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PATHOPHYSIOLOGICAL DYNAMICS OF PAIN SENSITIVITY IN BURNED PATIENTS, TAKING INTO ACCOUNT THE VALUE OF THE OXYGEN FRACTION IN THE INHALED GAS MIXTURE

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Abstract. ***Introduction.*** Pain (nociception) is an unpleasant subjective sensation, depending on its localization and strength, having a different emotional coloring, signaling damage or a threat to the existence of the body and mobilizing its defense systems, aimed at conscious avoidance of the action of a harmful factor and the formation of non-specific reactions, ensuring this avoidance. The nociceptive system perceives and conducts a pain impulse, forming a reaction to pain. The antinociceptive system is a hierarchical set of neural structures at different levels of the central nervous system, with its own mechanisms, capable of inhibiting the activity of the pain (nociceptive) system. **Purpose of the study.** To conduct a comparative pathophysiological study of the dynamics of pain sensitivity in burned patients, taking into account the value of the oxygen fraction in the inhaled gas mixture (FiO_2). ***Materials and methods.*** The study was conducted in the Department of Thermal Injuries of the St. Petersburg Scientific Research Institute of Emergency Medicine named after I.I. Dzhanelidze. The results of the examination of 106 burned patients of both sexes with deep burns were studied, who were supplied with an oxygen-air mixture in the following proportions during anesthesiological care and in the postoperative period during surgical necrectomy under artificial ventilation: FiO_2 30–35% — in 30% of those burned (45); FiO_2 50–55% — in 45% of those burned (37); FiO_2 75–80% — in 25% of those burned (24). The burned were divided into 3 groups, taking into account the fraction of oxygen in the inhaled gas mixture (FiO_2). ***Results.*** It was found that those burned in group 1 developed mild tissue hypoxia. At the same time, in order to provide full-fledged antinociceptive protection to those burned, an increase in doses of the opioid narcotic analgesic (fentanyl) by 18–20% was required. Normoxemia was noted in the burned patients of group 2 (control) and no increase in doses of the opioid narcotic analgesic (fentanyl) above the recommended doses was required, taking into account the nature and scope of surgical intervention. In the burned patients of group 3, the amount of opioid narcotic analgesic (fentanyl) necessary for adequate analgesia during anesthesia and the postoperative period practically did not differ from the control group. Our proposed method of increasing the oxygen fraction in the inhaled gas mixture (FiO_2). more than 50% under the control of the gas composition of arterial blood has reduced pain sensitivity by half and the frequency of administration of opioid narcotic. ***Conclusion.*** The use of a high fraction of oxygen in an inhaled gas mixture (FiO_2) of more than 50% over a period of time (from 180 to 720 minutes), reduces pain sensitivity by half and the frequency of intravenous, intramuscular and transdermal administration of an opioid analgesic (fentanyl) by 18–20%.

Keywords: burned, nociception, antinoception, opioid narcotic analgesic (fentanyl), anesthetic support, oxygen fraction in the inhaled gas mixture (FiO_2), gas composition of arterial blood https://doi.org/10.56871/RBR.2025.32.19.003

ПАТОФИЗИОЛОГИЧЕСКАЯ ДИНАМИКА БОЛЕВОЙ ЧУВСТВИТЕЛЬНОСТИ У ОБОЖЖЕННЫХ С УЧЕТОМ ВЕЛИЧИНЫ ФРАКЦИИ КИСЛОРОДА ВО ВДЫХАЕМОЙ ГАЗОВОЙ СМЕСИ

