Risk Factors of Intraoperative Oxygen Desaturation: A Case-Control Study of 152,314 Anesthetics

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Background: *The present study was part of the Thai Anesthesia Incidents Study (THAI Study) of anesthetic adverse outcomes.*
Objective: *To determine factors related to intraoperative oxygen desaturation ($SpO_2 \leq 85\%$ or $< 90\%$ for more than 3 min)*
Material and Method: *During a 12-month period (February 1, 2003 - January 31, 2004), a prospective multicentered registry of patients receiving anesthesia was conducted in 20 hospitals across Thailand. Anesthesia personnel filled up patient-related, surgical-related, and anesthesia related variables and adverse outcomes including intraoperative oxygen desaturation. A case-control (1:4) study of patients with and without intraoperative oxygen desaturation in the THAI Study database was done. Univariate and multivariate analysis were used to identify factors related to intraoperative oxygen desaturation. A p-value < 0.05 was considered as significant.*
Results: *Among 152,314 patients without preanesthetic desaturation in the database, 328 cases of intraoperative oxygen desaturation were matched with 1,312 control patients without desaturation. Variables that predict desaturation by multiple logistic regression were age less than 5 years old [OR 9.3 (95% CI 5.4-16.0)], ASA physical status 3, 4, 5 [OR 3.1 (95% CI 2.2-4.3)], history of upper respiratory tract infection [OR 10 (95% CI 1.9-51.6)], history of asthma [OR 2.9 (95% CI 1.0-9.5)], general anesthesia [OR 4.0 (95% CI 2.4-6.7)] duration of anesthesia 31-90 min [OR 1.9 (95% CI 1.2-3.0)], duration of anesthesia 91-150 min (OR 2.2 (95% CI 1.3-3.6)], and duration of anesthesia > 150 min [OR 2.0 (95% CI 1.2-3.4)].*
Conclusion: *Knowing the risk factors of intraoperative oxygen desaturation helps improving personnel to improve preanesthetic conditions and facilitate early detection as well as prompt treatment of intraoperative oxygen desaturation.*

Keywords: *Anesthesia, Desaturation, Complication, Adverse events, Risk factors, Case-control*

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The occurrence and possible pathogenesis of hypoxemia during anesthesia were described several years ago[1-3]. In these early studies using discontinuous and invasive techniques, the exact occurrence of hypoxemia was not described. With the development of the pulse oximeter, it is possible to measure oxygen saturation continuously and non-invasively[4,5]. The Royal College of Anesthesiologists of Thailand (RCAT) hosted the Thai Anesthesia Incidents Study (THAI Study) of anesthetic adverse outcomes for studying of incidence and factors related to anesthesia related complications[6,7]. The incidence of 24 hr perioperative oxygen desaturation in The THAI Study was 31.9:10000 anesthetics. Punjasawadwong et al reported 497 incidents of oxygen desaturation of which desaturation of which 88.4%, 8% and 3.2% of the incidents were related to respiratory events, cardiovascular events and problems with anesthetic machine or equipment failure respectively[8]. In their descriptive study, 74.6% of the oxygen desaturation incidents occurred during intraoperative period[8]. Therefore, the present study was aimed to analyze risk factors of intraoperative oxygen desaturation using the THAI Study's database.

Material and Method

The Thai Anesthesia Incidents Study (THAI Study) of anesthetic adverse outcomes was a prospective multi-centered registry of consecutive anesthesia performed in 20 hospitals: 7 university hospitals (Chiang Mai University, Chulalongkorn University, Khon-Kaen University, Siriraj Hospital and Ramathibodi Hospital Mahidol University, Pramonkutklao Medical College and Prince of Songkla University); 5 tertiary hospitals (Buddhachinaraj Hospital, Ratchaburi Hospital, Nakorn Sri Thammarat Hospital, Khon Kaen Hospital and Neurological institute); 4 general hospitals (Lampoon Hospital, Pichit Hospital, Baanpong Hospital and Trang hospital); and 4 district hospitals (Sanpatong Hospital, Nakorn-Thai Hospital, Kranuan Hospital and Nampong Hospital) across Thailand. The present study was approved by all institutional ethical review boards without additional written informed consent required.

