TRAMADOL HYDROCHLORIDE IN DYSFUNCTIONAL LABOUR A CLINICAL TRIAL

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SUMMARY

Inj. Tramadol hydrochloride, a weak opioid analgesic 100 mg I.M. was given a clinical trial in cases of dysfunctional labour as well as normal labour cases at North Bengal Medical College. The results observed were compared with those of conventional analgesics like pethidine.

Antinociceptive efficacy of tramodol was found comparable to pethidine. In tramadol group incidence of foetal distress was significantly reduced, duration of labour shortened and incidence of caesarean section decreased. Apgar score of 7 - 10 at 1 minute was far commoner in tramadol group than in the pethidine group. Uncorrected PNMR was observed 7 times less in the tramadol group, though baby-weights were comparable in both the groups. When corrected for prematurity and maternal factors, PNMR became nil in tramadol group.

INTRODUCTION

Pain in labour is unpleasant, and sometimes distressing to the parturient. Till date, there is no completely safe and satisfactory method for relief of pain in obstetric practice, since the commonly employed drugs readily cross the placenta causing respiratory depression in the foetus/ neonate.

Dysfunctional labour of hypotonic or hypertonic variety or cervical dystocia leads to prolonged labour in 25% of primigravidae

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and 2% of multigravidae (Dawn, 1995). This produces stress to the mother and carries the risk of maternal deaths upto 1% in uncared case while doubling the perinatal deaths.

The risks of commonly used opioids eg. morphine, pethidine & pentazocine are well-known. Tranquilisers like diazepam and lorazepam have no analgesic effect. Inhalation anaesthesia with Nitrous Oxide-O2 combination has limitations in routine use.

An ideal pain-relieving agent in labour should be safe to both mother & foetus with satisfactory analgesic potential. Tramadol hydrochloride, a weak opioid agonist acting mainly through descending monoaminergic pain inhibitory pathway has been given trial in both dysfunctional and normal labour to observe its safety & efficacy vis-a-vis other commonly used analgesics.

MATERIALS & METHODS

This prospective study was carried out at the Dept. of Obstetrics & Gynaecology, North Bengal Medical College, Siliguri, from April' 93 to March' 95.

Inj. Tramadol hydrochloride, 100 mg was administered I.M to both primi & Multi gravidae in 1st & 2nd stage to 112 cases of dysfunctional labour (Table I : Trial group I).

(Table I) Another 100 cases of uncomplicated normal labour cases (Group II) were included in this study for the purpose of pain relief only and to observe the effect to the drug on mother & neonate. A repeat dose of tramadol 100 mg in 25 cases of Group I & 15 cases of Group II and antispasmodics like epidosin I/V in 57 cases of Group I & 40 cases of Group II were also administered.

A third group of 100 cases were also

Table I
GRAVIDITY & STAGE OF LABOUR

Trial group with Tramadol 112 cases Group - I		Control group with Conventional analgesics 100 cases Group - III
	N (%)	N = %
Primi	- 77 (66%)	63%
Multi	- 38 (33.9%)	37%
1st stage	- 106 (94.6%)	95%
2nd stage	- 6 (5.4%)	5%

Table II
DISTRIBUTION OF CASES

Dysfunc. Labour		Trial Group	Control Group	
Uncomplicated group		51	38	
Complicated		61	62	
Postdated-	5		Postdated -	3
Elderly prime	3		Elderly primi	5
Post CS	4		Post CS	6
Twin Preg	2		Twin Preg.	2
PET	27		PET	10
Preterm	20		Preterm	36

included as retrospective study to serve as control group (Group III) where commonly used analgesics & tranquilisers e.g Inj. Pethidine 100 mg I/M, Inj. Pentazocine 30 mg I/M, Inj. diazepam 10 mg I/M I/V were used either single or in combination for comparing with the results of trial group of tramadol. In this group pethidine was used in 62 cases, diazepam alone in 23 cases and pentazocine & diazepam together in 15 cases.

Selection of cases : In trial group (dysfunctional labour) (1) All cases were clinically assessed properly & had cephalic presentation, (2) Hypertonic dysfunctional labour cases e.g. incoordinate uterine action, hyperactive lower segment, asymmetric uterine dysfunction etc. (3) Cervical dystocia, (4) in hypotonic dysfunctional labour cases, tramadol was administered following oxytocin drip when labour pain was well established with half dilatation of cervical os (5) CPD was excluded clinically.

Associated obstetric complications were comparable in each group as evident from Table II.

RESULTS

A. Relief of pain Degree of pain relief observed after tramadol administration in trial group was found satisfactory in 15 (13%), moderate in 42 (38%), mild in 53 (47%) cases and no relief in 2 (2%) cases. Pain relief was assessed by subjective method.

B. Pulse rate . No appreciable change was recorded after administration of tramadol.

C. BP : Rise of systolic BP was noted only in 7 (6.2%) cases by 5 - 10 mm Hg, that too in cases where initial BP was 140/90 mm Hg or more before application of tramadol. No or marginal changes were observed in diastolic BP.

D. Foetal distress observed as per Table III

F Type of delivery as per Table IV.

F. Apgar score at 1 min. as per Table V.

G Perinatal mortality - Fresh still birth (FSB) neonatal deaths (NND) and PNMR observed as per Table VI.

