INDUCTION OF LABOUR WITH DEAMINOOXYTOCIN

by

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Intravenous infusions of dilute solutions of oxytocin, developed and reported by Theobald *et al* (1948) and Hellman (1949) have been regarded as safe and effective means of inducing labour. Since oxytocin was found to be inactivated by plasma oxytocinase (Fekete, 1930, it was thought to be one of the factors responsible for the failure of oxytocin to induce labour.

Deaminooxytocin, an oxytocin analogue lacking free amino group of half cystine residue in the oxytocin molecule was found to possess greater vasodepressor and oxytocic activity (du Vigneaud *et al* 1960; Chan and du Vigneaud 1962; Ferrier *et al* 1965) and is not inactivated by plasma oxytocinase (Golubow *et al* 1963). Saameli (1964), Embrey (1965) and Bienziasz *et al* (1967) found deaminooxytocin 1.5 to 2 times more potent than oxytocin. Laine (1971) showed that the amount of deaminooxytocin required to induce labour by buccal route was remarkably less as compared to oxytocin. Deaminooxytocin infusion for induction of labour has not been asssessed fully, and needs trial. The only report is from Janson (1966) who studied the drug in 11 cases but no comparison with oxytocin was made. In the present study, an effort has been made to determine whether deaminooxytocin infusion has any advantage over oxytocin infusion.

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Material and Methods

The study was carried out on 51 patients at term admitted for induction of labour. Alternate patients were induced with deaminooxytocin (ODA. 914 Sandoz) and oxytocin (Syntocinon, Sandoz). "Physiological doses" consisting of 1 unit of oxytocin or deaminooxytocin in 500 ml. of 5% dextrose were used by slow intravenous infusion. Initially the infusion rate was maintained at 12 to 16 drops (1.6 to 2.0 mu) per minute and gradually increased to 20 to 40 drops (2.6 mu to 5.2 mu) per minute depending upon the foetal heart rate and uterine contractions. The maximum of 40 drops (5.2 mu) per minute was maintained. If the labour pains did not start, the infusion was discontinued at night and restarted the next morning. The infusion was continued in those patients who started labour pains and were likely to progress during night. Half hourly record of maternal pulse, blood pressure, foetal heart rate, intensity, duration and frequency of uterine contractions were kept in all patients.

Five ml. of blood was taken in a plain

vial before the start of induction of labour for the estimation of serum oxytocinase. The method followed was that of Harshey *et al* (1971) using L-cystine di P-nitroanilide as the substrate.

The induction of labour was considered successful if the vaginal delivery could be achieved. The outcome of induction was considered unsuccessful if caesarean section was required for (i) failure to initiate labour, (ii) failure to progress because of inefficient or abnormal uterine contractions or (iii) foetal distress. Various parameters such as latent period (a lag period from start of induction to onset of labour pains), induction delivery interval, duration of labour, amount of drug required till onset of labour pains and delivery, success rate and complications were used to compare the efficacy of deaminooxytocin to induce labour with that of oxytocin.

Results

Out of 51 patients induced, 25 patients were given deaminooxytocin and 26 patients received oxytocin. The two groups of patients were evenly matched as regards age, parity, gestation period, indication and serum oxytocinase levels (Table I & II). Table III shows the mode of deliveries in the two groups. Successful induction of labour was achieved in 21 out of 26 (80.8 per cent) patients in oxytocin group and 23 out of 25 (92.0 per cent) patients in deaminooxytocin group. (Table III).

Successful cases. The different parameters used to compare the efficacy of deaminooxytocin to induce labour in

TABLE I

Mean age, Parity, Gestation Period and Serum Oxytocinase

Factors	Oxytocin group (Mean ± S.D.)	Deaminooxytocin group (Mean ± S.D.)
Age Primi	24.5 ± 1.97	23 ± 2.24
Multi	26.1 ± 3.06	28 ± 4.29
Parity (excluding primigravida)	1.7 ± 0.74	1.7 ± 1.10
Gestation period (weeks)	39.5 ± 1.5	39.3 ± 1.9
Serum oxytocinase (Optical density)	0.45± 0.23	0.44 ± 0.17

TABLE II

Distribution of Patients as Regards Parity and Indications for Induction of Labour