For each patient undergoing a surgical procedure, the anesthesiologist or nurse anesthetist completed a preplanned structured data entry form 1, which included a series of patient-related, surgical-related and anesthesia-related variables in addition to the usual anesthetic record. After constructing form 1 and defining the variables, the involved research staff and personnel were trained through workshops and internal audits. This form had been piloted in six university hospitals before adoption at the other sites with a 1-month run-in period before recruitment of each site in the registry. As for the recording of patient related variables, the attending anesthesia personnel were requested to record preoperative medical conditions, the American Society of Anesthesiologists (ASA) physical status classification and demographic characteristics of the patients. Regarding the surgical procedure, the operations were recorded by converting the written operative procedure into groups by operated region. Factors related to anesthesia including monitors, main anesthetic technique, additional anesthetic technique employed, airway equipment, status of performance of anesthesia, and drug utilized were recorded. The anesthesia personnel or research nurses visited the patients to record their 24-hr perioperative (24 hr after induction of anesthesia) adverse outcomes. The adverse outcomes of cardiac arrest, death, oxygen desaturation ($SpO_2 \leq 85\%$ or $\leq 90\%$ for more than 3 min), infarction, pulmonary aspiration, reintubation, esophageal intubation and desaturation, anaphylaxis/anaphylactoid reaction, and drug errors were recorded purposes of analysis, timing of adverse events was divided into three periods: intraoperative period (during surgery), post anesthesia care period (at the recovery room), and postoperative period (since discharge from the recovery room until 24 hr of anesthesia). All record forms were reviewed by a research nurse or site manager for completeness. Correction was then made by each center including the verification of the major event recorded. Incompleteness after this step would be considered as missing.

All form 1's from each hospital during the 12 month period between February 2003 to January 2004 were entered in at the data management centre at Chulalongkorn University with double-entry technique to ensure the reliability of the data base.

Study population

With this prospective data collection, the authors conducted a case-control study with the ratio of 1:4.

The cases were patients who experienced oxygen desaturation ($SpO_2 \leq 85$ or ≤ 90 for more than 3 min). The patients with preoperative oxygen desaturation were excluded.

Controls were patients without oxygen desaturation recruited from the THAI Study database during the same period.

Sample size calculation

The sample size was based on the proportion of patients with ASA physical status 3,4 without oxygen desaturation of 0.07 such as in Moller's study for the estimated proportion of control[9]. The authors chose the odds ratio of 2 to have clinical significance. With an "a" of 0.05 and a "b" of 0.2, using formula for an unmatched unequal case-control ratio of Schlesselman[10] and corrected with multiple correlation, the calculated sample size was 320. Since the total number of patients who experienced intraoperative oxygen desaturation was 328, the authors therefore recruited all 328 patients as subjects (cases). To get 1,312 patients without oxygen desaturation, systematic random sampling was used with interval size of 115 to recruit the controls from the database.

Factors potentially associated with oxygen desaturation were assessed by using Chi-square test, (or Fisher's exact test when appropriated) for categorical variables. Magnitude of association was measured by using crude odds ratio with 95% confidence interval (CI). Variables with $p < 0.25$ were entered in the model. Multiple logistic regression with backward stepwise approach was then used to identify risk factors of intraoperative oxygen desaturation. All analyses were performed with the use of STATA (version 9.1). In all cases, two-tailed tests were performed, and p-value < 0.05 was considered statistically significant.

Results

During the period between February 1, 2003 and January 31, 2004, 152,314 patients without preoperative oxygen desaturation were enrolled in the database. Among these, 328 cases of intraoperative oxygen desaturation were recruited as subjects (cases). The 1,312 patients in control group were recruited by systematic sampling method with interval of 115 patients. The demographic, surgical and anesthesia characteristics of case and control are demonstrated in Table 1 and Table 2. From univariate analysis, the present study revealed that age, ASA physical status, history of recent upper respiratory tract infections, history of heavy smoking, site of surgery, anesthetic technique and duration of anesthesia were significantly related to oxygen desaturation.

Table 1. Demographic and preanesthetic characteristics of patients in case and control groups (univariate)

