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Therapy of acute postoperative respiratory failure with autosurfactant

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Abstract

Background

One of the important causes of acute postoperative respiratory failure may be a decrease in the surface activity of interfacial surfactant located at the air/liquid interface and providing surface tension of alveoli and bronchioles .The main problem with the use of exogenous surfactant obtained from animals (calves, lambs, pigs, etc.) by lung flushing and synthetic surfactant is that in the treatment of acute respiratory failure there are not enough convincing good results in the treatment of severe patients. Exogenous surfactant does not correspond to human surfactant in its biochemical composition, adsorption, distribution, surface-active properties, and excretion period.

Objectives

To investigate the effects of autosurfactant therapy on respiratory mechanics and oxygenation in patients with acute postoperative respiratory failure.

Methods

The examination and treatment data of 27 patients, operated in the thoracic department were included in this study. Central form of cancer in stage II-III was detected in all 27 patients. In the postoperative period all patients had complications from the side of respiratory organs, disorders of tracheobronchial patency with hypoventilation of one or two lung lobes in 26 patients, atelectasis of a lobe in one patient .Pulmonary complians was reduced and amount 38,2 ± 0,2 ml/mbar on ventilator Blood oxygen saturation (SaO2) was reduced and was 93 ± 04%. Due to the severity of the condition caused by the development of respiratory failure, prolonged ventilation in PSV Bronchoalveolar flush was obtained from healthy subsegmental bronchi of the lung contralateral to the pathological process before surgery during fibrobronchoscopic examination of the patient in the amount of 40–50 ml. It was filtered through sterile gauze and centrifuged at low temperature for 10 minutes. Surface tension was checked on a Wilhelmi scale. Supernatant containing surfactant with good surfactant properties was used for therapy of acute postoperative respiratory failure, where the surface tension minimum was 24 ± 3.0 mN/m. The supernatant fluid in the amount of 10–15 ml was injected into the right or left main bronchus in the presence of hypoventilation and atelectasis of the damaged lung in a patient identified using a fiberoptic bronchoscope.

Results

After application of autosurfactant, there was an increase in respiratory volume by 10.3 ± 0.2% (p = 0.02), lung compliance by 21.4 ± 0.35% (p 0.05), SaO2 93 ± 0,4% to 97 ± 0,3%. There was no antigenic

incompatibility of the thus obtained preparation with human surfactant, since this method is not organ and tissue transplantation.

Conclusions

The application of autosurfactant demonstrated significant clinical efficacy in improving pulmonary function for patients with acute postoperative faiulure. This innovative approach offers a promising therapeutic alternative for managing respiratory complications.

Introduction

Identification of causes and treatment of acute postoperative respiratory failure is one of the urgent problems of modern medicine. Acute respiratory failure is a severe complication in the immediate postoperative period, which develops in 3.4% of patients in relation to the total number of operated patients [1]. One of the important causes of acute postoperative respiratory failure may be a decrease in the surface activity of interfacial surfactant located at the air/liquid interface and providing surface tension of alveoli and bronchioles [2, 3, 4]. However, until recently, methods of surface tension correction in the lungs of patients with acute postoperative respiratory failure have been insufficiently developed [8].

With the introduction of the method of obtaining subsegmental bronchoalveolar flushes into clinical practice, the methodological opportunities for conducting targeted studies of the state of alveolar surfactant in operated patients and for elucidating the role of its dysfunction in the development of acute postoperative respiratory failure have expanded.

Pulmonary surfactant is a multicomponent natural complex consisting of 7 classes of phospholipids, neutral lipids, cholesterol, 4 protein groups. It is practically impossible to create a preparation of exogenous surfactant, which by its composition and biochemical composition would be identical to human surfactant. This explains the failure of the use of exogenous surfactant preparation obtained from animal lung extract by bronchoalveolar lavage and synthetic surfactant in the treatment of respiratory failure in adults [8,14]. Therefore, we propose to obtain surfactant from the patient before surgery by bronchoalveolar lavage and administer it to the patient in case of acute respiratory failure in the postoperative period.

Objectives.

To evaluate the efficacy of preoperatively harvested contralateral autologous surfactant (autosurfactant) in patients with acute postoperative respiratory failure and to assess its effects on pulmonary mechanics and oxygenation.

MATERIALS AND METHODS

Patients

The study protocol involves patients undergoing elective thoracic surgery with a high risk of developing postoperative pulmonary complications. This single-center prospective interventional clinical study was approved by the Ethics Committee of Astana Medical University. Written informed consent was obtained from all subjects. The examination and treatment data of 27 patients, operated in the Thoracic Department of Astana Medical University, were included in this study. Central form of cancer in stage II-III was detected in all 27 patients. All 27 patients with this pathology had changes in the form of atelectasis and hypoventilation of two lung lobes. In 15 patients pneumonectomy operation was performed, in 12 patients removal of two lung lobes was performed. In the postoperative period all patients had complications from the side of respiratory organs, disorders of tracheobronchial patency with hypoventilation of one or two lung lobes in 26 patients, atelectasis of a lobe in one patient according to chest X -ray examination date. Blood oxygen saturation (SaO2) was reduced and was 93 ± 0,4%, arterial oxygen tension (PaO2) – 76,2 ± 1,2 mmHg on ventilator. Due to the severity of the condition caused by the development of respiratory failure, prolonged ventilation in PSV mode up to 25.5 ± 1,3 hours was performed in all patients.