	Oxytocin group (Number of patients)	Deaminooxytocin group (Number of patients)
Parity		
Primigravida	12	15
Multigravida	14	10
Indications		
Pre-eclampsia	10	8
Postdate and Postmature	8	7
Premature rupture of membranes (>8 hours)	5	8
Placental insufficiency	1	2
Miscellaneous (Diabetes, Rh immunisation)	2	0

TABLE III
Mode of Deliveries

	Oxytocin group	Deaminooxytocin group
Normal	18	17
Outlet forceps	1	2
Low midforceps	2	1
Assisted breech	0	3
Caesarean section	5	2
Total	26	25

successful cases with those of oxytocin infusion are shown in Table IV. A significant reduction in the latent period ($P < 0.05$) and amount of drug required till onset of labour and delivery ($P < 0.05$ and $P < 0.01$ respectively) were observed in the de-aminooxytocin group. It was observed that 18 out of 23 (78.3 per cent) of patients in deaminooxytocin group and 13 out of 21 (61.7 per cent) in oxytocin group delivered within 24 hours after the start of induction (Table V).

Unsuccessful cases. Out of seven caesarean sections, 5 were in oxytocin group and 2 in deaminooxytocin group. All were primigravidae except 1 in oxyto-

TABLE IV
Comparison of Treatment With Deaminooxytocin and Oxytocin. The Results are Mean ± Standard Error

Parameters	Oxytocin group (21 cases)	Deaminooxytocin group (23 cases)	Ratio OXY: ODA	P-value
Latent period (Hours)	10.9 ± 2.46	4.47 ± 1.63	2.4:1	<0.05
Induction delivery interval (Hours)	22.3 ± 3.3	16.7 ± 3.3	1.3:1	>0.05
Duration of labour (Hours)	11.4 ± 1.6	12.2 ± 2.15	0.95:1	>0.05
Amount of drug till onset of labour pains (I.U.)	0.98 ± 0.21	0.4 ± 0.03	2.4:1	<0.05
Amount of drug till delivery (I.U.)	3.01 ± 0.43	1.4 ± 0.28	2.1:1	<0.01

TABLE V
Induction Delivery Interval

Hours	Oxytocin group	Deaminooxytocin group
Within 24	13 (61.9)	18 (78.3)
24-36	4 (19.05)	1 (4.3)
more than 36	4 (19.05)	4 (17.4)

Percentage given in parenthesis.

cin group. Since the number of patients was very small statistical analysis was not attempted. The indications for caesarean section in the oxytocin group were inco-ordinate uterine action with foetal distress in 3 cases and hypotonic uterine action and failed induction in 1 case each. In deaminooxytocin group first caesarean was required for failed forceps due to unrecognised midpelvic contraction and second was done for incidental detection of thick meconium stained liquor on amniotomy on third day of infusion This patient had previously no labour pains or other signs of foetal distress.

Complications. The complications encountered in this study are presented in Table VI. There was no significant difference in the apgar score of the babies at birth in the 2 groups. There was no perinatal or maternal loss in either group.

TABLE VI
Complications During Induction of Labour and Delivery

Complications	Oxytocin group	Deaminooxytocin group
Foetal distress	2	1
Inco-ordinate uterine action with foetal distress	4	—
Hypotonic uterine action	1	—
Postpartum haemorrhage and shock	1	—
Manual removal of placenta (cord snap)	—	1

Discussion

Although 'physiological' doses of oxytocin for induction of labour have been found to be safe, such doses usually result in about 30 per cent failures on the first day of infusion and prolonged induction delivery interval (Theobald, 1963). Turnbull and Anderson (1968) and Howie and MacVicar (1970) have recommended the use of titrating doses as high as 128 mu/minute to overcome these problems. In order to avoid accidents with such high doses it is essential to continuously monitor the uterine activity and foetal heart with a toco-cardiograph. Another approach to the problem is the use of an oxytocin analogue which is more potent and comparatively safer.

