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CLINICAL INVESTIGATIONS

# Nocturnal hypoxaemia in late pregnancy

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## Summary

We have measured arterial oxygen saturation ($Sp_{O_2}$) continuously overnight in 13 non-pregnant (NP), 13 pregnant normotensive (NPIH) and 15 pregnant patients with a diagnosis of pregnancy-induced hypertension (PIH). The two pregnant groups did not differ in duration of pregnancy (>35 weeks) and none was in labour. There was no significant difference in age between these three groups. Mean $Sp_{O_2}$ in group NP was 98.5 % (range 97–99 %). This was significantly higher than that in group NPIH (95.2 (91–98) %) and group PIH (94.9 (89–99) %). In seven pregnant patients, more than 20 % of the recording was spent with an $Sp_{O_2}$ < 90 %. We conclude that a significant number of pregnant women (>35 weeks' gestation) suffer from prolonged nocturnal hypoxaemia. (*Br. J. Anaesth*. 1995; **75**: 678–682)

**Key words**

Hypoxaemia. Pregnancy. Oxygen, saturation.

It has been known for many years that patients may be hypoxaemic for several days after operation [1]. More recent research, measuring arterial oxygen saturation after operation, has demonstrated that patients may experience profound hypoxaemic episodes on the second and third postoperative nights [2]. A reduction in functional residual capacity (FRC) [3] and an increase in REM sleep (which is associated with an enhanced tendency to respiratory obstruction [2]) are the major factors in the aetiology of desaturation. During these periods of desaturation, significant myocardial ischaemia may occur and this may be associated with increased cardiovascular morbidity and mortality in the postoperative period [4].

During pregnancy, there is a progressive reduction in FRC. This reduced FRC, in combination with increased oxygen consumption, may render the parturient more susceptible to hypoxaemia during periods of apnoea or airway obstruction.

We have measured nocturnal arterial oxygen saturation in three groups of women to determine the extent of any hypoxaemia episodes; those in group 1 were non-pregnant controls (NP), those in group 2 were pregnant and normotensive (NPIH), and those in group 3 were pregnant with a diagnosis of pregnancy-induced hypertension (PIH). A preliminary account of this work was presented to the Obstetric Anaesthetists Association and published elsewhere in abstract form [5].

## Patients and methods

The study was approved by the local Ethics Committee and written informed consent was obtained from all subjects. We recruited 44 subjects allocated to one of three groups. The non-pregnant group (NP) comprised healthy female volunteers of child bearing age recruited from staff of the Departments of Anaesthesia and Gynaecology. The normotensive group (NPIH) were ASA I patients studied before either elective Caesarean section (for breech or previous Caesarean section) or induction of labour. The hypertensive group (PIH) comprised patients admitted with this diagnosis for observation on the obstetric ward. They fulfilled the criteria for diagnosis of pregnancy-induced hypertension according to a recognized definition [6]. Patients in both pregnant groups were greater than 35 weeks' gestation and not in labour.

An Edentec Model 3711 digital recorder was used to record overnight pulse oximetry and respiratory pattern. This device comprises a lightweight bedside recorder with several non-invasive probes attached to the patient. These recorded the following variables: arterial oxygen saturation ($Sp_{O_2}$), heart rate, chest impedance and airflow at the nose.

At the beginning of each study a flexible $Sp_{O_2}$ probe (adult Nellcor D25 sensor) was attached to the first or second toe. $Sp_{O_2}$ levels were updated on every pulse, the result being a two-pulse average. The accuracy of $Sp_{O_2}$, as provided by the manufacturers, is $\pm 2$ % in the 70–100 % $Sp_{O_2}$ range and $\pm 3$ % in the 61–69 % $Sp_{O_2}$ range.

