension, chronic nephritis, diabetes mellitus, severe anaemia (haemoglobin percentage below 5 gm%), cardiac diseases, syphilis, Rh isoimmunisation and cervical incompetency were excluded from the present study.

In addition to the usual conservative line of treatment, in all cases initially intravenous infusions were given. To 500 ml. of physiological saline or 5% dextrose solution 30-60 mgm. of duvadilan was added, the drip running so that duvadilan did not exceed 0.5 mg/minute (approximately initially at 30-50 drops/minute going up to 50-80 drops/minute).

A close watch was kept on blood pressure, pulse rate, uterine contractions and foetal heart sounds, any variation in these being controlled by the rate of the drip. Naturally then depending on the effect on the uterine contractions and blood pressure the dose rate varied and it was possible to give a total of 30 to 60 mgm of duvadilan. The intravenous infusion was given till the uterine contractions were arrested. Thereafter the treatment was carried on with intramuscular injections, 1 ampoule (10 mg.) of duvadilan being given at 4-6 hours interval according to the progress shown; 24-48 hours treatment with intramuscular injections was quite sufficient to switch on to oral therapy, 1 tablet (10 mg.) given 3 times a day and was continued for 10 to 15 days, the whole dosage being varied a little ac-

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cording to the response shown by the patient. In view of the fact that intravenous isoxsuprine may occasionally produce sudden fall of blood pressure, measures to counteract shock, mephentermine sulfate, veritol, dexamethasone sodium phosphate and norepinephrine injections, were kept at the bed side of the patient.

A control group of 30 cases was subjected to a similar study and were treated with only rest, sedatives, analgesics etc.

*Observations*

The cases in the study group and control group were of almost identical ages and there was no significant difference in the incidence of various complications in the two groups as it would be apparent from Table I.

Previous history of premature labour was present in 11 cases of the study group and 6 cases in the control group.

In all the cases uterine contractions were felt. The condition of the cervix was noted in both the control and study group at the time of starting the treatment. In the control group (30 cases) os was closed in 6 cases, dilated 1 finger in 19 cases and 2 fingers in 5 cases. In the study group (50 cases) os was closed in 9 cases, dilated 1 finger in 34 cases and 2 fingers in 7 cases.

The results of therapy are given in Table II.

It was observed that the labour was postponed in most of the cases with isoxsuprine. In the study group labour was postponed by one week to 12 weeks in 38 (76%) out of 50 cases and in over 50% of the cases the labour was postponed by 3 weeks to 12 weeks. In the control group, 22 (73.3%) out of 30 cases delivered within 24 hours. Only in 6 cases (20%) labour could be postponed by one to seven days and in only 2 cases (6.7%) it was postponed by 1 to 3 weeks. In the study group 41 (82%) out of 50 babies could be salvaged, while in the control group only 17 (56.7%) out of 30 babies could be saved. All the cases in both the groups

TABLE I

*Showing the Complications of Pregnancy*

| No. of cases | Anaemia | Antepartum haemorrhage | Twins | Toxaemia | Cases without any apparent complication |
|---|---|---|---|---|---|
| A. Study group (50) | 20 | 8 | 4 | 6 | 12 |
| B. Control group (30) | 14 | 5 | 3 | 4 | 4 |

*Showing the Effects of Isoxsuprine on the Prolongation of Labour*

TABLE II

| No. of patients | Less than 24 hours | 1-7 days | 8-21 days | 22-35 days | 36-49 days | 50-63 days | 64-84 days |
|---|---|---|---|---|---|---|---|
| A. Study group (50) | 6 | 10 | 7 | 9 | 8 | 6 | 4 |
| B. Control group (30) | 22 | 6 | 2 | — | — | — | — |

were followed up through the pregnancy, labour and peurperium.

Out of the 50 cases, 4 cases who were initially relieved by the treatment had to be admitted repeatedly twice or thrice at 7 to 10 days interval for recurrence of the symptoms and every time the above regime was repeated with regression of symptoms till full-term babies were delivered.

One of the cases, a 2nd para, had a contracted pelvis and she had a pervious delivery by lower segment caesarean section. She went to term and delivered a full-term baby by lower segment caesarean section.

*Discussion*

In spite of the recent advances in the care of premature infants, prematurity continues to be the most important cause of neo-natal deaths. Therefore, however little the postponement of labour is important as the infant remains for a longer period in the ideal environment in the uterus, thus increasing its chance of survival.

In the present series labour was postponed by one week to 12 weeks in 76% of cases and in over 50% of the cases it was postponed by 3 weeks to 12 weeks under the effect of isoxsuprine. Bishop and Woutersz (1961) demonstrated the inhibitory effect of isoxsuprine on contractility of human uterus. They treated 120 patients of premature labour in 16th to 36th week of pregnancy. Premature uterine contractions ceased completely in 48 of their cases and resulted in full-term deliveries, while in 72 cases labour could be postponed for more than 24 hours. Whitelaw *et al* (1961) studied 22 cases of premature labour in which duvadilan therapy was given. They were able to obtain a full-term child in 50% cases and to postpone labour in 5 patients upto 96 hours. In 6 patients the treatment failed. Hendricks *et al* (1961) treated 13 patients who were between 20th and 34th weeks of pregnancy; in 4 of these cases membranes were already ruptured. In the latter four, treated with duvadilan, labour set in a few hours after infusion. In 3 others there was not any significant prolongation but in the remaning 6 cases it was sufficient to obtain a viable child. Prakash and Mehrotra (1966) tried isoxsuprine in 25 cases of premature labour. In 80% of cases there was complete subsidence of pain and os started reforming. Das (1969) reported that with isoxsuprine therapy, labour could be postponed by one to twelve weeks in 18 (72%) out of 25 cases of premature labour and 21 (84%) out of 25 babies could be salvaged. Our results are comparable with those of Prakash and Mehrotra and Das. In view of its inhibitory effect on the pregnant uterus, isoxsuprine may be helpful as a prophylactic measure in cases of habitual abortions.

*Side Effects*

Nausea and vomiting were seen in 8 cases (16%), palpitation and giddiness in 10 cases (20%), slight fall of blood pressure in 10 cases, and tachycardia in 9 cases (18%). In 4 cases there was severe giddiness and marked fall of blood pressure. The drug had to be discontinued in these cases and later on they were switched on to oral therapy. No ill effects were observed on the foetus or newly born babies in any case.

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