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# **Tramadol versus Nalbuphine in total intravenous anaesthesia for Dilatation and Evacuation**

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## **Abstract**

**Objective:** To compare the results of Tramadol with Nalbuphine for dilatation and evacuation with total intravenous anaesthesia technique.

**Methods:** A total of 70 patients (35 in each group) were included in this prospective, double blind randomized study. Intravenous tramadol 1.5mg/kg and nalbuphine 0.1mg/kg were compared in total intravenous anaesthesia (TIVA) using a propofol infusion in patients undergoing dilatation and evacuation (D and E). Changes in haemodynamic variables greater than 20% from the base line values were noted.

**Results:** There was no difference found in haemodynamic parameters. There was statistically significant difference found ( $p < 0.05$ ) in postoperative recovery between the two groups.

**Conclusion:** Quality of analgesia was better in nalbuphine group but both drugs provide suitable analgesic supplementation to TIVA (JPMA 57:67;2007).

## **Introduction**

Dilatation and Evacuation is a commonly daycare procedure in obstetrics. Due to requirement for an early discharge, this procedure requires an anaesthetic technique which can provide rapid recovery. With a better cardiovascular stability and a short time to emergence from anaesthesia, TIVA is considered to be better than inhalational technique for short day care procedures.<sup>1</sup>

The advantages of TIVA technique include reduction in the potential for administration of hypoxic gas mixtures, less environmental pollution and absence of exposure of patients and staff to nitrous oxide and volatile agents.<sup>2</sup> Rapid recovery of postoperative psychomotor performance appears to be an additional advantage of TIVA. Propofol remains the most suitable anaesthetic agent for TIVA, it allows for rapid changes in anaesthetic depth and a rapid clear-headed recovery.<sup>3</sup> Analgesia is provided either with nalbuphine or tramadol.

Nalbuphine is a partial kappa agonist /  $\mu$  antagonist opioid of phenanthrene series. It was synthesized in an attempt to produce analgesia without the undesirable side effects of a  $\mu$  agonist, notably respiratory depression and drug dependence. It has been observed that nalbuphine provides cardiovascular stability and there is less nausea and vomiting when used in the TIVA technique.<sup>4</sup>

Tramadol is a mixed compound, which not only stimulates all opioid receptors but also inhibits neuronal nor-epinephrine uptake and serotonin release. Analgesic doses of tramadol produce less respiratory depression than other opioids, owing in part to its non-opioid receptor mediated actions. Equiv-analgesic dose of tramadol has much less effect on respiratory center than pethidine. It has demonstrated that analgesic potential of tramadol relies to a considerable extent on non-opioid receptor mechanisms.<sup>5</sup> Tramadol is used intraoperatively in day care surgeries and post operative analgesic requirement is reduced.<sup>6,7</sup>

Despite these documented advantages of Tramadol, it has never been compared with nalbuphine. This study compares these two drugs for D and E with TIVA technique.

### Methods

The study was performed at a University Hospital after approval from Ethics Review Committee and the human subject protection committee of the Aga Khan University Hospital and after informed consent from the patient. The study included all patients of child bearing age with pregnancy of 12 to 14 weeks duration belonging to ASA I & II group. Excluded from the study were patients who did not give the consent, ASA III and above, previous hypersensitivity to any of the study drugs and anticipated difficult intubations.

It was a prospective randomized double blind study. Total of 70 patients were included, and were randomly divided into two groups 'A' and 'B', with 35 patients in each group undergoing D&E. All patients had standard monitoring throughout the procedure, consisting of non invasive blood pressure (B.P) heart rate (HR), ECG and oxygen saturation.

Group A patients were given intravenous injection Tramadol 1.5 mg/kg after rapid sequence induction with propofol 2mg/kg, succinylcholine 1-1.5mg/kg followed by intubation.

Group B patients received injection Nalbuphine 0.1mg/kg after rapid sequence induction with propofol 2mg/kg, succinylcholine 1-1.5mg/kg followed by intubation. The propofol dose regimen used was that described by Roberts et al.<sup>8</sup> The same regimen was used in both groups.

The analgesic efficacy and haemodynamic stability was monitored, by noting any change in arterial pressure greater than 20% of baseline value, change in heart rate greater than of 20% of baseline and any purposeful movement in response to pain was noted.

At the termination of succinylcholine action patients were allowed to breathe spontaneously. Respiratory rate, tidal volumes, and oxygen saturation were continuously monitored in all patients. Heart rate, Blood pressure, and Spo2 were noted at induction, 1 minute after study drug either nalbuphine or tramadol, then 2, 3 and 5 minutes and there after until the termination of surgery. To evaluate recovery time eye opening on command, and orientation from the end of infusion were recorded.

