PREVENTION OF PREMATURE LABOUR BY INTRAVENOUS ETHANOL†

by

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Alcohol has been used in obstetrics as an analgesic agent for many centuries. But, it was lately realised by Chapman and Williams (Quoted by Patel, 1969) that if given early in labour, Ethanol stops the uterine contractions. Fuchs F. *et al* (1965), and Fuchs A-R (1963-67-68) tried Ethanol in last decade in the patients in premature labour and found it to be quite effective in stopping the uterine contractions.

Material and Methods

The study was carried out in the Sassoon General Hospitals, Poona. A group of thirty patients between the twentieth and thirtysixth weeks of pregnancy, coming to the labour ward in premature labour was selected. The criteria applied for the selection of patients were as follows:

1. Labour beginning before thirtysixth week of pregnancy.
2. Membranes must be intact.
3. The cervix should not be more than 5 cms. dilated.
4. There should be no obvious cause for the onset of premature labour; e.g. antepartum haemorrhage, intrauterine death, etc.
5. There should be no maternal cardiac or liver disease (as these are the contraindications to the administration of Ethanol).
6. Regular uterine contractions must be occurring over a period of atleast thirty minutes.

These thirty patients were divided into two groups:

Group A: The twenty-five patients forming this group were admitted because of spontaneous onset of premature labour.

Group B: This group of five patients contains the patients who went in premature labour following some pelvic surgery. Four of them had undergone cervical tightening by the McDonald's technique while the fifth one was operated for a twisted ovarian cyst.

For control study, another group of thirty patients who came to labour room in premature labour was studied. Every control case was selected by the same criteria applied for the study group cases and was taken alternating with the cases selected for Ethanol infusion. Control cases were treated with intramuscular injection of 10 mgms. of Siquil, immediately after the diagnosis of premature labour.

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Technique and Dosage

Uterine activity was monitored by external tocography (Metrimplex Tocograph—Lorand system) in sixteen cases and by external palpation in fourteen cases.

In addition to the uterine activity, presence of show and cervical dilatation were looked for the diagnosis of premature labour.

Before starting intravenous infusion of Ethanol, every patient was given intramuscular injection of 10 mgms. of Siquil for prevention of vomitting.

The dose of Ethanol was calculated according to the weight of the patient by the following formula:

$$DE = 1.5 \times Wt.$$

where DE represents the dose of Ethanol (Absolute Alcohol) in milliliters and Wt. stands for the weight of the patient in Kilogrammes. This much calculated amount of Ethanol was dissolved in 5% Dextrose solution to make 10% solution of Ethanol. This solution was given to the patient through an intravenous drip in about one hour as the loading dose. For maintaining the blood levels of Ethanol, 1/10th of the loading dose was given every subsequent hour. The maintenance doses were continued till the uterine contractions stopped and for one hour thereafter. If inspite of Ethanol the labour continued to progress as evident by the tocographic tracings, and/or clinical examination, then Ethanol infusion was continued till the cervix became $\frac{3}{4}$th dilated, and then it was discontinued.

No special treatment was given to the patients in the post infusion period except for the twenty-four hours' rest in bed.

Observations and Results

The observations and results of Groups A and B were noted separately as well as together. They were analysed by the following parameters:

1. Successful: If the labour could be arrested and postponed for at least three days.
2. Equivocal: If the labour could be arrested but recurred within forty-eight hours or the pregnancy had to be terminated within this time for various maternal indications.
3. Failure: Where labour could be arrested or if the arrested labour recurred and delivery took place within twenty-four hours.

Table I shows the results of Ethanol infusion in both groups—A and B—sepa-

TABLE I
Results of Ethanol Infusion

Group	No. of cases	Successful	Equivocal	Failure
A	25	15	4	6
	100%	60%	16%	24%
B	5	5	—	—
	100%	100%	—	—
A+B	30	20	4	6
	100%	66.66%	13.33%	20%

rately and combined. It shows 60% success in group A and 100% success in group B. The combined success is 66.66%.

Table II shows the causes of unsuccessful results (equivocal + failure) analysed. It reveals that of the ten unsuccessful cases, eight were unsuccessful due to wrong selection of cases. Thus if those cases are omitted, the corrected figures read as 88% success in group A while 91% success in whole study group.

TABLE II

Causes of Unsuccessful Results

Causes	Equivocal	Failure
Undiagnosed I.U.D.	-	2
Undiagnosed Ruptured Membranes	-	1
Taken up Cervix	1	3
Chorioamnionitis	1*	-
No Cause Detected	2	-
Total	4	6

* Infection occurring after the Ethanol Infusion.

The graph shown in Fig. 1 shows the paritywise analysis of successful cases. The only striking feature in it is that the success rate in primigravid patients is nil (vide infra). Otherwise, parity does not seem to play any part in the prevention of premature labour by Ethanol.