Chest impedance and heart rate were recorded by attaching two electrodes to each side of the chest (middle axillary line at T4–5 level). Chest wall motion was measured by passing a constant current through the varying resistance of the chest wall and measuring the changes in voltage. Heart rate (QRS detection) was measured by a digital interval circuit and has an internal accuracy of $< \pm 4$ beat $min^{-1}$ (range 25–200 beat $min^{-1}$). Nasal airflow was measured by a thermistor attached between the upper lip and the nose.

All subjects were shown how to disconnect and reconnect the recorder to enable visits to the toilet, etc. All overnight recordings were downloaded on to a desktop computer and analysed using an ETS (Infiniti Medical) software program.

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*Table 1* Description of patients with pregnancy-induced hypertension. F = face, H = hand, A = ankle, Ab = abdomen

| Subject No. | Arterial pressure (mm Hg) | Proteinuria | Oedema |
|---|---|---|---|
| 1 | 130/95 | Nil | Nil |
| 2 | 130/100 | Nil | Nil |
| 3 | 180/120 | Trace | F, H, A |
| 4 | 150/105 | 2+ | H, A, Ab |
| 5 | 140/100 | Nil | Nil |
| 6 | 140/90 | Nil | F, A, H |
| 7 | 130/100 | 2+ | F, A |
| 8 | 140/100 | Trace | Nil |
| 9 | 140/100 | 1+ | Nil |
| 10 | 150/95 | Trace | H, A |
| 11 | 150/110 | 2+ | H, A |
| 12 | 160/90 | Nil | H, A, F, Ab |
| 13 | 150/100 | 1+ | A |
| 14 | 135/90 | 2+ | H |
| 15 | 145/100 | Nil | Nil |

DATA ANALYSIS

For each overnight recording, mean $Sp_{O_2}$ was calculated and a cumulative saturation plot constructed. Wilcoxon rank sum test was used to compare mean $Sp_{O_2}$, gestation and Apgar scores, and ANOVA was used to compare age, body mass index (BMI) and duration of recording between the three groups.

The pregnant subjects were classified into those with mean $Sp_{O_2} > 95\,\%$ and mean $Sp_{O_2} \leqslant 95\,\%$ and the Student's $t$ test was used to compare fetal birth weight and BMI. Fisher's exact test was used to compare smokers. The hypoxic pregnant subjects ($Sp_{O_2} \leqslant 95\,\%$) were compared with the non-pregnant subjects using Fisher's exact test. $P < 0.05$ was regarded as significant.

*Table 2* $Sp_{O_2}$ data (%) obtained from non-pregnant volunteers (NP), patients with a normal pregnancy (NPIH) and those with a diagnosis of pregnancy-induced hypertension (PIH). (ETS software only calculates mean $Sp_{O_2}$. The lower quartile is extrapolated from the cumulative saturation plot to the nearest whole number)