Table III
FOETAL DISTRESS

Trial Group - with tramadol	I- N (%)	Control Group - III with pethidine N (%)
Mild	8 (7.1%)	29 (29%)
Severe	6 (5.4%)	13 (13%)

Table IV
TYPE OF DELIVERY

	Trial Group - I N (%)	Control Group - III N (%)
. Spot. vaginal	77 (69.8%)	55 (55%)
Forceps	15 (13.4%)	22 (22%)
. CS	20 (17.9%)	23 (23%)

Table V
APGAR SCORE AT 1 MIN

Score	Trial Group I N = (%)	Control Group III N = (%)
0 - 3	1 (0.9%)	7 (7%)
4 - 6	9 (8.0%)	29 (29%)*
7 - 8	37 (33.0%)	62 (62%)
9 - 10	67 (59.9%)	4 (4%)

* Including two twins in each group

Table VI
PERINATAL MORTALITY

	FAB	NND	PNMR
Trial Group	1*	2**	26.8
Control group	7	11	180

* Premature 2nd twin
** Maternal influenza - 1. ** Premature 2nd twin - 1.

Table VII
GROUP II : EFFECT ON FOETUS & TYPE OF DELIVERY

Foetal distress 5%
Drug-delivery interval between 1-8 hours in 92%
Forceps - 20% CS - 8%

Apgar Score at 1 min	4 - 6	=	5%
	7 - 8	=	34%
	9 - 10	=	61%

Group II : 100 cases of normal labour at term where Inj. tramadol 100 mg I/M was used. Here primigravidas were 48 cases. 95 cases were in stage I labour and 5 cases were in stage II labour. Pain relief in this group was satisfactory in 24% cases, moderate in 40% and mild in 36% cases. In this group baby weights were between 2 to 2.49 kg in 28% cases and above 2.5 kg in 72% cases. Effect of tramadol administration on the foetus and type of delivery observed are as per Table VII. No perinatal death in this group.

DISCUSSION

Tramadol hydrochloride, a centrally acting drug with low affinity for opioid receptors and acting mainly through activation of descending monoaminergic pain inhibitory non-opioid pathway (70%), when used during labour, produces a low incidence of respiratory and cardiac depression in

the neonate and also produces effective analgesia in the labouring mother with minimum adverse effects (Lee et al, 1993).

Tramadol is a synthetic 4-phenyl-piperdine analogue of codeine & has the chemical structure : (+)- trans-2-(dimethyl aminomethyl)-1-(m-methoxyphenyl)-cyclo-hexanol hydrochloride. To have its anti-nociceptive effectiveness, tramadol activates only 30% opioid pathway (Besson & Vickers, 1994) as tested by naloxone (an opioid antagonist) antagonism. The remaining 70% antinociception is attained by activation of the serotonergic & noradrenergic descending monoaminergic pain inhibitory pathway. Tramadol inhibits re-uptake of both serotonin & noradranaline (Lee et al, 1993). Tramadol shows some selectivity for μ opioid receptor (Raffa et al, 1992), but its only active metabolite o-demethyl tramadol (M1) shows higher affinity for this receptor (Hennies et al, 1988). However, this metabolite was not found to contribute to the analgesic effect of a single dose of tramadol 100 mg orally (lee et al, 1993). Excepting a few, most clinical studies have been performed by German researchers and it was only in early 1990s that more international interest arose on tramadol as a safe & effective analgesic (Lehmann, 1994). In the present series we observed moderate to satisfactory pain relief during dysfunctional labour in 51% cases. Prasertswat et al (1985) reported satisfactory analgesia in 78% caes and also reported insignificant difference with pethidine & morphine in analgesic potential. Nausea & vomiting following tramadol were insignificant.

Husslein et al (1987), and Kaintz et al (1992) observed no adverse effects on mother/neonates after using tramadol 100 mg I/M during labour. We observed foetal distress more than 3 times less with tramadol than with pethidine (12.5% vs 43%). In the trial group with tramadol 90% deliveries occurred within 1-8 hours (cf. 55% in the control group). Incidence of spontaneous vaginal deliveries were higher in trial group than in control group (69.8% vs 55%). Caesarean sections were less in trial group than in control group (17.9% vs 23%). Apgar score of 7-10 at 1 min. were far better in trial than in control group (92.9% Vs 66%), baby weight being comparable in both the groups. Suvonnakote et al (1986) using tramadol 100-150 mg slow I/V in 55 labour cases reported neonatal respiratory depression in 7% cases while using pethidine 100-150 mg slow I/V the neonatal respiratory depression observed was 31% i.e. more than 4 times.

Uncorrected perinatal mortality rate observed in our series in the trial group was almost 7 times less than in the control group (26.8 Vs 180) though baby weights were comparable in both the groups. When corrected for prematurity & maternal ailments perinatal mortality in tramadol group was nil.

In groups II cases of normal labour where tramadol was used results observed were better in all parameters and there was no perinatal death, moderate to satisfactory analgesia in 64% cases (trial group I 51% cases), duration of labour was lowered; drug-delivery interval between 1-8 hours was in 92% cases (90% in trial group I; 55% in control group) and caesarean section

rate was also lowered to 8% (in trial group I 17.9%, control group 23%). There was no maternal death in any group.

CONCLUSION

Tramadol hydrochloride, a weak opioid agonist analgesic which acts mainly through activation of the non-opioid descending monoaminergic pain inhibitory pathway was given a trial in this study. It was found to be a Safe & effective analgesic during labour both dysfunctional & normal, it did not cause maternal morbidity, and it did not cause intranatal/neonatal CVS/respiratory depression. Therefore (4) tramadol hydrochloride is strongly recommended to be used in labour.

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