TABLE III

Perinatal Mortality

Group	No. of Babies	Survival	Deaths
A + B	30	24	6
	100%	80%	20%
Control	30	15	15
	100%	50%	50%

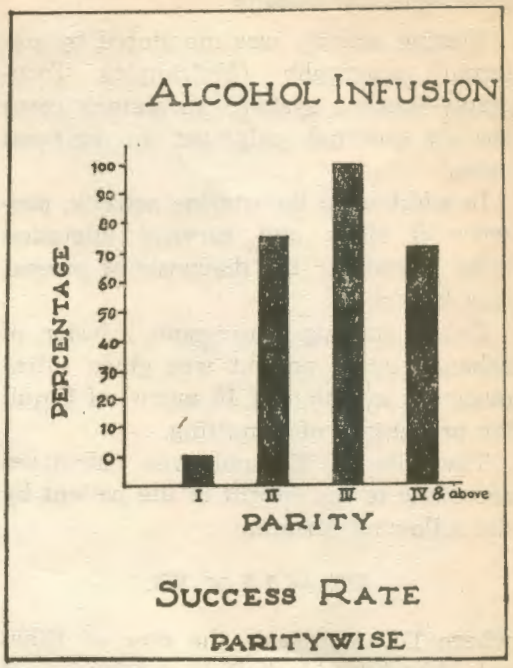

Fig. 1
Success rate parity wise.

Perinatal Mortality

Table III shows that due to Ethanol infusion for postponing the premature labour, the perinatal mortality, which is 50% in control group is reduced to only 20%.

Discussion

1. *Mode of Action of Ethanol:*

(i) On Posterior Pituitary: Fuchs *et al* and many others believe that Ethanol arrests the labour by suppressing the posterior pituitary secretions—antidiuretic hormone and oxytocin. The fact that Ethanol suppresses labour and also in lactating rabbits the lactation, proves its mode of action through oxytocin suppression.

(ii) On Myometrium: Initially it was thought that Ethanol acts directly on the

myometrium and makes it relax. But E. M. Countinho (1968), Wilson *et al* (1969) and Bueno-Montano (1966); all have come to the conclusion after their experiments on myometrial strips, that in therapeutic dosages, Ethanol acts on uterine activity not by its direct action on myometrium but by some other means, because the concentration of Ethanol required in the muscle bath (12.8 mgm.%) was eight times that of the concentration after therapeutic dose (1.6 (mgm.%).

(iii) As Calcium Antagonist: Hervitz, von Hegan and Joines (1967) think that Ethanol in higher concentrations is an indirect calcium antagonist at the level of cell membrane.

(iv) Osmotic Effect: According to Wilson and Fuchs, the transient action of Ethanol in low concentrations is due to its osmotic effect, as increased extracellular osmolarity has been shown to cause inhibition of contractile activity in vascular smooth muscle.

(v) On Membrane Dynamics: Bueno-Montano *et al* in 1966 stated that this action of Ethanol is by shortening of action potential and depolarization of membrane, thus ultimately by disturbing the membrane dynamics.

(vi) Foetal Role: According to Horiguchi *et al* (1971), Ethanol may reduce the foetal needs when the relation between foetal metabolic requirements and the supply via placenta is adversely affected. Thus the necessity for the foetus to escape the unfavourable environment may be abolished and the foetal mechanism for initiation of the labour may not be triggered.

(vii) Antagonism of Oxytocin: In humans, in therapeutic dosages, Ethanol acts, according to Mantell and Liggins (1970), not only by inhibition of oxytocin release but also by the non-competitive antagonism of oxytcin.

Of the various modes of action of Ethanol mentioned above, the one suggested by Fuchs *et al*, that Ethanol in therapeutic doses suppresses oxytocin release to arrest the labour is a more plausible explanation.

2. *Safety of Ethanol*:

The study has proved Ethanol to be quite a safe drug even by the intravenous route. But for few minor side effects mentioned below, Ethanol did not cause any trouble to the patients.

Side effects: (i) Elation: Elation was found in all the thirty cases exclusively. This finding is contradictory to the findings of Fuchs *et al*, who have noted elation in none of their patients. Could this be because women of the Sassoon Hospital class of patients in India are not used to alcoholic beverages as are the Western women?

(ii) Diuresis: In our study, diuresis also was a constant finding. As the mode of action of Ethanol is by suppression of posterior pituitary, along with oxytocin, antidiuretic hormone also is suppressed leading to diuresis.

(iii) Nausea and Vomiting: Only ten of the thirty patients receiving Ethanol suffered from this minor side effect. This can be explained as due to the central stimulation of vomiting and satiety centres by Ethanol.