Variables	Case (n = 328)	Control (n = 1312)	Crude odds ratio (95% CI)	p-value
Age (year)				
< 5	103 (31.4%)	58 (4.4%)	9.3 (5.7-15.1)	<0.001
5-9	16 (4.9%)	43 (3.3%)	1.9 (0.9-3.8)	
10-19	28 (8.5%)	112 (8.5%)	1.3 (0.7-2.2)	
20-54	116 (35.4%)	77.5 (59.1%)	0.7 (0.5-1.1)	
55-65	30 (9.1%)	140 (10.7%)	1.1 (0.6-1.9)	
> 65	35 (10.7%)	184 (14.0%)	1	
Gender				
Female	164 (50.0%)	716 (54.6%)	1	0.14
Male	164 (50.0%)	596 (45.4%)	1.2 (0.9-1.5)	
Body mass index				
< 25	242 (73.8%)	994 (75.8%)	1	0.75
25-29.9	59 (18.0%)	215 (16.4%)	1.1 (0.8-1.6)	
≥ 30	27 (8.2%)	103 (7.8%)	1.0 (0.7-1.7)	
ASA physical status				
1-2	219 (67.0%)	1152 (87.8%)	1	<0.001
3-5	108 (33.0%)	160 (12.2%)	3.6 (2.6-4.8)	
History of:				
Recent URI	11 (3.3%)	2 (0.1%)	22.7 (4.9-211.5)	<0.001
Asthma	7 (2.1%)	10 (0.8%)	2.8 (1.0-8.3)	0.06
Smoking	15 (4.6%)	106 (8.1%)	0.5 (0.3-0.9)	0.03

Value shown as frequency (%)
Abbreviation : URI = upper respiratory tract infection

Table 2. Surgical and anesthetic characteristics of patients in case and control groups (univariate)

Variables	Case (n = 328)	Control (n = 1312)	Crude odds ratio (95% CI)	p-value
Site of surgery				
Others	210 (64.0%)	697 (53.1%)	1	<0.001
Extremity	29 (8.8%)	283 (21.6%)	0.3 (0.2-0.5)	
Lower abdomen	31 (9.5%)	79 (6.0%)	1.3 (0.8-2.0)	
Upper abdomen	58 (17.7%)	253 (19.3%)	0.8 (0.6-1.1)	
Anesthesia technique				
Regional anesthesia	18 (5.5%)	390 (29.8%)	1	<0.001
General anesthesia	310 (94.5%)	919 (70.2%)	7.3 (4.4-12.6)	
Duration of anesthesia				
< 30 min	33 (10.1%)	211 (16.1%)	1	0.01
31-90 min	146 (44.5%)	608 (46.4%)	1.5 (1.0-2.3)	
91-150 min	88 (25.0%)	280 (21.3%)	1.9 (1.2-2.9)	
> 150 min	67 (20.4%)	213 (16.2%)	2.0 (1.3-3.2)	

Value shown as frequency (%)

Table 3. Factors related to intraoperative oxygen desaturation (multiple logistic regression)

Factors	Adjusted odds ratio (95%CI)	p-value
Age < 5 yr	9.3 (5.4-16.0)	<0.001
ASA physical status		
1-2	1	
3-5	3.1 (2.2-4.3)	<0.001
History of URI	10 (1.9-51.6)	0.01
History of asthma	2.9 (1.0-9.5)	0.04
General anesthesia	4.0 (2.4-6.7)	<0.001
Anesthesia duration		
< 30 min	1	
31-90 min	1.9 (1.2-3.0)	0.005
91-150 min	2.2 (1.3-3.6)	0.002
> 150 min	2.0 (1.2-3.4)	0.005

Abbreviation : URI = upper respiratory tract infection

From multiple logistic regression analysis, factors significantly associated with intraoperative oxygen desaturation are shown in Table 3.

Discussion

As a consequence of discontinuous measurements, the incidence and degree of hypoxemia were not investigated in early studies on hypoxemia during anesthesia[1-3]. Another non-invasive continuous measuring technique, transcutaneous PO_2, has been available for many years[11]. The continuous, non-invasive and accurate technique of pulse oximetry can permit a more thorough study of hypoxemia during anesthesia. A randomized controlled study by Moller et al confirmed that pulse oximetry could detect early hypoxemia and related events, which therefore facilitated early management[12]. In the authors' previous descriptive study, 10.7%, 20.9%, 31.0% and 12.0% of the incidents of oxygen desaturation occurred during induction, intubation, maintenance and emergence periods respectively[8]. Therefore, in the present case-control study the authors analyzed the risk factors of oxygen desaturation that only occurred during the intraoperative period.

Since the authors' were able to enroll 152,314 patients without preanesthetic oxygen desaturation during the 12-month period, the presented approach was successful in obtaining sufficient prospective data for investigation. Studying too few patients, on the one hand, provides results with too little discriminatory power; studying too many patients, on the other hand, requires unaffordable luxuries in funding and time. The THAI Study provided prospective data collection allowing retrospective analysis of risk factors related to anesthesia adverse events.