The student t-test was applied for continuous variables such as HR, BP, MAP and recovery time. The chi square test was applied for categorical variables such as, nausea vomiting and pain score. Data analysis was conduct-

ed through statistical package of social sciences (SPSS 10).

### Results

There was no statistically significant difference in demographic values between the two groups and also in the variables as Heart rate, Systolic and Diastolic blood pressure, Mean arterial pressure (MAP), and oxygen saturation from induction of anaesthesia to end of surgery.

There was a statistically significant difference between the two groups in the recovery profile. Tramadol had a more sedating effect than nalbuphine. Patients receiving nalbuphine woke up earlier and well oriented compared to tramadol. (Table 1 and 2).

During the study, we also evaluated the pain score by visual analogue scale of the patients in both groups. This was noted as (0= No pain, 1= Mild pain, 2= Moderate pain, and 3= Severe pain. In nalbuphine group, 80% of patients had no pain, 19% had mild pain. In the tramadol group, 51% of patients had no pain, 48% had mild pain and no patient complained of moderate or severe pain in both groups in post anaesthesia recovery room (Figure).

### Discussion

Total intravenous anaesthesia (TIVA) is a popular

**Table 1. Haemodynamic variables**

Variables	Nalbuphine	Tramadol	p-value
Heart Rate at Baseline (min)	89.25 ± 15.1	81.09 ± 13.9	0.07
Systolic B.P at Baseline (mmHg)	128.29 ± 12.6	121.00 ± 14.9	0.09
Diastolic B.P at Baseline (mmHg)	78.69 ± 10.4	73.91 ± 9.0	0.14
MAP at Baseline (mmHg)	94.72 ± 10.5	88.97 ± 10.6	0.22
Heart Rate at Induction (min)	109.78 ± 12.1	106.74 ± 11.6	0.28
Systolic B.P at Induction (mmHg)	122.97 ± 23.9	124.80 ± 21.8	0.73
Diastolic B.P at Induction (mmHg)	75.47 ± 19.0	79.60 ± 16.3	0.32
MAP at Induction (mmHg)	90.80 ± 20.7	94.26 ± 17.9	0.45
Heart Rate at 1 to5 min after study drug (min)	93.25 ± 13.8	97.94 ± 13.0	0.14
Systolic B.P at 1 to5 min after study drug (mmHg)	123.22 ± 20.3	122.74 ± 20.2	0.92
Diastolic B.P at 1 to5 min after study drug (mmHg)	76.17 ± 17.2	75.14 ± 14.4	0.78
MAP at 1 to5 min after study drug (mmHg)	91.11 ± 17.0	90.34 ± 15.2	0.84
Heart Rate at 10 min after study drug (min)	82.97 ± 10.0	88.56 ± 11.5	0.05
Systolic B.P at 10 min after study drug (mmHg)	120.69 ± 10.8	119.24 ± 10.0	0.55
Diastolic B.P at 10 min after study drug (mmHg)	69.39 ± 9.0	70.12 ± 7.3	0.71
MAP at 10 min after study drug (mmHg)	85.17 ± 8.5	86.35 ± 7.1	0.53

**Table 2. Recovery from anaesthesia**

Variable	Nalbuphine	Tramadol	p-value
Time to orientation from the end of TIVA (min)	19.39 (5.7)	23.77 (7.8)	< 0.05
Time to opening of eyes from the end of TIVA (min)	8.39 (3.0)	11.46 (3.8)	< 0.05

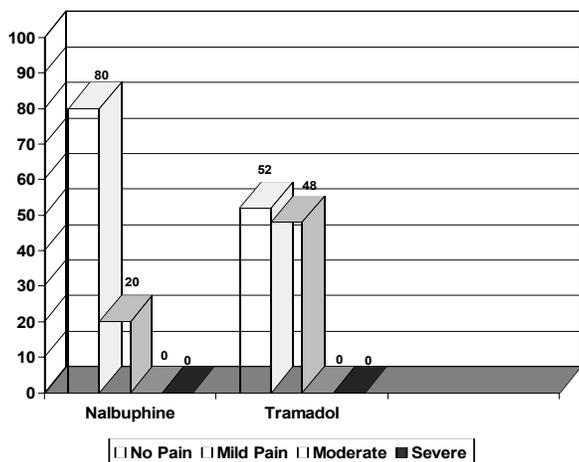


Figure. Comparison of pain scores.

