PREDICTIVE FACTORS OF OXYGEN DESATURATION OF PATIENTS SUBMITTED TO ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY UNDER CONSCIOUS SEDATION

Suzana MÜLLER, João Carlos PROLLA, Ismael MAGUILNIK and Helenice Pankowski BREYER

ABSTRACT - Background and Aims - Hypoxemia can occur during endoscopic retrograde cholangiopancreatography probably induced by the analgesia and sedation done. Moreover the patient's prone position difficults the adequate ventilation. The hypoxemia and hypoventilation may not be noticed by nursing staff. A transversal study was used to investigate possible predictive factors of oxygen desaturation in sedated patients with midazolam associated to meperidine undergoing endoscopic retrograde cholangiopancreatography. 

Patients and Methods - A total of 186 patients were monitored with continuous pulse oximetry. Poisson regression was used to measure the independent effect of each factor adjusted for effects of each of the other factors. The variables studied were: age, gender, hematocrit and hemoglobin levels, scopolamine use, diagnostic or therapeutic exam, American Society of Anesthesiologists Scores (ASA), duration time of exam, sedative used midazolam in the average of 0.07 mg/kg and analgesic drug meperidine in the average of 0.7 mg/kg that was titrated according patient's reaction. 

Results - No desaturation was found in 113 (60.8%) patients, mild desaturation (SpO2 ≤92%) in 22 (11.8%) and severe desaturation (SpO2 ≤90%) in 51 (27.4%). This desaturation was recognized only by the pulse oximeter. There was no need to use any antagonist drug of the sedatives in patients who had severe desaturation, they were just stimulated to deep breaths and oxygen was offered at 2 liters per minute via catheter. The variables found to predict desaturation were age ≥60 years old and ASA score III. The duration of exam was barely significant for desaturation. 

Conclusions - The variables of age of 60 years old or more, and ASA III score are identified as increased risk for desaturation for patients who undergo endoscopic retrograde cholangiopancreatography under conscious sedation. Long time of exam suggests the patient oxygen desaturate. Such patients require very close monitoring to desaturation and hypoventilation by the assistants and nursing staff alerting to respiratory depression. The use of pulse oximeter and asking for deep breaths during the exam helps to diminish such risks.


INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) carries all the standard risks of endoscopic procedure, including those due to sedation, drug idiosyncrasy, and cardiorespiratory dysfunction. Of the early procedure-related events, bleeding, pancreatitis, retrodudenal perforation and sepsis can occur with approximately equal frequency (1%-2% each) and, along with cardiac incidents, constitute the main causes of death(6, 7).

Such procedure can be painful and cause considerable anxiety. Most patients are given some form of sedation and/or analgesia, often termed “conscious sedation”. Since medication induces respiratory depression, this is probably the most common cause of endoscopy-related death(8). ERCP demands a patient's prone position which increases the ventilatory resistance. The thorax is compressed against the exam bed, and in addition the upward displacement of abdominal visceras against the diaphragm difficult normal breathing(12).

One effect of sedation is hypoxia(5, 22) which may produce cardiac events such as myocardial ischemia and cardiac arrhythmias(1) when oxygen saturation is under 90%(41).

The aims of this transversal study were to identify possible predictive factors of oxygen desaturation in patients undergoing ERCP under conscious sedation, analyzing the influence in the oxygen saturation variation of drugs administered.

Another purpose of this study is to verify if exists association of the variables age, gender, diagnostic or therapeutic exam,
duration time of procedure, hematocrit and hemoglobin values and the physical status of the patients according to the American Society of Anesthesiologists (ASA) system\(^\text{(2)}\) (Figure 1), with the oxygen saturation variation.

**ASA classification according to ARMSTRONG\(^\text{(2)}\)**

I. Healthy patient;

II. Mild systemic disease, patient in use of drugs;

III. Severe systemic disease with definite functional limitation, not incapacitating, controlled by drugs;

IV. Severe systemic disease, with constant threat to life, incapacitating;

V. Moribund patient, unlikely to survive 24 hours.

**Observation:** Add E for emergency cases.

FIGURE 1 – Classification of physical status by the American Society of Anesthesiologists

**PATIENTS AND METHODS**

The study group comprised 186 patients consecutively referred for ERCP in the “Hospital de Clínicas” of Porto Alegre, RS, Brazil. Patients under 15 years old, with pulmonary illness, using oxygen or a cardiac pacemaker, and those whose basal oxygen saturation was under 94% were excluded. The study design was approved by the Ethics Committee of the hospital, and steps were taken to ensure confidentiality of patient data. All patients received both midazolam and meperidine. The dosages were stipulated by mg/kg as shown in Table 1. These dosages were offered to the endoscopists based in the average dosage and they were free to choose one of them (lower, equal or higher than average), without the intervention of the main author (SM). They chose according the clinical health status of patients. In the room, drugs antagonists, flumazenil and naloxone respectively, were available. Three jets of lidocaine spray were used in the patient’s oropharynx. Material for cardio-respiratory resuscitation was available in the exam room, and the assistant nurses were trained in emergencies and ERCP.

