The Effects of Entonox and Epidural Analgesia on Arterial Oxygen Saturation of Women in Labour

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The arterial oxygen saturation of 60 mothers in the first stage of labour was monitored using pulse oximetry. Half the mothers received epidural analgesia and the other half inhaled Entonox for pain relief. Eight women in epidural group had at least one episode of significant arterial oxygen desaturation (SpO2 < 90%) as compared to twelve women in Entonox group (P = 0.273). There was little difference in the number of hypoxic episodes experienced by either group, there were 22 periods in epidural group as compared to 36 periods in Entonox group, although their mean duration of these hypoxic episodes was longer in women of Entonox group that is (12 – 72 seconds) while in epidural group that (12 – 36 seconds) (P = 0.002). The severity of these hypoxic episodes was greater in the Entonox group than the epidural group (P = 0.02)

Key Words: Anesthesia = Obstetrics, Analgesics = Entonox, Anesthetic Techniques = Regional epidural, Hypoxia.

Introduction
Methods commonly used during labour for pain relief have great concern of its safety both to the mother and the fetus. Entonox has been regarded as safe and satisfactory analgesic for the management of pain in labour. However there is growing body of evidence for hypoxic episodes which points to increasing concerns about the overall safety of this method of pain relief. Epidural analgesia for labour pains has become very popular amongst the mothers, obstetricians and anesthesiologists alike. During the past two decades, it has served a real benefit for pain relief and wonder for mothers. The effects of epidural analgesia on maternal oxygenation needs to be compared with the Entonox inhalation for pain relief.

Methods
This study was performed at Shaikh Zayed Hospital / FPGMHI Lahore, proper approval of the study was taken from the hospital ethical committee and college of physicians and surgeons Pakistan. Sixty mothers of age 20—35 years and weight 35 – 60 kg having ASA status I, II undergoing normal labour were selected. Informed consent of the patients were taken.

Criteria of inclusion was antenatally booked cases who agreed with either of procedures, belonging to ASA I, II, age 20—35 years, weight 35—60 kg with good obstetric and medical history. Criteria of exclusion was eclampsia, pre-eclamptic toxemia, chronic obstructive airway disease, diabetes mellitus, ischemic heart disease, any coagulopathies, hypovolaemia, patient’s informed refusal, neurological disorder, symptoms associated with herniated disc, systemic infection, marked obesity.

To start with a good I/V line. Mothers were randomly allocated in two groups depending on their choice of analgesia. Group I received epidural analgesia Group II received entonox analgesia. In Group I, I/V line started with Ringer lactate and 500cc infused as pre-load. Heart rate and blood pressure was recorded. Women in first stage of labour and having a cervical dilatation of more than 2cm, SpO2 was recorded using pulse oximetry with a finger probe. Epidural injection and catheter was placed at the L3-4 or L2-3 with analgesic level extending to the T10 level. Maintenance of analgesia was done with bolus injections of 0.25% bupivacaine if needed. The labouring mother will be pain free. Maternal oxygen saturation SpO2 was continuously monitored for 40 – 50 minutes using pulse oximetry.

The second group received Entonox for pain relief. The mothers received entonox breath at the start of their contractions and a wright spirometer was used to measure the volume of Entonox inhaled during each contraction. Maternal arterial oxygen saturation was measured continuously for 40 – 50 minutes using pulse oximetry. Contractions occurring during the period was recorded.

Results
Sixty parturients were included in the study during first stage of labour. Thirty parturients in each group with similar characteristics Table 1 for baseline readings of heart rate, blood pressure, arterial oxygen saturation, cervical dilatation, and study duration. The number of uterine contractions recorded during study period ranged from 11 – 14.

In Table 2, there were 6095 assessment periods, each of 12 second duration in the entonox group and 5500 assessment periods in epidural group. The median number assessed per mother was 211 (range 200 – 230) in epidural group and 203 (range 200 – 225) in entonox group. Eight women in epidural group had at least one episode of significant arterial oxygen desaturation in epidural group as compared to twelve women.
in entonox group (p 0.273). The total number of periods of significant desaturation of SpO₂ < 94% was greater in entonox group (104 periods) as compared to the epidural group (45 periods). (P=0.00002), which is statistically significant. Hypoxic episodes SpO₂ < 90% noticed in both groups there were 22 periods