| | BMI | Smoker | Mean $Sp_{O_2}$ | Initial $Sp_{O_2}$ | Lower quartile $Sp_{O_2}$ | % Time $Sp_{O_2}$ <90 % |
|---|---|---|---|---|---|---|
| NP subjects | | | | | | |
| 1 | 20.8 | No | 98 | 99 | 96 | 0 |
| 2 | 20.2 | No | 99 | 100 | 98 | 0 |
| 3 | 20.8 | No | 99 | 100 | 98 | 0 |
| 4 | 17.4 | No | 98 | 100 | 97 | 0 |
| 5 | 31.1 | No | 99 | 100 | 98 | 0 |
| 6 | 17.9 | No | 99 | 100 | 97 | 0 |
| 7 | 31.3 | No | 97 | 98 | 96 | 0 |
| 8 | 21.5 | No | 99 | 100 | 98 | 0 |
| 9 | 22.8 | No | 99 | 99 | 98 | 0 |
| 10 | 25.2 | No | 98 | 100 | 97 | 0 |
| 11 | 24.5 | No | 99 | 100 | 98 | 0 |
| 12 | 22.6 | No | 99 | 100 | 97 | 0 |
| 13 | 21.1 | No | 98 | 98 | 96 | 0 |
| NPIH patients | | | | | | |
| 1 | 22.4 | Yes | 97 | 98 | 96 | 0 |
| 2 | 28.3 | No | 91 | 98 | 89 | 40 |
| 3 | 32.2 | No | 95 | 97 | 94 | 0 |
| 4 | 30.1 | No | 96 | 96 | 95 | 0 |
| 5 | 33.5 | No | 98 | 99 | 97 | 0 |
| 6 | 29.4 | No | 94 | 98 | 93 | 2 |
| 7 | 29.1 | No | 92 | 93 | 90 | 21 |
| 8 | 25 | Yes | 98 | 99 | 97 | 0 |
| 9 | 24.2 | Yes | 96 | 97 | 95 | 0 |
| 10 | 29.4 | No | 93 | 98 | 90 | 20 |
| 11 | 28 | No | 94 | 96 | 92 | 0 |
| 12 | 29.4 | No | 98 | 99 | 96 | 0 |
| 13 | 34.5 | No | 96 | 98 | 93 | 2 |
| PIH patients | | | | | | |
| 1 | 43.2 | No | 99 | 100 | 97 | 0 |
| 2 | 23.9 | No | 97 | 98 | 96 | 0 |
| 3 | 38 | No | 92 | 100 | 90 | 28 |
| 4 | 27.3 | No | 93 | 100 | 91 | 5 |
| 5 | 29.4 | No | 96 | 96 | 95 | 0 |
| 6 | 32.2 | No | 92 | 97 | 90 | 25 |
| 7 | 35.7 | No | 92 | 94 | 90 | 26 |
| 8 | 25.7 | No | 98 | 100 | 95 | 0 |
| 9 | 26.4 | No | 96 | 99 | 95 | 0 |
| 10 | 36.6 | No | 95 | 96 | 94 | 0 |
| 11 | 31.2 | No | 97 | 97 | 95 | 0 |
| 12 | 41.1 | Yes | 89 | 96 | 87 | 72 |
| 13 | 26.8 | Yes | 98 | 100 | 97 | 0 |
| 14 | 34.5 | Yes | 97 | 98 | 96 | 0 |
| 15 | 28 | Yes | 93 | 96 | 92 | 4 |

## Results

Data from three subjects were rejected because of non-compliance. The remaining 41 subjects comprised 13 non-pregnant, 13 normotensive and pregnant, and 15 pregnancy-induced hypertensive women. Patients in the hypertensive group had systemic arterial pressures varying from 130/90 to 180/120 mm Hg, proteinuria ranging from 0 to 2+, and all were asymptomatic (table 1). Patient characteristics and oxygenation data for all groups are shown in tables 2 and 3. One patient was receiving carbamazepine for epilepsy (subject No. 3, PIH). No other patients were receiving drugs during the study.

The duration of recording for the non-pregnant group was significantly longer than that for both pregnant groups ($P < 0.01$). There was no difference between the mean ages of the three groups (table 3). As expected, BMI (weight/height$^2$) was significantly larger in the pregnant groups ($P < 0.01$) compared with the non-pregnant group.

Mean overnight $Sp_{O_2}$ for both pregnant groups was significantly lower than that in the non-pregnant group ($P < 0.001$). There was no difference between groups PIH and NPIH (table 3). There were significantly more pregnant subjects with hypoxaemia ($Sp_{O_2} \leqslant 95\,\%$) than non-pregnant subjects ($P = 0.002$) (table 3).

The pregnant subjects were classified into those with mean $Sp_{O_2} \leqslant 95\,\%$ ($n = 13$) and those with $Sp_{O_2} > 95\,\%$ ($n = 15$). There was no significant difference between fetal birth weight, Apgar scores at 1 and 5 min, BMI or the number of smokers between these two groups (table 4).

In seven subjects, all from the pregnant groups, more than 20 % (range 20–73 %) of the period of their overnight recordings revealed an $Sp_{O_2} < 90\,\%$. The cumulative saturation plot for one of these subjects is shown in figure 1A (subject No. 12, PIH).