The procedures were executed by only two endoscopists (IM, HPB) using duodenoscopes Pentax ED 3401 or 3410.

**TABLE 1 - Groups of patients, according to dosages of sedatives and analgesics**

<table>
<thead>
<tr>
<th>Group</th>
<th>Midazolam (mg/kg)</th>
<th>Meperidine (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td><strong>lower dosage than average</strong></td>
<td><strong>higher dosage than average</strong></td>
</tr>
<tr>
<td>Group B</td>
<td>0.05 — 0.07</td>
<td>0.5 — 0.7</td>
</tr>
<tr>
<td>Group C</td>
<td>0.07 — 0.1</td>
<td>1.0</td>
</tr>
</tbody>
</table>

* Average dose: midazolam 0.07 mg/kg

* Average dose: meperidine 0.7 mg/kg

* Group of patients who received a low dose of midazolam and a high dose of meperidine as well as those who received a high dose of midazolam and low dose of meperidine

The criteria of oxygen desaturation were: mild desaturation SpO\(_2\) ≤92%, and severe desaturation SpO\(_2\) ≤90%.

Basal oxygen saturation was recorded after positioning the patient in prone position, and before sedation. The oxygen saturation was recorded at each minute of the exam, as well as the cardiac frequency by a Distal pulse oximeter (DX-2405 Oxypleth) finger probe\(^{\text{11}}\). Gender, age, ASA score, time of scopolamine administration, time of oxygen use, sedatives dosage, total time of the exam, time of oxygen desaturation and hematocrit/hemoglobin levels were also recorded. Supplemental oxygen at 2 liters per minute was administered in nasal catheter when the patient was in severe desaturation (SpO\(_2\) ≤90%), and they were stimulated take deep breaths.

**Statistical Analyses**

In exploratory analysis the relationship between quantitative variables and desaturation level was determined by Student’s \(t\) test. The chi-square test, and chi-square test with Yates correction analyzed qualitative variables. Poisson regression\(^{\text{25}}\) with robust variance estimates was used to measure independent effect of each factor adjusted for the effects of each of the other factors. Differences were considered significant if \(P < 0.05\). This statistical analysis allow us to estimate, as measure of effect, the prevalence ratio with confidence interval of 95%.

The results were analyzed using the Statistical Package for the Social Sciences (SPSS)\(^{\text{21}}\) and Stata version 7.0 analytic software.

**RESULTS**

Of the 186 patients studied, 113 (60.8%) did not desaturate, 22 (11.8%) had mild desaturation, and 51 (27.4%) had severe desaturation. The desaturation occurred at 7 (SD ± 6) minutes after the initial sedative administration. In the patients who had severe desaturation (≤90%) they were stimulated to deep breaths and the oxygen at 2 L/min using a catheter was installed.

Of the 186 patients, 122 (65.6%) were female and 64 (34.4%) were male. The gender did not show association with oxygen desaturation (\(\chi^2\) Yates \(P = 0.6\)). The patients’ age varied from 15 to 93 years old, with mean of 53 years old (SD ± 18). Dichotomous age ≥60 had a significant association with oxygen desaturation (\(\chi^2\) Yates \(P = 0.004\)) (Table 2).

**TABLE 2 - Association of age with oxygen saturation variation**

<table>
<thead>
<tr>
<th>Age</th>
<th>Desaturation</th>
<th>No desaturation</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>≥60 years</td>
<td>38 (52.8)</td>
<td>34 (47.2)</td>
<td>72 (100)</td>
</tr>
<tr>
<td>&lt;60 years</td>
<td>35 (30.7)</td>
<td>79 (69.3)</td>
<td>114 (100)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>73 (39.2)</td>
<td>113 (60.8)</td>
<td>186 (100)</td>
</tr>
</tbody>
</table>

* Yates \(P = 0.004\)

The patients were classified into three groups of ASA score: ASA II \(n = 69\) (37.1%), ASA III \(n = 83\) (44.6%), and ASA IV \(n = 34\) (18.3%). There were no patients ASA I and V. There was a significant association of ASA score with oxygen desaturation (\(\chi^2\) \(P = 0.013\)) as shown in Table 3. The proportion of patients ASA III who desaturated 41 (49.4%) was significantly higher than the proportion of patients ASA II 18 (26.1%).

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The group of patients ASA IV, 14 (41.2%) had a similar proportion with desaturation as the total sample and were closest in that proportion to the group of patients who were ASA III.