<table>
<thead>
<tr>
<th>Table 1: Baseline.</th>
<th>Group I</th>
<th>Group II</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical dilatation (cm)</td>
<td>4.9 ± 0.1394</td>
<td>4.1 ± 0.9850</td>
<td>0.4950</td>
</tr>
<tr>
<td>Heart Rate (minute)</td>
<td>83.9071 ± 0.5950</td>
<td>81.0921 ± 0.9895</td>
<td>0.4350</td>
</tr>
<tr>
<td>Blood pressure systolic (mmHg)</td>
<td>115.93 ± 0.9650</td>
<td>117.70 ± 1.2015</td>
<td>0.5321</td>
</tr>
<tr>
<td>Blood pressure diastolic (mmHg)</td>
<td>78.2541 ± 0.9912</td>
<td>81.0902 ± 1.1010</td>
<td>0.4958</td>
</tr>
<tr>
<td>SpO₂</td>
<td>98.01 ± 0.1030</td>
<td>98.05 ± 0.9310</td>
<td>0.5431</td>
</tr>
<tr>
<td>Study duration (minutes)</td>
<td>42.10 ± 0.9875</td>
<td>42.5 ± 9535</td>
<td>0.6017</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Table 2: Effect of Analgesic Technique on Maternal Arterial Oxygen Saturation.</th>
<th>Group I Epidural (n = 30)</th>
<th>Group II Entonox (n = 30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. 12 seconds periods of SpO₂ Total number</td>
<td>5500</td>
<td>6095</td>
<td>0.4950</td>
</tr>
<tr>
<td>Assessed per mother</td>
<td>211 (200 – 230)</td>
<td>203(200 – 225)</td>
<td>0.4950</td>
</tr>
<tr>
<td>Total number of desaturations SpO₂ &lt; 94%</td>
<td>45</td>
<td>104</td>
<td>0.00002</td>
</tr>
<tr>
<td>Number of mothers desaturating</td>
<td>8</td>
<td>12</td>
<td>0.273*</td>
</tr>
<tr>
<td>Hypoxic episodes SpO₂ &lt; 90% total number</td>
<td>22</td>
<td>36</td>
<td>0.146</td>
</tr>
<tr>
<td>Duration (seconds)</td>
<td>17 (12 – 36)</td>
<td>29.8 (12 – 72)</td>
<td>0.002</td>
</tr>
<tr>
<td>Severity</td>
<td>89% (87 – 89%)</td>
<td>88% (89 – 84%)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

P < 0.05 significant
+ (Chi Square = 23.3624 df = 1)
* (Chi Square = 1.20 df = )

in epidural group as compared to 36 periods in entonox group.

The mean duration of these hypoxic episodes was longer in women of entonox group that is 29.8 seconds (12 – 72 seconds) while in epidural group 17 seconds (12 – 36 seconds) (p = 0.002). The severity of these hypoxic episodes was greater in the entonox group (median 88% range 84 – 89%) than the epidural group (median 89% range 87 – 89%) (p = 0.02).

Qualitative data were analysed for their assistance and significance of the proportions using non-parametric Chi-square test values of chi-square with respective degrees of freedom (df) are provided where necessary. Student’s t – test for independent samples is utilized to test the possible significance of difference between the means of two groups for quantitative data. A value of P < 0.05 is considered as significant.

**Discussion**

The results of our study show that mild hypoxaemic episodes (SpO₂ < 94%) occur more frequently in entonox group of parturients. Hypoxic episodes (SpO₂ < 90%) are more in duration and severity in entonox group of parturients as compared to epidural group. Although significant desaturations occur in both groups (Table 3).

In our study certain limitations were present:

1. Control group of parturients comprising of no analgesia was not included.
2. Time lag of significant arterial desaturation episode of parturient and reading on pulse oximetry was there because of fixed response time of pulse oximeter.
3. In Entonox inhalation, time lag between the onset of uterine contractions and perception of pain with the initiation of inhalation of entonox and its maximum analgesic effect.
4. Measurements of minute ventilation, ETO₂, ET-CO₂, ETN₂O could not be done.
5. Apgar score of baby was not included in our study.
6. Study period was limited to 40-50 minutes of first stage of labour.

Results of other study are supporting our findings Reed et al (1989),\(^1\) studied the oxygen saturation during first and second stage of labour. Study was carried on three groups of parturients receiving entonox, pethidine, and combined pethidine and entonox. A control group of parturients comprises of no analgesia. They concluded that SpO\(_2\) < 90% were recorded during normal labour without analgesia and hypoxic episodes recorded in three groups. Severe hypoxic episodes were marked in last hour of first stage of labour. They studied the Apgar scores of babies and noticed no adverse effect on neonatal outcome. This study did not measure minute ventilation, ETCO\(_2\), ETN\(_2\), ETO\(_2\) and the degree of analgesia to equal effectiveness in all groups.

Einarsson et al (1996)\(^2\) studied about the mechanism of diffusion hypoxia using N\(_2\)O during labour and they measured minute ventilation, ETCO\(_2\), ETO\(_2\), ETN\(_2\).O. The results showed the periods of significant desaturations in two parturients out of twenty four. In this study, there was associated decrease in ETO\(_2\) concentration with these periods of desaturations, ETN\(_2\)O concentration was also low at that time therefore diffusion hypoxia could not be attributed. In this study, they measured the ETO\(_2\) but its exact time with pulse oximeter may be a lag because of response time. This study made clear that hypoxic episodes occurred in entonox analgesia which are more attributable to reduced maternal oxygen reserves during uterine contractions with increased oxygen consumption.