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Резюме. *Введение.* Боль (ноцицепция) — это неприятное субъективное ощущение, обладающее в зависимости от его локализации и силы различной эмоциональной окраской, сигнализирующее о повреждении или об угрозе существованию организма и мобилизующее системы его защиты, направленные на осознанное избегание действия вредоносного фактора и формирование неспецифических реакций, обеспечивающих это избегание. Ноцицептивная система воспринимает и проводит болевой импульс, формируя реакцию на боль. Антиноцицептивная система — это иерархическая совокупность нервных структур на разных уровнях центральной нервной системы (ЦНС), с собственными механизмами, способная тормозить деятельность болевой (ноцицептивной) системы. ***Цель исследования.*** Провести сравнительное патофизиологическое изучение динамики болевой чувствительности у обожженных с учетом величины фракции кислорода во вдыхаемой газовой смеси (FiO_2). ***Материалы и методы.*** Исследование проводилось в отделе термических поражений ГБУ «Санкт-Петербургский научно-исследовательский институт скорой помощи им. И.И. Джанелидзе». Изучены результаты обследования 106 обожженных обоего пола с глубокими ожогами, которым во время проведения анестезиологического обеспечения и в послеоперационном периоде при выполнении хирургических некрэктомий в условиях искусственной вентиляции легких подавалась кислородно-воздушная смесь в следующих соотношениях: FiO_2 30–35% — у 30% обожженных (45); FiO_2 50–55% — у 45% обожженных (37); FiO_2 75–80% — у 25% обожженных (24). Обожженные были разделены на три группы с учетом фракции кислорода во вдыхаемой газовой смеси (FiO_2). ***Результаты.*** Установлено, что у обожженных 1-й группы развивалась тканевая гипоксия легкой степени. При этом для обеспечения полноценной антиноцицептивной защиты обожженным требовалось повышение доз опиоидного наркотического анальгетика (фентанила) на 18–20%. У обожженных 2-й группы (контрольной) отмечалась нормоксемия, и не требовалось повышение доз опиоидного наркотического анальгетика (фентанила) выше рекомендованных доз с учетом характера и объема оперативного вмешательства. У обожженных 3-й группы количество опиодного наркотического анальгетика (фентанила), необходимого для адекватной аналгезии в процессе анестезиологического обеспечения и послеоперационном периоде, практически не отличалось от контрольной группы. Предложенный нами способ увеличения фракции кислорода во вдыхаемой газовой смеси (FiO_2) более 50% под контролем газового состава артериальной крови позволил снизить болевую чувствительность в два раза и частоту введения опиоидного наркотического анальгетика (фентанила) на 18–20%. ***Заключение.*** Применение высокой фракции кислорода во вдыхаемой газовой смеси (FiO_2) более 50% в течение времени от 180 до 720 минут снижает болевую чувствительность в два раза и частоту внутривенного, внутримышечного и трансдермального введения опиоидного анальгетика (фентанила) на 18–20%.

Ключевые слова: обожженные, ноцицепция, антиноцицепция, опиоидный наркотический анальгетик (фентанил), анестезиологическое обеспечение, фракция кислорода во вдыхаемой газовой смеси (FiO_2), газовый состав артериальной крови

INTRODUCTION

It is believed that the oxygen fraction in the inhaled gas mixture (FiO2) affects the parameters of nociceptive receptors, but we have not found any clinical studies conducted according to the criteria of evidence-based medicine. The sensitivity of the receptor apparatus, including opioid receptors, depends on a number of external and internal factors, including, apparently, hypoxia [3, 4, 8]. When arterial blood oxygen saturation decreases in high altitude conditions, patients need to increase the doses of opioid analgesics for adequate pain relief [9, 11], as their pain sensitivity threshold decreases [7, 8] due to the fact that developing hypoxemic hypoxia changes the sensitivity of opioid receptors towards a decrease [6]. Conversely, when hemoglobin is saturated with oxygen, using hyperbaric oxygenation, the intensity of pain syndrome decreases in patients [2]. Therefore, these studies served as the basis for this study on the possible connection between oxygenation and antinociception in burn patients during anesthesia and in the postoperative period during surgical necrectomies.

AIM

The aim of the study is to conduct a comparative pathophysiological study of the dynamics of pain sensitivity in burn patients, taking into account the oxygen fraction in the inhaled gas mixture (FiO_2).