All except two subjects who exhibited periods of overnight hypoxaemia (mean $Sp_{O_2} \leqslant 95\,\%$) had $Sp_{O_2} > 95\,\%$ when the Edentec monitor was attached at the beginning of the study. Both these patients had an $Sp_{O_2}$ of 98 % at the end of the study (subject No. 7, PIH, and subject No. 7, NPIH).

The nature of the desaturations can be classified generally into two types: continuously low baseline $Sp_{O_2}$ (fig. 2) or combinations of this with episodic features. The lower quartile $Sp_{O_2}$ values were generally only slightly lower than the mean $Sp_{O_2}$ values suggesting a relatively steady baseline $Sp_{O_2}$ with little variability.

Analysis of chest impedance and airflow signals suggested that none of the hypoxaemic events could be attributed to apnoea or obstructive episodes.

*Table 4* Fetal birth weight, BMI, Apgar (mean (SEM) or median (range)) and number of smokers in patients with high and low $Sp_{O_2}$. Note that both normal and pregnancy-induced hypertensive patients feature in both subgroups

| | $Sp_{O_2} \leqslant 95\,\%$ ($n = 13$) | $Sp_{O_2} > 95\,\%$ ($n = 15$) |
|---|---|---|
| Birth weight (kg) | 3.15 (0.10) | 3.23 (0.17) |
| BMI(kg m$^{-2}$) | 31.9 (1.25) | 29.3 (1.41) |
| Apgar 1 min | 9 (6–9) | 9 (3–10) |
| Apgar 5 min | 10 (9–10) | 10 (8–10) |
| Smokers (No.) | 2 | 5 |

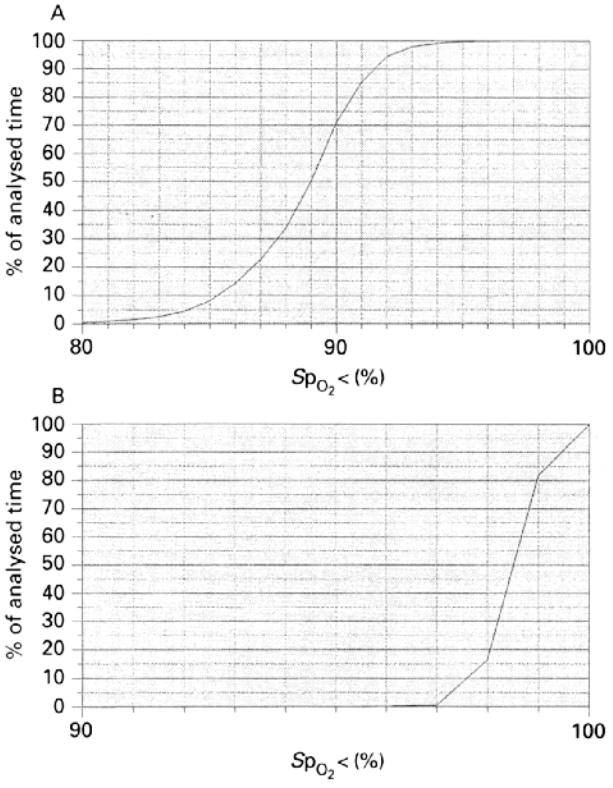


*Figure 1* Duration of period of recording spent at various levels of arterial oxygenation. A: Duration of recording in this patient (subject No. 12, PIH) was 231 min. B: Duration of recording was 451 min (subject No. 11, NP).