In contrast to the findings of Horiguchi *et al* (1971), in their experiments on Rhesus monkeys, we failed to notice the progressive foetal asphyxia and maternal respiratory depression during Ethanol infusion. The cause for their observation can be very well attributed to the general anaesthesia used by them during their experiment. This aspect has already

been dealt with in details by P. V. Dilts (Jr.) (1970) in his various excellent experiments in different animals.

3. *Comparison with the Results of Other Workers*:

Table IV summarises the results of different workers as compared with our results. Accordingly, the successful results of Ethanol infusion in the present series as in the series of other workers in the ruptured membranes cases are nil. In the cases with intact membranes, our figures (65% success) are worth comparing with those of Fuchs *et al* (1967) (69% success) and Patel *et al* (1969) (60% success). While in their other series, Fuchs *et al*, have got much better results than ours (88% success in 1965 and 100% success in 1968). Such high results are probably due to scrupulous scrutiny in the selection of the cases.

TABLE IV

Results of Ethanol compared with Others

Worker	Total No.	No. of cases		Successful		Equivocal		Failure	
		M+	M—	M+	M—	M+	M—	M+	M—
F. Fuchs (1965)	25	17	8	15	—	—	—	2	8
F. Fuchs, A. R. Fuchs (1967)	68	52	16	35	—	10	7	7	9
-do- (1968)	81	65	16	65	—	—	—	—	16
Patel et al (1969)	30	30	—	18	—	—	—	12	—
Present Series	25	23	2	15	—	3	1	5	1

M+ = Membranes Intact

M— = Membranes Ruptured

4. *Primigravida and Taken up Cervix*:

Though the main cause of failure was wrong selection of the cases, these two aspects require a special mention as they also form quite a bulk of unsuccessful cases. As in primigravid patients, the cervix is taken up long before the patient goes in labour, both these conditions leading to unsuccessful results can be explained on the same basis, i.e. the taken up cervix is the point of no return in labour. Therefore, we would rather put these two conditions in addition to the list of contraindications for the infusion of Ethanol for prevention of premature labour.

Otherwise, the unsuccessful results are mainly due to missed contraindications while selecting the cases as it is evident from Table II.

5. *Uterine Activity*: (Figs. 2 and 3)

If the tracings of uterine activity are seen from the Figs. 2 and 3, marked change is observed in the pattern of uterine contractions before and after the Ethanol infusion. In successful cases, the contractions go on diminishing progressively in amplitude duration and

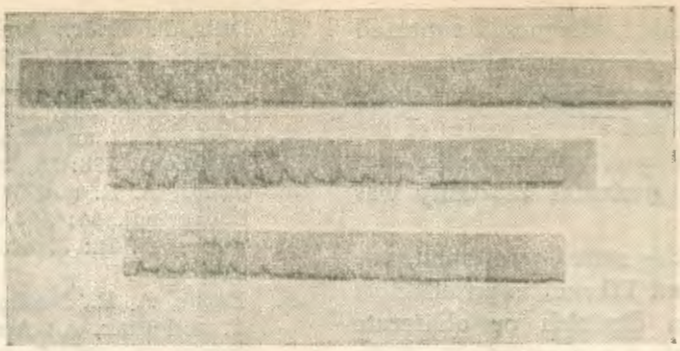

Fig. 2
Uterine tracing showing suppression of Uterine activity after Ethanol in successful cases.

Fig. 3
Uterine tracings showing failure of Ethanol.

frequency, to stop ultimately. While in unsuccessful cases, with Ethanol, the contractions diminish in amplitude, duration and frequency for some time and then they start again till the patient is delivered. In short, even in established labour in irreversible stage, Ethanol can relax the uterus for some time. Does it not call for its use in cases of intrapartum hypercontractility and occasionally for the manipulations during the second stage of labour?

Summary and Conclusions

1. Thirty cases coming in with premature labour were studied to test the efficacy of Ethanol for prevention of premature labour.

2. Another group of thirty cases was studied as control.

3. In the study group, there were twenty-five cases who went into spontaneous premature labour and in five cases premature labour occurred subsequent to some pelvic surgery.

4. In twenty-five cases, results with Ethanol were 60% successful, 16% equivocal and 24% failure.

5. In the remaining five cases, the results were 100% successful.

6. Of the thirty control cases, only in 6 (20%) could the labour be prolonged, for more than three days.

7. The main causes of failure were primigravid patients, and taken up cervix. The other causes were undiagnosed

intrauterine death, undiagnosed ruptured membranes and chorioamnionitis.

8. Perinatal mortality rate in the study group was 20% but all the babies of the successful cases survived, while in control cases the perinatal mortality was 50%.

9. Though the series was small, the results show that Ethanol is an effective agent that can diminish or obliterate uterine contractions in cases of premature labour and reduces the perinatal mortality due to prematurity and increases the foetal salvage rate.

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