There were no significant association of sedative dosage and oxygen desaturation (P = 0.206) because of the distribution of the sedatives dosages for patients.

Endoscopists chose lower dosages for critical patients and higher for healthier ones shown in the association of ASA score and dosages of sedatives (P = 0.021) (Table 5). ASA III patients were administered lower dosages than ASA II patients. For ASA IV sedatives patients’ dosage distribution was similar to total of sample.

Chi square test showed association of sedatives dosage and dichotomized age (P = 0.001), as shown in Table 5. Patients 60 years old or more received lower dosages than mean (group A).

The duration of exam was barely significant for desaturation (P = 0.047). The variables: hematocrit (P = 0.791); hemoglobin (P = 0.803); diagnostic or therapeutic exam (P = 0.9); scopolamine use (P = 0.242); sedatives dosages (P = 0.206) were not significant for oxygen desaturation as shown in Table 4.

The elderly patients are at risk for oxygen desaturation during endoscopic procedures[6, 10, 14, 26], but this was not confirmed for others authors[15, 16]. In our study it was significant (P = 0.004; relative risk: 1.5; confidence interval: 1.12-1.93) for desaturation. Of the 186 patients, 72 (38.7%) were 60 years old or more, of these 38 (52.8%) desaturated, as found by some authors[6, 10, 14, 26].

We observed association between dosages of sedatives and analgesics and age. Patients 60 years old or more received less dosages of drugs (P <0.001), showing that the age influenced the endoscopist when choosing drug dosages, even though, oxygen desaturation occurred in this group.

The low level of hemoglobin and hematocrit are controversial in relation to oxygen desaturation[11, 18, 19]. Our study did not find significant association of low level of hematocrit (P = 0.791) and hemoglobin (P = 0.803) with oxygen desaturation. According to GUYTON and HALL[23], in anemia there is a compensatory increase of cardiac debit and because of it, there is only a diminishing in oxygen transportation speed to the tissues. This may be the explanation for the maintenance of oxygen saturation in anemic patients.

The health conditions of patients are considered to be a risk factor for oxygen desaturation[1, 10]. Our study showed statistical significance

### Table 3 - Association of ASA score and oxygen saturation variation

<table>
<thead>
<tr>
<th></th>
<th>Desaturation</th>
<th>No desaturation</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA II</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>26.1</td>
<td>51</td>
</tr>
<tr>
<td>ASA III</td>
<td>41*</td>
<td>49.4</td>
<td>42</td>
</tr>
<tr>
<td>ASA IV</td>
<td>14</td>
<td>41.2</td>
<td>20</td>
</tr>
<tr>
<td>TOTAL</td>
<td>73</td>
<td>39.2</td>
<td>113</td>
</tr>
</tbody>
</table>

Test: Pr = 0.013

**Difference in relationship to the group ASA II, analysis of adjusted residues.

### Discussion

Our results in 186 patients undergoing ERCP under conscious sedation show decrease of oxygen saturation in 39.2% of the patients. Mild desaturation occurred in 22 (11.8%) of patients and severe desaturation in 51 (27.4%), no desaturation occurred in 113 (60.8%) of patients. These findings are similar to other studies: WONG et al[28] found 50% of patients desaturated. CRANTOCK et al[8] found 47% of patients not receiving supplementary oxygen desaturated. Only MISTRY et al[21] study identified the hypoxemia in EGD as transitory and benign in unsedated patients. The data about gender were not significant, same finding of other authors[1, 16].

Endoscopic sphincterotomy changed ERCP from diagnostic to therapeutic[22]. In our study, a diagnostic exam was done in 40 (21.5%) patients, while 146 (78.5%) were therapeutic exams. This distinction was not significant for desaturation (P = 0.9). But we observed that the duration time of therapeutic exam (18.6 min SD ± 8.1) is longer than diagnostic exam (12 min SD ± 6.2), (P <0.001). The duration time of exam was barely significant for oxygen desaturation (P = 0.047): patients who desaturated had a longer time of exam than those who did not desaturate. The time of exam among those who desaturated was 19 minutes and those who did not desaturate was 16.4 minutes. The total time of exam varied from 5 to 54 minutes. The references about duration time of exam and desaturation are poor in medical literature, only IWAO et al[16] referred not having found a significant association with oxygen desaturation in the duration time of endoscopy exams (P = 0.27). IBER et al[15] identified that anaemia and apnea may occur in two different times: a few minutes after the sedative and analgesia administration, and after 20 minutes of exam.