## Discussion

We have found that a significant number of pregnant women (both PIH and NPIH groups) exhibited arterial desaturation ($Sp_{O_2} \leqslant 95\,\%$) for prolonged

*Table 3* Duration of recording, patient characteristics, mean saturation (mean (SD or range)) and number of subjects with a mean $Sp_{O_2} \leqslant 95\,\%$. NP = Non-pregnant, NPIH = normal pregnant patient, PIH = pregnancy-induced hypertensive patient. ** $P < 0.01$, *** $P < 0.001$ compared with both pregnant groups

| | NP ($n = 13$) | NPIH ($n = 13$) | PIH ($n = 15$) |
|---|---|---|---|
| Record length (min) | 480 (61)** | 330 (91) | 385 (103) |
| Age (yr) | 28 (21–38) | 30 (17–42) | 31 (21–39) |
| BMI (kg m$^{-2}$) | 22.9 (4.3)** | 28.9 (3.5) | 32 (5.9) |
| Mean $Sp_{O_2}$ (%) | 98.5 (97–99)*** | 95.2 (91–98) | 94.9 (89–99) |
| No. of subjects with mean $Sp_{O_2} \leqslant 95\,\%$ | 0 | 6 | 7 |

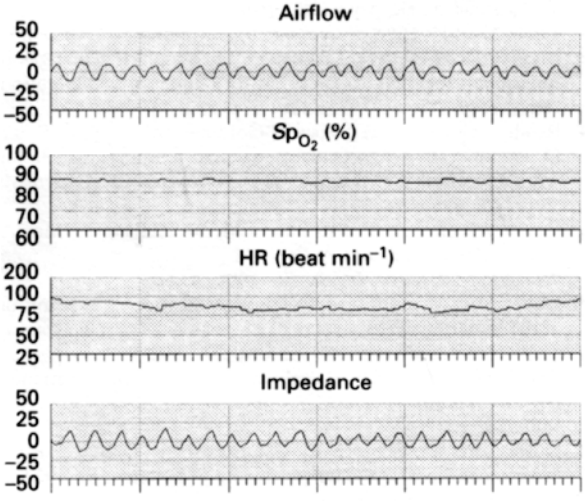


*Figure 2* Record obtained from the Edentec recorder showing a 60-s period. Top tracing represents airflow at the nose assessed by nasal thermistor, below arterial oxygenation measured by pulse oximeter, below heart rate (HR) from ECG recording (note change of scale if > 100 beat min$^{-1}$) and at the bottom, chest impedance recording from chest electrodes indicating respiration (subject No. 2, NPIH, at 05:58). Note the continuous $Sp_{O_2}$ value of approximately 85 % and the absence of respiratory obstruction.

periods during the night compared with non-pregnant women. The cause of this desaturation is not clear from our data but from analysis of chest impedance and airflow recordings during the periods of desaturation, we have excluded apnoea and airway obstruction as potential causes. The difference in BMI between the pregnant and non-pregnant groups is unlikely to explain this difference in overnight $Sp_{O_2}$ but it would be difficult to obtain non-pregnant matching controls to totally exclude body weight alone as the explanation for this phenomenon. The durations of recording were longer in the non-pregnant group because more pregnant subjects removed the monitoring probes earlier in the morning.

One of the most consistent changes in pulmonary function during pregnancy is a reduction in functional residual capacity (FRC) and residual volume (RV). These are reduced by approximately 21 % and 22 %, respectively, at term compared with respiratory volumes in non-pregnant patients [7]. Norregaard and colleagues observed that there was a significant reduction in FRC and RV when the parturient changed from the sitting to the supine position. They found that supine FRC in the third trimester was less than half the predicted value but there was no change in arterial saturation [8]. Bevan and colleagues observed that in a group of 20 patients, the closing volume was greater than the FRC in the last month of pregnancy in 10 sitting and six supine patients [9]. We were unable to record the sleeping position of our subjects but we believe that a reduction in FRC must have contributed to the desaturation.

An increase in REM sleep is associated with increased frequency of hypoxaemic episodes after major surgery [2]. In this situation, the respiratory disturbance is similar to that of patients with sleep apnoea syndrome, that is apnoeic episodes with transient periods of oxygen desaturation. We were not assessing if REM sleep was present but there were no apnoeic episodes (either central or obstructive) recorded by the monitor.