MATERIALS AND METHODS

A total of 106 burn patients of both sexes with deep skin burns were examined. During anesthesia and in the postoperative period, while undergoing surgical necrectomy under artificial lung ventilation, they were administered an oxygen-air mixture in the following ratios: FiO_2 30–35% — in 30% of burn patients (45); FiO_2 50–55% — in 45% of burn patients (37); FiO_2 75–80% — in 25% of burn patients patients (24). The study was conducted in the thermal injury department of the I.I. Dzhanelidze St. Petersburg Research Institute of Emergency Care.

Surgical necrectomies, characteristics of burn patients, and photographs of the artificial lung ventilation (ALV) device with the set oxygen fraction FiO_2 are presented in Table 1 and Figures 1–3.

The study design is a single-center prospective study conducted in accordance with the principles of the World Medical Association's Declaration of Helsinki, “Ethical Principles for Medical Research Involving Human Subjects” (2013) and the Rules of Clinical Practice in the Russian Federation (No. 266, dated June 19, 2003). This study was approved by the local Ethics Committee at the I.I. Dzhanelidze St. Petersburg Research Institute of Emergency Care (protocol No. 1-02 dated February 11, 2025).

Anesthesiological support: total intravenous anesthesia using 1% propofol, 50 mg rocuronium bromide, 0.005% fentanyl, with an increase in dose if necessary. The three-component anesthesia model provided reliable antinociception, early awakening, and highly effective pain relief. Oro/tracheal intubation of the trachea and artificial ventilation of the lungs with an air-oxygen mixture were performed..

Intraoperative monitoring

- The following parameters were recorded using the Mindray e PM 15 monitor:
  – non-invasive blood pressure;
  – cardiac monitoring;
  – blood oxygen saturation (SpO_2%);
  – capnometry ($EtCO_2$%);
  – peripheral perfusion index (PI).

Table 1

Surgical necrectomy, lesion area and characteristics of the burned

Таблица 1

Хирургические некрэктромии, площадь поражения и характеристика обожженных

Характеристика обожженных / Characteristics of burnt	Хирургическая некрэктомия / Surgical necrectomy
	S=поверхностного >10% / S=surface level >10% S=глубокого>5% / S=deep>5%
Мужчины / Men	57 (54%)
Женщины / Women	49 (46%)
Возраст <18 лет / Age <18 years old	Средний возраст от 35 до 75 лет / The average age is from 35 to 75 years
Продолжительность и объем хирургических некрэктомий / Duration and volume of surgical necrectomies	Зависит от площади поверхностного и глубокого поражения тканей (в %) / It depends on the area of the superficial and deep tissue damage (in %)

Group 1 of those burned, taking into account the value of the oxygen fraction in the inhaled gas mixture FiO_2 30–35%

1-я группа обожженных с учетом величины фракции кислорода во вдыхаемой газовой смеси FiO_2 30–35%

Fig. 1. Drager Savina 300 apparatus with an established oxygen fraction in the inhaled gas mixture FiO_2 30–35%

Рис. 1. Аппарат Drager Savina 300 с установленной фракцией кислорода во вдыхаемой газовой смеси FiO_2 30–35%

Group 2 burned, taking into account the value of the oxygen fraction in the inhaled gas mixture FiO_2 50–55%

2-я группа обожженных с учетом величины фракции кислорода во вдыхаемой газовой смеси FiO_2 50–55%

Fig. 2. Drager Savina 300 apparatus with an established oxygen fraction in the inhaled gas mixture FiO_2 50–55%

Рис. 2. Аппарат Drager Savina 300 с установленной фракцией кислорода во вдыхаемой газовой смеси FiO_2 50–55%

- $PaCO_2$ in mm Hg was determined in arterial blood samples using gas analysis.

Balanced polyionic solutions were used for infusion therapy. The rate and volume of infusion therapy were assessed based on the pulse wave index, blood pressure, and hourly diuresis.