From univariate analysis, the authors have identified age, ASA physical status, recent upper respiratory tract infection, history of smoking as significant factors related to intraoperative desaturation. As for surgical and anesthetic characteristics, site of surgery, general anesthesia, and duration of anesthesia were also significant factors related to desturation.

However, the presented analyses failed to demonstrate gender, body mass index, history of asthma as significant risk factors. In the authors' previous study, anesthesia contributed to more than 90% of desaturation incidents. Therefore, gender is less likely to be significant risk factors. In the present study, obesity or high body mass index did not relate to desaturation which was similar to other studies[9,13,14]. In contrast, Russell et al reported that greater body weight was more likely to experience oxygen desaturation at the postanesthesia care unit[15]. Although a history of pulmonary disease such as asthma, chronic obstructive pulmonary disease and bronchiectasis was found to be an independent factor for desaturation at the postanesthesia care unit, history of asthma was not a statistically significant factor in univariate analysis but was a risk factor in multivariate analysis.

The multivariate analysis identified the following factors significantly associated with intraoeprative desaturation: age, ASA physical status, history of upper respiratory tract infections, history of asthma, anesthetic technique and anesthesia duration.

In the present study, patients aged less than 5 years had greater risk than older age. Small children have many physiologic factors related to respiratory system such as decreased functional residual capacity, small airways and high oxygen consumption, which can make them more susceptible to hypoxemia. The association between age and desaturation also agreed with previous reports[13-15,17].

The current study suggests that patients with ASA physical status classification of 3, 4 and 5 are at increased risk of intraoperative desaturation. This finding is consistent with Muller's study[18]. The possible explanation is that ASA physical status 3, 4 and 5 patients were associated with moderate to severe systemic disease such as respiratory system, cardiovascular system with greater risk of hypoxemia. However, Moller et al showed no association between ASA physical status and occurrence of oxygen desaturation[9]. The lack of correlation in Moller's study might be due to the small number of patients studied.

The association between history of recent upper respiratory tract infections and oxygen desaturation is well established in the literatures with a two- to three fold increase in the relative risk of transient desaturation[19-21]. The present study reported adjusted odds ratio of 10 for desaturation in patients with a history of upper respiratory tract infections. However, studies grading the severity of severity of respiratory events found significant increases in the severity of surrogate events such as coughing, breath holding, and secretions[19,20,22]. Episodes of laryngospasm or bronchospasm in these studies were no more frequent or severe in those with upper respiratory tract infections, whereas true outcomes such as unanticipated hospital admission pneumonia, and death were rare[19,20,22].

The authors also analyzed the effects of the type of anesthesia on intraoperative hypoxemia. The authors found that patients receiving general anesthesia were at a higher risk (adjusted odd ratio of 4.0) of desaturation. This result agreed with previous studies by McKay and Noble, which reported that the incidence of arterial desaturation during anesthetic induction, maintenance and emergence was significantly lower in patients having regional anesthesia[23]. The effects of general anesthesia on pulmonary function could be the reason for this in perioperative oxygen saturation in patients having general or regional anesthesia.

It is noteworthy that the authors also identified duration of anesthesia as a risk factor for intraoperative desaturation. The present results reported adjusted odds ratio of 1.9, 2.2 and 2.0 for duration of anesthesia of 31-90 min, 91-150 min, and $\geq$ 150 min compared with duration of $\leq$ 30 min respectively. This conforms with previous studies[9,14,15]. The possible explanations were 1) anesthetic agents such as opioid, volatile anesthetics or muscle relaxant may contribute to hypoventilation resulting in perioperative desaturation 2) the longer duration of anesthesia the more chances of airway incidents occurring throughout the operation.

Although the design of the present study allowed the authors to examine the influence of many factors on occurrence of oxygen desaturation, there were limitations that necessitate caution in interpreting the results. In particular, this is a nonrandomized, nonblinded study and as such may be subject to some selection or observer bias. However, the authors believe that the anesthesia personnel had no vested interest in the several outcomes of the THAI Study. Another concern in the present study was the retrospective analysis of prospective collected database, which might suffer from missing data. Although the authors acknowledge these limitations, the potential of bias would be minimized by the large sample size.

Conclusion

In conclusion, predictive factors of intraoperative oxygen desaturation were less than 5 years

of age, ASA physical 3, 4, 5, history of upper respiratory tract infection, history of asthma, general anesthesia and duration of anesthesia more than 30 min. Knowing the risk factors helps the anesthesia personnel in reducing possibility of desaturation by improving the preanesthetic condition, early detection and prompt treatment of intraoeprative oxygen desaturation.