The data analysed in our study represented the readings obtained from the whole period when the probes were attached, that is when the patient was both awake and asleep, and we do not know what proportion of the total recording time was spent with the patient asleep. The majority of patients had $Sp_{O_2}$ > 95 % when initially attached to and detached from the monitor. This may suggest that desaturations occurred only during periods of sleep. If this is so, then our analyses underestimated the severity of hypoxaemia present during sleep, but unfortunately we cannot analyse this aspect further.

Inaccurate $Sp_{O_2}$ values may be caused by artefacts produced predominantly by motion or poor contact of the probe [10]. The ETS software program analysis automatically excludes data of poor quality or where heart rate derived from the oximeter differs from that recorded from the chest leads. All probes were attached securely with tape and we have surveyed all the recordings by visual inspection and are satisfied that we have rejected all recordings that could be artefact. To exclude probe position as a cause of artefact, we have recruited another 10 pregnant patients (>36 weeks' gestation) and recorded both toe and finger overnight $Sp_{O_2}$ simultaneously. Of these patients, four had a lower mean $Sp_{O_2}$ recorded from the toe probe compared with the finger probe. One of these four patients had a toe/finger $Sp_{O_2}$ difference greater than the Edentec error allowance. In two patients, toe $Sp_{O_2}$ was greater than finger $Sp_{O_2}$. We feel therefore that in this preliminary study we have excluded artefact to the best of our ability and that hypoxaemia in the pregnant groups compared with the non-pregnant subjects was a genuine finding. However, confirmation is required in larger studies.

Several studies have shown that episodic maternal hypoxia occurs during labour and delivery but with no effect on neonatal Apgar scores or changes in umbilical cord pH/$Pa_{O_2}$ values [11, 12]. Deckardt and colleagues showed that there was a significant decrease in maternal arterial saturation and a significant decrease in neonatal cord pH in patients using opioid and Entonox analgesia compared with extradural analgesia, but there was no difference in Apgar scores [13]. Our study differs from these in that our pregnant patients were not in labour and we believe that this is the first study to reveal that some non-labouring patients in late pregnancy have *continuous* nocturnal hypoxaemia, but we do not know for how long nocturnal hypoxaemia persists. It is well known that pregnant women living at high altitude (1600–4602 m with approximate $Sp_{O_2}$ 95–80 %) experience chronic hypoxaemia and this is associated with a higher incidence of intrauterine growth retardation and a higher infant mortality, primarily in preterm infants [14, 15]. Although our small study has shown no difference in birth weights and Apgar scores between hypoxaemic and non-hypoxaemic patients, the power of the study is clearly inadequate to examine this issue.

Templeton and Kelman observed that although there was no difference in $Pa_{O_2}$ there was a significant increase in alveolar to arterial $PO_2$ difference and increased physiological shunt in nine patients with severe pre-eclampsia (proteinuria $>2$ g litre$^{-1}$) compared with normal pregnant controls. They also showed that 22 patients with moderate pre-eclampsia had no significant change in pulmonary function. They suggested that impairment of gas exchange in severe pre-eclampsia may result from maldistribution of pulmonary blood flow [16]. It is possible that failure to demonstrate a difference in $Pa_{O_2}$ resulted from increased alveolar ventilation in those with severe pre-eclampsia and we suggest that this compensation is likely to be less effective during sleep and it is possible that our data are consistent with this hypothesis.

From tables 1 and 2 there is a suggestion that patients with more severe degrees of PIH (oedema and proteinuria) may have suffered the greatest degree of hypoxaemia. Again, the size of our study is too small to permit formal evaluation of this observation but clearly this is important and warrants further investigation in a large-scale study.

In summary, in this preliminary study, we have shown for the first time that a significant number of pregnant women ($>35$ weeks' gestation) suffer from significant prolonged nocturnal hypoxaemia. Clearly, the duration, magnitude and aetiology of this hypoxaemia during pregnancy and pre-eclampsia, together with any effects on fetal outcome, require further investigation.

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