In our study oxygen desaturation occurred at the time of 7 (SD ± 5.77) minutes after the sedative administration. The midazolam and meperidine dosages in our study varied from 0.05 to 1.0 mg/kg for midazolam, and 0.5 to 1.0 mg/kg for meperidine. Dosage was not in association with oxygen desaturation (P = 0.206). We conclude that the sedation association with analgesia, as standardized in this study, was not a risk factor for desaturation, if administered in low dosages and monitoring the patient. The patients who suffered severe oxygen desaturation (SpO2 <90%) received supplemental oxygen at 2 liters per minute, reversing immediately. There was no need to use the antagonists to reverse the sedative and analgesic effects. Hypoxemia during endoscopy is most commonly attributed to sedation-induced hypoventilation[17].

**Table 4 - Poisson regression test**

<table>
<thead>
<tr>
<th>Variables</th>
<th>PR</th>
<th>P</th>
<th>CI 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 60 years old</td>
<td>1.58</td>
<td>0.02</td>
<td>1.04-2.39</td>
</tr>
<tr>
<td>Gender female</td>
<td>1.41</td>
<td>0.09</td>
<td>0.94-2.11</td>
</tr>
<tr>
<td>Group C</td>
<td>0.94</td>
<td>0.80</td>
<td>0.57-1.52</td>
</tr>
<tr>
<td>Group B</td>
<td>0.92</td>
<td>0.72</td>
<td>0.59-1.42</td>
</tr>
<tr>
<td>ASA III</td>
<td>1.80</td>
<td>0.01</td>
<td>1.13-2.88</td>
</tr>
<tr>
<td>ASA IV**</td>
<td>1.66</td>
<td>0.07</td>
<td>0.94-2.94</td>
</tr>
<tr>
<td>Therapeutic exam***</td>
<td>0.86</td>
<td>0.56</td>
<td>0.53-1.40</td>
</tr>
<tr>
<td>Scopolamine (Yes)</td>
<td>1.42</td>
<td>0.20</td>
<td>0.82-2.45</td>
</tr>
<tr>
<td>Hb altered</td>
<td>0.95</td>
<td>0.83</td>
<td>0.61-1.45</td>
</tr>
</tbody>
</table>

* Compared to group A
** Compared to group ASA II
*** Compared to diagnostic exam

**Table 5 - Association of doses of sedatives and analgesics, chosen by endoscopists, with age**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Age</th>
<th>&lt; 60 years</th>
<th>≥ 60 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td></td>
<td>30 (42.3%)</td>
<td>41 (57.7%)</td>
</tr>
<tr>
<td>Group B</td>
<td></td>
<td>69 (83.1%)</td>
<td>14 (16.9%)</td>
</tr>
<tr>
<td>Group C</td>
<td></td>
<td>15 (46.9%)</td>
<td>17 (53.1%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>114 (61.3%)</td>
<td>72 (38.7%)</td>
</tr>
</tbody>
</table>

Test: Pr <0.001
for oxygen desaturation in relationship to ASA scores ($P = 0.013$) as shown in Table 4. Of the 73 (39.2%) patients who desaturated, 41 (49.4%) were ASA III. This data is significant when analyzed in relationship to ASA II n = 18 (26.1%).

We observed that patients ASA III received lower dosages of sedatives when compared to ASA II group ($P = 0.021$). It shows that the patient's health status influenced the selection of midazolam and meperidine dosages by the endoscopists. The dosage of patients ASA IV varied among the groups A, B and C. The oxygen saturation variation in this group had similar distribution between the desaturated and the saturated group. In spite of the fact that endoscopists chose lower dosages of sedation for patients greater than or equal to 60 years old, desaturation was more frequent in this group. Other authors have not found this.

Scopolamine use was not significant for desaturation ($P = 0.242$). An increase in cardiac frequency may be produced by scopolamine use$^{14,15}$, or by patient discomfort$^{16}$. The increase of the cardiac frequency in our study was approximately 30 beats per minute. Considering this increase demands higher cardiac oxygenation$^{17}$, we believe to be necessary closer monitoring of cardiac patients.

The pulse oximetry was a very important method of monitoring oxygen saturation in our study. All the episodes of desaturation were identified only by the pulse oximeter, as other authors also observed$^{18,19}$. The darkness of the room permitting better fluoroscopy and video visualization makes more difficult to detect the later signals of desaturation as cyanosis, and it is worth to remember that cyanosis appears only when oxygen saturation is below 90%.

**CONCLUSIONS**

In conclusion, predictive factors of oxygen desaturation were: more than 60 years of age and ASA III score. Sedation and analgesia doses were not desaturation factors in our study. The doses selected for this study were within a safe level for the patients. Scopolamine use, hematocrit and hemoglobin levels, gender, diagnostic or therapeutic exam were not associated with oxygen desaturation. The utilization of a pulse oximeter is essential for all ERCP's patients and especially important in older, sicker patients to safe monitoring by the nursing staff.

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**REFERENCES**


