ORIGINAL ARTICLE

Labour analgesia: Tramadol versus Pentazocine

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Abstract:
Objective: To compare the efficacy and safety of intramuscular Tramadol and Pentazocine during labour, in our women.
Design: Double blind randomised trial.
Setting and duration: Aga Khan Hospital for Women - Garden from July 06, 2010 to December 11, 2010.
Methods: 231 women, 114 in Tramadol group and 117 in Pentazocine group, were included in the analysis, with term singleton pregnancy, cephalic presentation that were in active phase of labour and had a baseline VAS score of more than 7. Tramadol 100 mg and Pentazocine 30 mg intramuscular were given to assigned subjects. Pain was assessed at 30 and 60 minutes of drug administration on VAS score (0 – 10) and maternal satisfaction on Likert's scale (1 – 5) two hours after delivery.
Results: The mean VAS score declined significantly in both the groups after analgesia (p-value<0.001), but no significant difference was observed between the two groups (p-value=0.839). Overall maternal satisfaction recorded at 2 hours of delivery, showed significantly more women satisfied in Pentazocine group (p-value=0.05). No significant difference was observed for maternal and neonatal outcomes. Sedation was found to be significantly more in Pentazocine group (p-value<0.001).
Conclusion: Both the drugs significantly reduced pain and were found to be equally safe and effective for labor analgesia.

Keywords: Labour Analgesia, opioids in labour, Tramadol, Pentazocine.

Introduction:

Pain management is an essential component of intrapartum care and a basic principle in modern obstetrics. The demand for pain relief in labour is increasing as individual pain threshold seems to be decreasing, sometimes to the extent of refusal for further trial of labour and request for caesarean section. Over the past decade, research has proved that good pain relief during labour controls wide spread maternal sympathetic stimulation and pain induced hyperventilation and hypocapnia. This also improves uteroplacental circulation and prevents dysfunctional labour. Therefore progress of labour is expected to be expedited in addition to some relief in pain and anxiety of the labouring women. [1,2,3]

A good analgesic should be effective, rapid in action, affordable, safe, with less side effects and one that does not hinder labour progress. Epidural analgesia is considered as the most effective analgesic available. [4,5,6]

However resource limitation, that is, the cost of equipment, personnel and intense monitoring during its administration, limits its availability in most obstetric units of developing countries likes Pakistan.

Pethidine has been widely used in many obstetric units worldwide in spite of reservations regarding its safety profile. Apart from early maternal and neonatal side effects, behavioural and feeding problem have been observed up to 6

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weeks in the baby. [7,8,9] The two other most commonly used drugs are Pentazocine and Tramadol and studies show them to be 'as effective as Pethidine and with less side effects. [3,4,10]

In Pakistan many hospitals catering women from middle and lower socioeconomic class do not offer labour analgesia. Labour is an extremely painful and for many young women a fearful experience. [4,11] Although opioids are readily available, easy to use and economical, their use is not common in Pakistan. The reasons probably are lack of realization of the analgesic requirement of the labouring women and reservations regarding safety of the drug from neonates' perspective. We decided to conduct a study comparing Tramadol and Pentazocine in our setup. This would have helped to develop protocol for labour analgesia with limited resources in our setting.

The objective of the study is to compare the efficacy and safety of intramuscular Tramadol and Pentazocine during labour, in our women.

Material and Methods:

The study was conducted in Aga Khan Hospital for Women - Garden, a secondary care unit of Aga Khan Hospital and Medical College Foundation. The duration of study was from July 06, 2010 to December 11, 2010. It was a double blind randomised study. Women with term (37 – 42 weeks), singleton pregnancy, cephalic presentation, in active phase of labour i.e. 3cm dilated with 2 or more regular contractions in 10 minutes lasting for 40- 60 seconds, were included in the study. Non cephalic presentation, preterm labour, multiple pregnancies, fetal anomalies, IUGR, significant maternal illness (uncontrolled diabetes, liver and renal impairment, cardiovascular and neurological diseases, etc), women on psychotropic drugs and women with an effaced cervix dilated >7 cm were excluded from the study.