Deaminooxytocin which is 1.5 to 2 times more potent than oxytocin has been compared with physiological doses of oxytocin for induction of labour in the present study. Using physiological doses (2.5 mu/minute) 13 out of 21 (61.9 per cent) and 18 out of 23 (78.2 per cent) cases delivered within 24 hours after starting induction with oxytocin and deaminooxytocin respectively. The results of deaminooxytocin infusion can be compared with those of oxytocin infusions reported by Maxwell (1964) and Turnbull and Anderson (1968). In Maxwell's (1964) series 78.8 per cent of patients delivered within 24 hours but the average dose of oxytocin was 13.9 units. Turnbull and Anderson (1968) reported 80 per cent patients delivering within 24 hours after amniotomy and oxytocin infusion in titrating doses as high as 16 to 32 units per 540 ml of dextrose. Thus, deaminooxytocin is effective in achieving the same results even with the low doses.

Even though the latent period was significantly ($P < 0.05$) reduced in the deaminooxytocin group, the duration of labour was similar in the 2 groups. This

is not surprising since increased activity of "Tissue oxytocinase" in blood has been found during labour (Branda *et al* 1968) which inactivates deaminooxytocin and this could affect the duration of labour.

Successful induction of labour was more often encountered with deaminooxytocin than oxytocin (Table III). However, it is not possible to draw a definite conclusion regarding the low incidence of caesarean section in deaminooxytocin group as the number of cases was small. A study of larger sample may be helpful to find out whether the caesarean section rate is significantly lower with deaminooxytocin infusion. Complications were also few with deaminooxytocin. No case of inco-ordinate or hypotonic uterine action or inability to initiate labour was found with deaminooxytocin infusion. No foetal mortality occurred during the study. Thus, it appears that deaminooxytocin may offer an advantage over the routine use of "physiological doses" oxytocin infusion for induction of labour.

Summary

In a comparative study, induction of labour was tried with intravenous infusions of deaminooxytocin and oxytocin. Eighteen out of 25 cases of the deaminooxytocin group and 13 out of 26 cases of the oxytocin group delivered within 24 hours. A significant reduction in the latent period ($P < 0.05$) and the amount of drug required till delivery ($P < 0.01$) was observed in the deaminooxytocin group. The complications encountered in this group were also less.

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References

1. Bienziasz, A., Drewniak, K. and Klimek, R.: Amer. J. Obst. & Gynec., **98: 535, 1967.**
2. Branda, L. A., Ferrier, B. M., Archmaut, G., Marchelli, E. A. and Rucanski, B.: Science, **160: 81, 1968.**
3. Chan, W. Y. and du Vigneaud, V.: Endocrinol. **71: 977, 1962.**
4. du Vigneaud, V. Winestock, G., Murti, V. V. S., Hope, D. B. and Kimbrough, R. D. Jr.: Journal of Biological Chemistry. 235: 64, 1960.
5. Embrey. M. P.: J. of Endocrinol. **31: 185, 1965.**
6. Fekete, K.: Endocrinol. **7: 364, 1930.**
7. Ferrier, B.M., Jarvis, D. and du Vigneaud, V.: Journal of Biological Chemistry. **240: 4264, 1965.**
8. Golubow, J., Chan, W. Y. and du Vigneaud, V.: Proceedings of the society for Experimental Biology and Medicine. **113: 113, 1963.**
9. Harshey, A. D., Mathur, V. S. and Gupta, A. N.: Bulletin of Postgraduate Institute of Medical Education and Research, Chandigarh (India). **5: 101, 1971.**
10. Hellman, L. M.: Amer. J. Obst. & Gynec. **57: 364, 1949.**
11. Howie, P. W. and MacVicar, J.: J. Obst. & Gynec. Brit. Cwlth. **77: 813, 1970.**
12. Jonson, I.: Acta. Obst. et Gynec. Scandinav. **45: 29, 1966.**
13. Laine, J.: Acta Obst. et Gynec. Scandinav. **50: 229, 1971.**
14. Maxwell, A. F.: J. Obst. & Gynec. Brit. Cwlth. **71: 37, 1964.**
15. Saameli, K.: Brit. J of Pharmacol. **23: 176, 1964.**
16. Theobald, G. W., Graham, A., Campbell, J., Gange, P. D. and Driscoll, W. J.: British Medical Journal, **2: 123, 1948.**
17. Theobald, G. W.: Modern trends in obstetrics. Butterworths, London, P. **87.**
18. Turnbull, A. C. and Anderson, A. B.: J. Obst. & Gynec. Brit. Cwlth. **75: 32, 1968.**