## Discussion

Total intravenous anaesthesia (TIVA) is a popular and established anaesthetic technique, mainly because of the availability of newer anaesthetic drugs with short half lives and advances in infusion pump technology making the administration of these drugs easier. Currently propofol is regarded as the most suitable anaesthetic agent for TIVA due to its short duration of action, minimal side effects and rapid recovery profile.<sup>9,10</sup>

Ideally a short half life narcotic agent should be used with propofol, as propofol has no analgesic properties; this will also reduce the dose of intravenous anaesthetic, resulting in lesser side effects. Fentanyl<sup>11</sup> alfentanil<sup>12</sup> sufentanil<sup>13</sup> and remifentanil<sup>14,15</sup> have all been used during TIVA. In a multicenter study of 6,161 patients, using TIVA with propofol and remifentanil proved to be safe, tolerable and effective with a high degree of acceptance by the patients.<sup>16</sup> It was found that postoperative pain reduced with TIVA technique, and also there were reduced analgesic requirements.<sup>17</sup>

One of the challenges of working in a developing country is the non-availability of newer short acting narcotics. This diverts anaesthesiologists to look for other alternatives. Longer acting narcotics, like pethidine and morphine, have been used in TIVA<sup>18</sup> and found to be safe alternatives. Agonist-antagonist narcotics have been used instead of short acting narcotics in both developed and less affluent countries. Their use has been reported by a number of investigators.<sup>19</sup>

However due to undesirable side effects of pethidine

and morphine, we decided to use tramadol and nalbuphine with TIVA, as these are not controlled drugs, and easily available on demand. Effects of nalbuphine have not been directly compared with tramadol, and their use in short gynaecological and obstetrical procedures, has not been published in literature.

Nalbuphine is chemically related to naloxone. It has a ceiling effect on respiratory depression and is said to cause less nausea and vomiting compared to morphine, pethidine or pentazocine.<sup>20</sup> In our study in nalbuphine group we did not encounter nausea and vomiting, although a 2-22% of nausea has been previously reported.<sup>21</sup> In this study, dose of nalbuphine was 0.1mg/kg and tramadol 1.5mg/kg given as a bolus dose. Haemodynamic stability was present in both groups.

Previously a double-blind investigation was undertaken to compare the efficacy of nalbuphine and fentanyl in the prevention of pain in patients undergoing termination of pregnancy in day care surgery. Patients who received nalbuphine had significantly lower pain scores compared to fentanyl and it proved to be more satisfactory for day surgery than the more commonly used fentanyl.<sup>22</sup>

Tramadol has been used clinically; it binds to  $\mu$ -opioid receptors with lower affinity than morphine, which suggests that the antinociceptive action of tramadol may not be due to opioid receptor binding only. Several studies have shown evidence that tramadol inhibits the reuptake of monoamines, as do antidepressant drugs such as desipramine. Tramadol inhibits the reuptake of nor epinephrine and serotonin.<sup>23</sup> Recently tramadol has been used with TIVA, and results shows that it can be safely administered pre- and intraoperatively as pre-emptive or preventive analgesia without modification of the depth of anaesthesia.<sup>24</sup> Tramadol has been previously used effectively for management of gynec-obstetric pain.<sup>25</sup>

Robert's regimen<sup>8</sup> was used for the TIVA technique. This manual scheme was designed to achieve a blood propofol concentration of 3-4 $\mu$ g/kg within five minutes. The use of manual regimens is now replaced by Target Controlled Infusion (TCI) pumps in developed countries, but again these are not generally available in the developing world. Robert's regimen was effectively used for TIVA in our study, and no case of awareness and recall was reported during the study.

The recovery profile in our study showed the nalbuphine group to have early recovery from anaesthesia as compared to the tramadol group. In a previously described study<sup>22</sup> nalbuphine was compared with a short acting narcotic "fentanyl". The recovery profile of nalbuphine group was not significantly different from the fentanyl group.

Our study showed that recovery from anaesthesia was early in nalbuphine group. Tramadol caused sedation in 2.4%.<sup>26</sup>

## Conclusion

In conclusion, both drugs were found to be satisfactory for use in TIVA. In a situation where short acting narcotics are not available, nalbuphine or tramadol provided adequate analgesia in combination with propofol.

In our study, nalbuphine had a better haemodynamic stability and an early post operative recovery with better pain control in comparison with tramadol, Nalbuphine would be a better choice when using TIVA technique in the day care surgery for D and E.

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