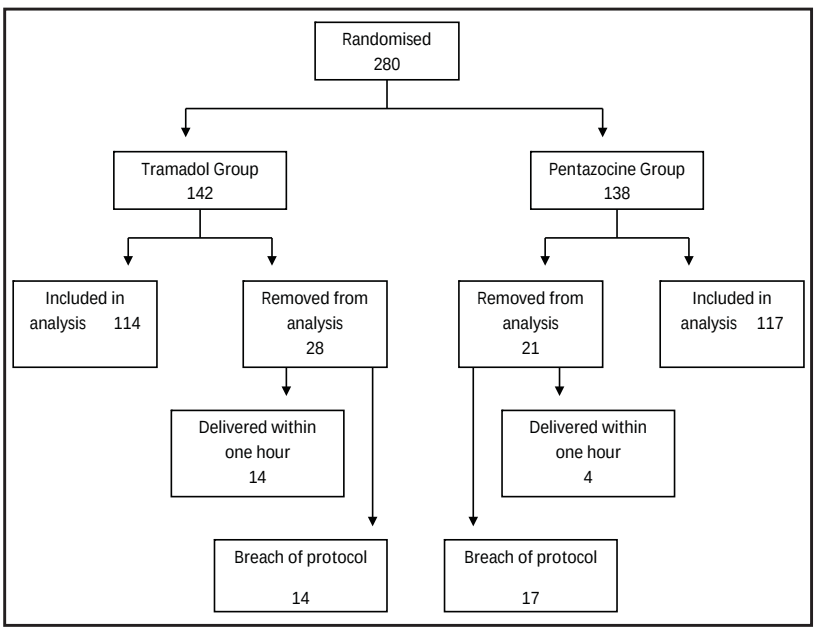

Figure 1:

Approval of the study was taken from the ethical review committee of the university and informed consent was taken from all women. The randomization sheet was retained in the pharmacy. The request for study drug was generated by labour ward medical officer, on a randomization authorization slip, for each subject. On receiving request, the pharmacist dispensed the drug in an opaque envelope, labeled either drug A or drug B, containing the ampoule hidden with white tape. The subject, investigators, labour ward medical officers and midwives were blinded of the drugs given. The codes A and B were broken by the pharmacist after the study analysis was completed. A total of 280 women were randomised, 142 in Tramadol group (A) and 138 in Pentazocine group (B). Of these 49 women, 28 from Tramadol group and 21 from Pentazocine group, were removed from the study. (Figure 1)

In Tramadol group (n=114), 100mg of Tramadol and in Pentazocine group (n=117), 30mg of Pentazocine were given intramuscular at baseline VAS score >5. Maternal pulse, blood pressure, respiratory rate, pain intensity, nausea, vomiting and sedation status was assessed by the assigned labour ward medical officer or midwife immediately before, at 30, and 60 minutes after drug administration. Pain was assessed on 10 point Visual Analog Scale (VAS). 0 = no pain, 1- 4 = mild, 5 – 7 = moderate and 8 – 10 = severe. Nausea was marked as 0 = nil, 1 = mild, 2 = moderate, 3 = severe. Vomiting was marked 0 = nil, 1 = mouthful, 2 = more than mouth-

ful. Sedation was assessed on Fischer scale as 1 = alert, 2 = drowsy, 3 = non arousable to voice, 4 = non arousable to command, 5 = unarousable. Overall maternal satisfaction was assessed two hours after delivery on Likert's scale. Time interval from drug administration to vaginal delivery was noted in minutes. Mode of delivery and APGAR scores at 1 and 5 minutes of birth, NICU admission and need for Naloxone were recorded. Repeat dose of analgesia drug was given 4 hours after the first if VAS score was more than 5 and cervix less than 7 cm dilated.

Results:

A total of 231 women, 114 women from Tramadol group and rest of them from Pentazocine group were included for the analysis. Maternal characteristics age, height, weight, education level, socio economic status, parity, gestational age and cervical dilatation at the time of drug administration were compared for the two groups. Only educational level and parity were found to be significantly associated with group status (Table 1).

Mean VAS score between the two groups were significantly different. The mean VAS score declined significantly for both the groups, but the pattern remained same and no interaction was observed. No significant difference was observed between percentage change in pain score from baseline between the two groups (p>0.999). Overall maternal satisfaction recorded at 2 hours of delivery, showed marginally significant difference in both the groups, with more women satisfied in Pentazocine group, although a larger proportion reported very good in Tramadol group as compared to Pentazocine group [Table 2].

Table 1: *Maternal Characteristics at the time of Drug Administration*

Characteristics	Tramadol	Pentazocine	p- value
Age (years)	25.2±(4.3)	24.5±(4.4)	0.249
Height (cm)	156.8 ±(5.1)	157.4±(4.7)	0.329
Weight (kg)	68.7 ±(14.3)	66.3 ±(10.8)	0.148
Education Level n(%)			
Up to Matric	102 (89.5%)	96 (82.1%)	0.012
Intermediate & above	12 (10.5%)	21 (17.9%)	
Socio economic status n(%)			
Poor/Lower Middle	50 (44.2%)	50 (42.7%)	0.103
Upper Middle/upper	63 (55.8%)	67 (57.3%)	
Parity n(%)			
Primi	58 (50.9%)	69 (59%)	0.027
Multi	50 (43.9%)	46 (39.3%)	
Grand Multi	6 (5.3%)	2 (1.7%)	
Gestational Age (weeks)	38.8 ±(1.09)	38.6 ±(1.08)	0.144
Cervical Dilatation (cm)	3.69 ±(0.7)	3.64 ±(0.62)	0.626

Table 3 shows the association of treatment group with maternal and neonatal outcomes. No significant difference was observed for maternal and neonatal outcomes.