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ปัจจัยเสี่ยงของภาวะความอิ่มตัวของออกซิเจนในเลือดต่ำระหว่างผ่าตัด: การศึกษาแบบ case-control ในผู้ได้ยาระงับความรู้สึก 152,314 ราย

สมรัตน์ จารุลักษณานันท์, สุวรรณี สุรเศรณีวงศ์, ยอดยิ่ง ปัญจสวัสดิ์วงศ์, วรรณา สมบูรณ์วิบูลย์, สุรีรัตน์ ศรีสวัสดิ์, ธารทิพย์ ประณุทนรพาล, ธวัช ชาญชญานนท์, วราภรณ์ เชื้ออินทร์, นิรันดร์ อินทรัตน์

***ภูมิหลัง**: การศึกษานี้เป็นส่วนหนึ่งของโครงการศึกษาภาวะแทรกซ้อนทางวิสัญญีในประเทศไทย*

***วัตถุประสงค์**: ในการหาปัจจัยเกี่ยวข้องกับภาวะระดับความอิ่มตัวของออกซิเจนต่ำ ($SpO_2 \leq 85\%$ หรือ $< 90\%$ นานกว่า 3 นาที)*

***วัสดุและวิธีการ**: ช่วงระยะเวลา 12 เดือน (ระหว่าง 1 กุมภาพันธ์ พ.ศ. 2546 – 31 มกราคม พ.ศ. 2547) มีการเก็บข้อมูลแบบทะเบียนโรคของการให้ยาระงับความรู้สึกสำหรับการผ่าตัดในโรงพยาบาล 20 แห่งในประเทศไทย ผู้ให้ยาระงับความรู้สึกทำการบันทึกข้อมูลเกี่ยวกับผู้ป่วยศัลยกรรม และการให้บริการทางวิสัญญีตลอดจนภาวะแทรกซ้อนต่าง ๆ รวมทั้งการเกิดภาวะระดับความอิ่มตัวของออกซิเจนในเลือดต่ำ ทำการวิเคราะห์แบบ univariate และ multivariate เพื่อหาปัจจัยเกี่ยวข้องกับการเกิดอุบัติการณ์ โดยค่า $p < 0.05$ ถือว่ามีนัยสำคัญทางสถิติ*

***ผลการศึกษา**: จากจำนวนผู้รับบริการทางวิสัญญีซึ่งไม่มีภาวะระดับความอิ่มตัวของออกซิเจนในเลือดต่ำก่อนให้ยาระงับความรู้สึก 152,314 ราย เปรียบเทียบรายที่เกิดภาวะระดับความอิ่มตัวของออกซิเจนต่ำระหว่างการผ่าตัด 328 ราย กับรายที่ไม่เกิดภาวะระดับความอิ่มตัวของออกซิเจนต่ำ 1312 รายถือเป็นกลุ่มเปรียบเทียบ พบว่าปัจจัยเกี่ยวข้องกับภาวะระดับความอิ่มตัวของออกซิเจนต่ำ ได้แก่ อายุน้อยกว่า 5 ปี [OR 9.3 (95% CI 5.4-16.0)], สภาวะกายภาพ ASA 3, 4, 5 [OR 3.1 (95% CI 2.2-4.3)], ประวัติการติดเชื้อระบบหายใจส่วนบน [OR 10 (95% CI 1.9-51.6)], ประวัติหอบหืด [OR 2.9 (95% CI 1.0-9.5)], การได้ยาระงับความรู้สึกแบบทั้งตัว [OR 4.0 (95% CI 2.4-6.7)], ระยะเวลาที่ได้ยาระงับความรู้สึก 31-90 นาที [OR 1.9 (95% CI 1.2-3.0)], ระยะเวลาได้ยาระงับความรู้สึก 91-150 นาที (OR 2.2 (95% CI 1.3-3.6)], ระยะเวลาได้ยาระงับความรู้สึก > 150 นาที [OR 2.0 (95% CI 1.2-3.4)] ตามลำดับ*

***สรุป**: การทราบปัจจัยเกี่ยวข้องกับการเกิดภาวะระดับความอิ่มตัวของออกซิเจนต่ำระหว่างการผ่าตัด ทำให้สามารถเตรียมผู้ป่วยก่อนให้ยาระงับความรู้สึกและช่วยในการวินิจฉัยและการแก้ไขภาวะระดับความอิ่มตัวของออกซิเจนต่ำได้เร็วขึ้น*