Features of artificial lung ventilation in patients with burns during surgical necrectomies, necessary for further analysis

A Drager Savina 300 device was used.

Group 3 burned, taking into account the fraction of oxygen in the inhaled gas mixture FiO_2 75–80%

3-я группа обожженных с учетом фракции кислорода во вдыхаемой газовой смеси FiO_2 75–80%

Fig. 3. Drager Savina 300 apparatus with an established oxygen fraction in the inhaled gas mixture FiO_2 75–80%

Рис. 3. Аппарат Drager Savina 300 с установленной фракцией кислорода во вдыхаемой газовой смеси FiO_2 75–80%

Ventilation mode: VC-SIMV, tidal volume — 6–7 ml/kg of body weight, PEEP — from 5 mm Hg.

The oxygen content (FiO_2%) in the inhaled mixture during mechanical ventilation during anesthesia was as follows:

- FiO_2 30–35% — in 30% of patients (45);
- FiO_2 50–55% — in 45% of patients (37);
- FiO_2 75–80% — in 25% of patients (24).

At the end of the operation (surgical necrectomy) and the anesthesia period, the amount of fentanyl required for adequate intravenous and transdermal analgesia was calculated in mcg/kg per hour.

Tissue oxygenation was assessed using the following techniques: pulse oximetry, which determines the degree of oxygen saturation in arterial blood and reflects oxygen delivery to tissues (SpO_2%); cerebral/somatic oximetry, which allows the degree of oxygen saturation of venous blood hemoglobin to be assessed (rSO_2%). The difference between SpO_2% and rSO2% reflects the tissue oxygen utilization coefficient (KuO_2%). The electrodes of the cerebral/somatic oximeter were placed on the patient's forehead. Using the INVOZ cerebral/somatic oximeter, the degree of oxygen saturation of venous blood hemoglobin (rSO_2%) in the brain was recorded.

A general view of the cerebral/somatic oximeter and SomaSensor sensors attached to both sides of the patient's forehead are shown in Figures 4–6.

The acid-base status (ABS) parameters were determined in the arterial blood gas composition using a Cobas b221 (Roche, Switzerland) multiparameter analyzer for blood gases, electrolytes, oximetric parameters, and metabolites (Fig. 6).

The obtained research materials were processed using parametric and nonparametric analysis methods. The accumu-

Fig. 4. **General view of the cerebral/somatic oximeter**

Рис. 4. **Общий вид церебрального/соматического оксиметра**

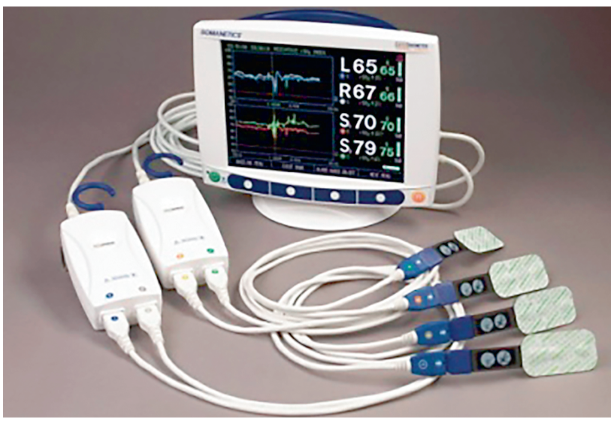

Fig. 5. **General view of the cerebral/somatic oximeter with "SomaSensor" sensors**

Рис. 5. **Общий вид церебрального/соматического оксиметра с датчиками (сенсорами) SomaSensor**

lation, correction, systematization of the initial information, and visualization of the obtained results were carried out in Microsoft Office 365 (Excel) spreadsheets. Statistical analysis was performed using STATISTICA 10.0 (developed by StatSoft). The Mann–Whitney U test was used to compare independent populations in cases where there were no signs of normal data distribution. The data are presented as the median with the interquartile range (IQR). To study the dependence of the probable optimal oxygen saturation of venous blood hemoglobin on the parameters of the dosage of opioid analgesics required for effective relief of postoperative pain syndrome in burn patients, Karl Ludwig von Bertalanffy's equation with modifications was adopted as the basic mathematical model [15].