Table 4 shows the effects of drugs on hemodynamic variables of women. Only systolic blood pressure was declined in both the groups at different time. Nausea and vomiting were significantly increased at different time points in both the groups but there was no difference between the groups. Sedation was found to be significantly different in the two groups at different time points as well as the interaction of groups with time was also found to be significant that is, more in Pentazocine group.

Discussion:

Pain relief is a crucial factor in labour management but unfortunately, there is no objective way of measuring pain, so the assessment remains very subjective. Epidural analgesia provides the most effective pain relief in labour. But where it is not available or the women do not opt for it, opioids remain the most suitable option. [5] Opioids do not greatly reduce labour pain but by virtue of their mode of action, but they do decrease anxiety and discomfort and put the labouring women at some ease. In our study both the drugs showed modest pain relief, 27% decline in VAS score in Tramadol group and 28 % decline in VAS score in Pentazocine group. Although the pain relief was comparable in both the groups, overall maternal satisfaction was marginally significantly more in Pentazocine group. This can be explained by significantly more women being sedated and less proportion of women (not statistically significant) having vomiting in this group. More than 80% of women in both the group rated analgesia as good, very good or excellent in our study .This was much higher than reported 32 to 65% in the

Table 2: *Pain Relief and Maternal Satisfaction*

	Tramadol Mean (SD)	Pentazocine Mean (SD)	p- value Time (T)	Group (G)	TxG Interaction
VAS Baseline	7.88±(1.26)	7.91±(1.25)	F= 268.18 p< 0.001	F= 28337.8 p< 0.001	F= 0.176 p= 0.839
VAS at 30 minutes	5.54±(1.5)	5.64±(1.6)			
VAS at 60 minutes	5.72±(1.48)	5.68±(1.55)			
Pain Relief (in %) from baseline	27.4%	28.2%		>0.999	
Maternal Satisfaction-2 hours after Delivery (Likert's Scale)	n(%)	n(%)			
Poor	7 (6.1%)	5 (4.3%)		0.05	
Satisfactory	10 (8.8%)	9 (7.7%)			
Good	50 (43.9%)	60 (51.3%)			
Very Good	45 (39.5%)	35 (29.9%)			
Excellent	2 (1.8%)	8 (6.8%)			

literature.[3,4,5]

Pentazocine is a benzomorphan derivative with both agonist and weak opioid antagonist activity Tramadol is a centrally acting weak synthetic opioid that displays its analgesic effect by modifying transmission of pain impulses by altering monoamine re-uptake mechanism [2,12]. Literature reports it to be a good analgesic and better than Pentazocine for post operative pain and equally effective in acute pain. [13] The edge of Tramadol over Pentazocine is not seen in labour pain, probably because labour pain is associated with anxiety and the nature of pain is different, that is arising at intervals and the intensity increasing with time. Our study found it to have efficacy equivalent to Pentazocine in labour pains. The C-Section rate was similar with comparable number performed for non progress of labour and fetal distress in both the groups. The duration of labour was also comparable in both the groups. Similar findings are reported by Kuti and colleagues where Pentazocine was compared with Tramadol and by Elborne and colleagues in their review of 16 trials comparing Pethidine and Tramadol. [4,14] Khoshedeh ha has shown Tramadol to significantly reduce duration of labour. [3] In our study 14 women delivered within one hour of drug administration in Tramadol group compared to 4 in Pentazocine group, though they were not included in analysis . Later than one hour the mean duration of labor was comparable in both the groups.

Lot of fear is found regarding safety of Opioids in labour but our study has shown both Tramadol and Pentazocine to be safe for the mother and the neonate .Tramadol and Pentazocine did not alter the hemodynamic markers accept for decline in systolic blood pressure. There was no respiratory depression in either group. Nausea and vomiting were found in small (though significant) number of women comparably in both the groups. Sedation was significantly more in

Table 3: *Maternal and Neonatal Outcome*

	Tramadol	Pentazocine	p- value
Drug to delivery interval (minutes)	239 SD: 134.7	232.8 SD: 137.8	0.751
Mode of Delivery n(%)			0.533
Spontaneous Vaginal Delivery	95(83.3%)	92 (78.6%)	
Instrumental Delivery	2 (1.8%)	5 (4.3%)	
Cesarean Section	17 (14.9%)	20 (17.1%)	
Indications; Fetal Distress	08	08	
Non Progress	08	11	
Others	01	01	
Mean APGAR score at 1 minute	8	8	-
Mean APGAR score at 5 minutes	9	9	-
APGAR score < 7 at 1 minute (n)	0	2	-
APGAR score < 7 at 5 minutes (n)	0	0	-
Use of Nalaxone	0	0	-
Admission to NICU	4 (3.5%)	3 (2.6%)	>0.099
Reasons;	1 RDS 1 Swallowed maternal blood 1 Transient Tachypnea of Neonate 1 Presumed Sepsis	1 RDS 1 Jaundice 1 Low birth weight	