Griffen et al (1995),\(^3\) studied maternal arterial oxygen saturation from the last hour of first stage until delivery. They divided four groups of parturients comprising of no analgesia, pethidine with intermittent entonox, extradural bupivacaine and extradural infusion of bupivacaine with fentanyl. The results showed the SpO\(_2\) < 94%, the lowest median saturation in extradural group 0 min / hour in the last hour of first stage. The incidence of desaturation was significantly lower than in the pethidine/etonox group (1.4 min / hour) and the extradural bupivacaine/fentanyl group (0.9 min/hour) and no analgesia group (3min/hour). They found no correlation between maternal arterial oxygen saturation in second stage and any adverse neonatal outcome, which included Apgar score and umbilical artery and vein blood gases.

In this study, the results showed the low incidence of hypoxaemia in extradural group in last hour of first stage. This finding of extradural analgesia is like our finding although we measure arterial oxygen saturation in initial hours of first stage of labour. In this study, effect of entonox is studied with systemic administration of pethidine which indicates inadequate analgesia in last hour of first stage of labour.

Hyperventilation in association with use of 50% N\(_2\)O in oxygen is believed to be an important cause of desaturation (Latto et al 1973)\(^4\) by reducing the ventilatory drive as a results of hypocapnia. This secondary hypoventilation combined with a reduced oxygen reserve may cause hypoxia. Nitrous oxide may depress the ventilatory drive further by reducing the response to hypoxia.\(^5\)

Hagerdal et al (1983)\(^6\) studied the oxygen consumption (VO\(_2\) and minute ventilation VE) were measured between and during uterine contractions in the first stage of labour before and after lumbar epidural analgesia in eleven women, who served as their own controls. VO\(_2\) and VE between contractions were unchanged by lumbar epidural analgesia to T\(_10\). Before lumbar epidural analgesia both VO\(_2\) and VE were increased significantly during contractions by 63% and 74% respectively. After lumbar epidural analgesia there was no significant increase of VO\(_2\) or VE during contractions. In the second stage of labour, VO\(_2\) and VE were measured in seven patients those have no analgesia or sedation and ten patients having complete pain relief produced by lumbar epidural analgesia. Measurements were taken 5 – 10 minutes before delivery. During contractions with pushing, VO\(_2\) and VE were decreased by 25% and 31% respectively, in patients having lumbar epidural analgesia as compared with patients having no analgesia or sedation.

These results show the increase in VO\(_2\) and VE are due primarily to pain associated with uterine contractions and lumbar epidural analgesia decreases the work of breathing and the oxygen consumption of the parturient in both the first and second stages of labour.

The findings of this study are attributed to maternal physiological demands during labour pains and benefit of effective analgesia to reduce work of breathing during labour.

Porter et al (1996),\(^7\) studied the incidence of desaturation in last hour of first stage and second stage. They also studied neonatal outcome. Extradural analgesia was used by local anaesthetic in one group and fentanyl in second group. The results show increased incidence of desaturation in the extradural fentanyl group to SpO\(_2\) < 95% during the whole of the second stage compared with controls (P < 0.01). They assessed fetal well being using umbilical arterial and venous blood samples at delivery for measurement of acid base and blood gas status. In this study, arterial oxygen desaturations may be related to act of pushing, perhaps due to breath holding. They found, that plasma fentanyl levels are not significantly raised to have any systemic effects on ventilation. The study duration was limited to the last hour of first stage and second stage. The result show that significant desaturations of maternal oxygenation occurred with extradural analgesia, with increased incidence in mothers...
with extradural fentanyl.

Why significant arterial desaturations occurred in normal labour and during analgesia? The physiological changes during pregnancy and labour reduces the ventilatory functions and increase in oxygen consumption. Functional residual capacity and residual volume are reduced. Oxygen consumption increased due to pain and resulting hyperventilation are the main cause of increased oxygen requirement in painful labour. Hyperventilation during uterine contractions causes reduced ventilatory drive by causing hypocapnia and a period of apnoea combined with the reduced oxygen reserve of labouring woman may cause hypoxia (Yacoub et al 1976). In addition; nitrous oxide can depress ventilatory drive further by reducing the response to hypoxia.

Significant arterial desaturations SpO₂ < 94% were also found in epidural analgesia, although their duration and severity was less as compared to entonox analgesia as shown in Table II. The reason for arterial oxygen desaturations in the epidural group is unclear. It may be related to the reduced oxygen reserve in all labouring women. The minute ventilation, ETO₂, and oxygen consumption were not measured in our study. It may be possible that some hyperventilation occurred with resulting apnoea in spite of good analgesia.

What level of hypoxia should be considered clinically significant and what duration of desaturation is regarded as critical and potentially harmful to mother and fetus? It has been suggested that SpO₂ < 85% for 6 min/hour may be harmful to adults. Reeder (1991) based this definition of severe hypoxia on ECG changes on holter monitoring after abdominal vascular surgery.

In our study, none of women fulfilled this definition of arterial oxygen desaturation. The effect of maternal hypoxaemia on the baby also depends on maternal PaCO₂. A low PaCO₂ from pain induced hyperventilation results in respiratory alkalosis abolishing the Bohr effect and causing vasoconstriction reducing uterine blood flow (Levinson and Shnider 1974).

It is concluded that the maternal oxygen saturation should be monitored during entonox inhalation and epidural analgesia, greater vigilance and monitoring is required in high risk parturient.

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References