PRESULTS AND DISCUSSION

Fentanyl consumption and monitoring indicators for burns during surgical necrectomies

The parameters of intraoperative monitoring of burns during surgical necrectomies are shown in Table 2.

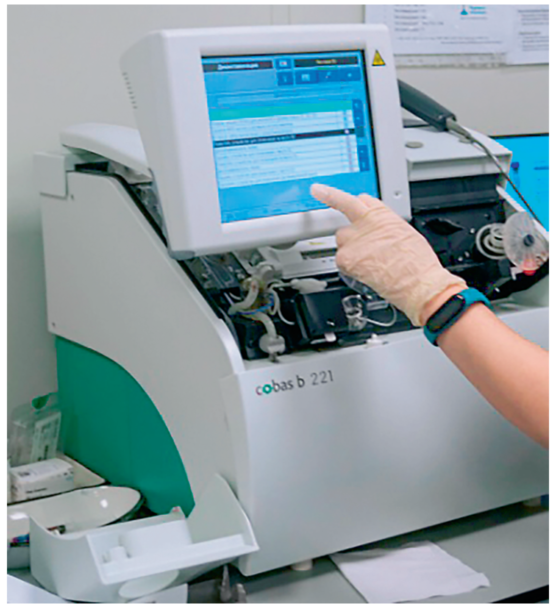

Fig. 6. **Multiparameter analyzer of blood gases, electrolytes, oximetric parameters and metabolites Cobas b221 (Roche, Switzerland). (Photos from the official website of the I.I. Dzhanelidze Research Institute of Emergency Medicine)**

Рис. 6. **Мультипараметровый анализатор газов крови, электролитов, оксиметрических параметров и метаболитов Cobas b221 (Roche, Швейцария). (Фотография с официального сайта НИИ скорой помощи им. И.И. Джанелидзе)**

The results presented in Table 2 are presented according to the following principle: the reference point is taken as the figure corresponding to the oxygen fraction in the inhaled mixture (FiO_2%) of 50–55%. This group of burn patients serves as a control.

The consumption of the opioid analgesic fentanyl in the group of burn patients with a FiO_2% fraction of 30–35% was statistically significantly higher than in the control group of burn patients by 18–20%. In the group of burn patients with FiO_2% of 75–80%, the amount of fentanyl required for adequate analgesia during anesthesia did not differ from the control group.

The oxygen tension in arterial blood samples in burn patients with FiO_2% 30–35% was statistically significantly lower (hypoxemia) than in the group of burn patients with FiO_2 50–55% and statistically significantly higher in the group of burn patients with FiO_2 75–80% (hyperoxia).

The acid-base status indicators in arterial blood samples indicated the presence of compensated mixed acidosis in patients burned with an oxygen fraction of 30–35%. Oxygen tension in venous blood samples (PvO_2) in the group with an oxygen fraction of 30–35% was higher than similar values recorded in burn patients in the control group.

An increase in lactate concentration in arterial blood was recorded in burn patients with FiO_2% 30–35%, while the same value did not differ from the values in the control group of burn patients with FiO_2% 75–80%.

Arterial blood oxygen saturation (SpO_2%) values in burn patients with FiO_2% 30–35% were statistically significantly lower than in burn patients in the control group. In burn patients with an oxygen fraction in the inhaled mixture of 65–80%, venous blood oxygen saturation did not differ from that in burn patients in the control group.

The carbon dioxide content in exhaled air ($EtCO_2$%) and in venous blood samples (pCO_2) was statistically significantly lower in the group of burn patients with FiO_2% 30–35% compared to the control group (FiO_2% 50–55%). In burn patients with FiO_2% 75–80%, the carbon dioxide content in the exhaled mixture and its concentration in venous blood samples did not differ from the values recorded in the control group.