Table 4: *Maternal Side Effects*

Variables	Drugs	Baseline Mean(SD)	At 30 Min Mean(SD)	At 60 Min Mean(SD)	p-Value		
					Time (T)	Group (G)	TxG Interaction
Pulse (beats/min)	Tramadol	85.76 (7.76)	85.25 (6.65)	84.54 (6.64)	F=1.212 p=0.298	F=0.992 p=0.320	F=1.389 p=0.250
	Pentazocine	84.26 (6.9)	84.52 (6.94)	84.33 (7.61)			
Systolic Blood Pressure (mm/hg)	Tramadol	113.14 (8.05)	114.7 (11.2)	111.69 (10.19)	F=5.955 p=0.003	F=0.911 p=0.341	F=0.835 p=0.435
	Pentazocine	112.84 (8.57)	112.7 (10.9)	111.09 (9.63)			
Diastolic Blood Pressure (mm/hg)	Tramadol	70.77 (7.81)	71.3 (2.5)	71.35 (7.46)	F=0.672 p=0.511	F=0.270 p=0.604	F=0.055 p=0.946
	Pentazocine	70.44 (7.31)	71.13 (7.6)	70.77 (6.60)			
Respiratory Rate (per minute)	Tramadol	19.42 (2.19)	19.41 (1.8)	19.28 (1.64)	F=0.076 p=0.927	F=0.490 p=0.485	F=0.64 p=0.528
	Pentazocine	19.23 (2.19)	19.15 (1.9)	19.29 (1.71)			
Nausea	Tramadol	0.03 (0.16)	0.10 (0.30)	0.97 (0.30)	F=5.02 p=0.007	F=0.001 p=0.97	F=0.684 p=0.505
	Pentazocine	0.05 (0.22)	0.08 (0.27)	0.94 (0.29)			
Vomiting	Tramadol	0.03 (0.16)	0.09 (0.28)	0.105 (0.31)	F=10.88 p<0.001	F=1.935 p=0.166	F=0.670 p=0.512
	Pentazocine	0.01 (0.09)	0.03 (0.18)	0.077 (0.27)			
Sedation	Tramadol	1.04 (0.18)	1.08 (0.27)	1.10 (0.297)	F=18.92 p<0.001	F=0.812 p=0.005	F=6.94 p=0.001
	Pentazocine	1.03 (0.18)	1.25 (0.49)	1.23 (0.50)			

Pentazocine group. Pentazocine is reported to be associated with sedation but overall safety profile of both the drugs is reported to be better than Pethidine. [1,4] Mean APGAR scores was 8 at one minutes and 9 at five minutes after birth, in both the groups. Only two babies were born with APGAR score less than 7 in Pentazocine group but the scores raised to more than 7 within five minutes of birth in both the babies. None of the babies in either group had respiratory depression. Studies have shown that intramuscular Tramadol and Pentazocine do not cause respiratory depression in the neonate. The risk of respiratory depression is postulated to be associated with intravenous route and when given within two to three hours of the delivery. [3] Although we had not given drugs after 7 cm dilatation, many women delivered within one to three hours of drug administration and none of the neonates had respiratory depression or required Naloxone. Overall none of the drugs was found to be better than the other. Both were found to be safe and equally effective. Bricker and colleagues in systemic review of 85 trials concluded that epidural is better than opioids and that if women opt for systemic opioids; there is no strong preference for any opioids. He recommends that in view of large number of women who use opioids in labour and the paucity of evidence, well designed large-sized trials should be conducted. [9] Elbourne and colleagues concluded in systemic review of 16 trials of that there is not enough evidence to evaluate comparative efficacy and safety of the various opioids used for analgesia in labour. [14] More recently, Roz Ullman and colleagues mentioned in their review of 54 trials comparing different opioids with intramuscular and intravenous routes, that opioids provide some pain relief and moderate satisfaction. The reviewers did not find sufficient evidence to recommend preferable opioid for labour analgesia.[15]

Conclusion:

Tramadol and Pentazocine were found to be safe and equally effective for labour analgesia with comparable maternal and neonatal outcomes. There was significantly more sedation and marginally significant more maternal satisfaction in Pentazocine group. Either of these drugs can be used for labour analgesia until evidence is obtained in favor of any particular opioid.

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