The perfusion index (PI) was statistically significantly reduced in the group of burn patients treated with FiO_2% 30–35% compared to the control group of burn patients and did not differ from the control group treated with FiO_2% 75–80%.

Hourly diuresis was statistically significantly lower in burn patients with FiO_2% 30–35% and did not differ from the control group of burn patients with FiO_2% 75–80%.

CONCLUSION

The use of a high oxygen fraction in the inhaled gas mixture (FiO_2) of more than 50% for a period of 180 to

Table 2

Parameters of intraoperative monitoring of those burned during surgical necrectomy, depending on FiO_2% in the oxygen-air mixture

Таблица 2

Параметры интраоперационного мониторинга обожженных при хирургических некрэктомиях в зависимости от FiO_2% в кислородно-воздушной смеси

Анализируемые параметры / Analyzed parameters	Величина параметров при FiO_2% / The value of the parameters at FiO_2%		
	30–35%	50–55%	65–80%
Расход фентанила (мкг/кг/ч) Median (IQR) / Consumption of fentanyl (mcg/kg/hr) Median (IQR)	10,6 (5,1–6,1) p=0,0456	5,9 (5,1–6,1)	5,8 (5,1–6,0) p=0,5568
rSO_2% (лобная область) Median (IQR) / rSO_2% (frontal area) Median (IQR)	82,2 (81,5–84,0) p=0,0500	70,3 (70,5–67,0)	70,5 (70,0–69,5) p=0,6692
pH / Median (IQR)	7,38 (7,33–7,40) p=0,0471	7,39 (7,37–7,40)	7,42 (7,38–7,42) p=0,7131
pCO_2 (мм рт.ст. / mmHg) Median (IQR)	29 (27,0–31,0) p=0,0493	39,5 (37,0–42,0)	38,7 (36,0–41,0) p=0,8113
pO_2 (мм. рт.ст. / mmHg) Median (IQR)	73,1 (70,3–75,1) p=0,0414	65,8 (64,3–72,4)	68,5 (65,1–71,3) p=0,6543
BE (ммоль/л / mmHg) Median (IQR)	–2,8 (2,3–2,9) p=0,0461	+1,0 (1,0–1,6)	+1,1 (1,0–1,5) p=0,8614
Концентрация лактата в артериальной крови (ммоль/л) Median (IQR) / Concentration of lactate in arterial blood (mmol/l) Median (IQR)	1,16 (1,11–1,21) p=0,04678	0,74 (0,72–0,81)	0,70 (0,67–0,73) p=0,6564
SpO_2% Median (IQR)	98,6 (98–100) p=0,0465	99,8 (99–100)	99,9 (99–100) p=0,7922
PaO_2 (артериальная кровь) (мм рт.ст.) PaO_2 (arterial blood) (mmHg)	64 (60–72) p=0,031	94 (91–101)	121 (112–136) p=0,039
$EtCO_2$% Median (IQR)	28,7 (27–32) p=0,0423	38,6 (37–43)	38,8 (36–42) p=0,6543
PI Median (IQR)	70,5 (71–74) p=0,6432	70,7 (70–75)	70,9 (79–64) p=0,6792
Диурез (мл/ч) Median (IQR) / Diuresis (ml/hr) Median (IQR)	48,3 (48,2–50,3) p=0,0502	54,3 (56,0–61,4)	55,1 (56,9–60,3) p=0,7023

Note: p — relative to the group of burned patients who received a fraction of FiO_2% = 50–55%.

Примечание: p — по отношению к группе обожженных, получавших фракцию FiO_2% = 50–55%.

720 minutes reduces pain sensitivity by half and the frequency of intravenous, intramuscular, and transdermal administration of the opioid analgesic (fentanyl) by 18–20%.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

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Consent for publication. Written consent was obtained from the patient for publication of relevant medical information within the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Информированное согласие на публикацию. Авторы получили письменное согласие пациентов на публикацию медицинских данных.

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