This research was conducted in 2025. .

3.1.1. Inclusion criteria for the Main Study Phase

(1) The age between 40–65 years old ;

(2) lung cancer, grade II -III;

(3) participants of box sexes ;

(4) planned surgical interventions;

(5) signed informed consent.

3.1.2. Exclusion Criteria

(1) Pregnancy

(2) hypertensive disease

(3) coronary artery diseases

(4) preoperative hemodynamic instability, defined as use of vasopressors.

Only elective patients with the American Society of Anesthesiologists (ASA) physical status II-III were included in this study.

Investigation Design and Procedure

Respiratory parameters were evaluated before and after autosurfactant administration in the same patients.

Bronchoalveolar Lavage Collection

Following completion of the clinical protocol, bronchoalveolar lavage (BAL) was obtained using a standardized lavage technique .The collected BAL fluid was immediately centrifuged at 4°C at 1500 rpm for 10 minutes to separate the cellular component from the supernatant. Bronchoalveolar flush was obtained from healthy subsegmental bronchi of the lung according recommendation ATS/ERS contralateral to the pathological process before surgery during fibrobronchoscopic examination of the patient in the amount of 40–50 ml. Supernatant containing surfactant with good surfactant properties was used for therapy of acute postoperative respiratory failure, where the surface tension minimum was 24 ± 3.0 mN/m in the amount of 10–15 ml. Autosurfactant was injected into the right or left main bronchi where there was hypoventilation, atelectasis of the damaged lung patient using a fibrobronchoscope.

Assessment of Surface-Active Properties

Surface tension characteristics of BAL fluid were measured using a Wilhelmy balance. The following parameters were analyzed:

- • Static surface tension (γstatic)
- • Maximum surface tension (γmax)
- • Minimum surface tension (γmin)
- • Stability index (SI)

Statistical Analysis

Data are presented as mean ± standard error of the mean (SEM). Statistical analyses were performed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA).

Comparisons between pre-treatment and post-treatment measurements were performed using the paired Student's t-test. For variables that did not meet assumptions of normality, the Wilcoxon signed-rank test was used. A two-sided p value < 0.05 was considered statistically significant.

Table 1
Demographic, Anthrometric Data, Surgical Volume (n -27)Indicator

Sex	
Male	19
Female	8
Age	58 ± 7,1
Weight, kg	71 ± 8,4
Height, cm	169 ± 4,5
Duration of surgery,hour	2,5 ± 0,3
Volume of operation :	15
Pneumonectomy	12
Removal of two lung lobes	

Results

All patients were comparable in terms of anthropometric data, weight, baseline blood pressure. After application of autosurfactant, there was an increase in respiratory volume by 10.3 ± 0.2% (p = 0.02), lung compliance by 21.4 ± 0.35% (p 0.05), SaO2 93 ± 0,4% to 97 ± 0,3% (p0.05) (Table 2). No adverse hemodynamic changes or allergic reactions were observed throughout the postoperative period. All 27 patients survived.

Table 2
Tidal volume, Compliance lungs, SaO2 before and after autosurfactant therapy Indicator

Before	**After therapy**
Tidal volume ,ml 390 ± 10	430 ± 2,3 (p< 0,05)
Complians lungs,ml/mbar 38,2 ± 0,2	46,1 ± 0,16 (p <0,05)
SaO2 93 ± 0,4%	97 ± 0,3% (p0.05)

Discussion

Surfactant dysfunction contributes significantly to the development and outcomes of various lung diseases, as demonstrated by numerous studies [3–5]. In 1959, surfactant deficiency was identified as the principal pathogenetic factor underlying neonatal respiratory distress syndrome (RDS). Consequently, surfactants derived from animal lungs and bronchoalveolar lavage fluid were developed, followed by

synthetic and semi-synthetic surfactant preparations [13]. Surfactant replacement therapy has demonstrated substantial clinical benefits in neonatal RDS.

A comprehensive search of the PubMed, EMBASE, Cochrane Library, CNKI, and Wanfang databases identified studies published up to December 2024. Only multicenter randomized controlled trials involving children aged 1 month to 18 years with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) were included [32]. This systematic review and meta-analysis demonstrated that surfactant therapy was associated with reduced mortality and fewer adverse events in critically ill children with ARDS; however, no significant reduction in the duration of mechanical ventilation was observed [32].

In contrast, the efficacy of surfactant therapy in adults with acute respiratory failure remains controversial. The use of exogenous surfactants in adult patients has been investigated for several decades; however, study results have been inconsistent. While large international multicenter trials have generally failed to demonstrate a reduction in mortality, several smaller studies have reported favorable clinical outcomes.

Rosenberg et al. [14] evaluated the efficacy of early endotracheal administration of surfactant in mechanically ventilated patients with established ARDS. The authors concluded that the timing of surfactant administration and the therapeutic efficacy of Surfactant-BL were the most important determinants of treatment success. Among 58 patients with ARDS, approximately 80% responded favorably to surfactant therapy. Within 6–24 hours after treatment initiation, the PaO_2/FiO_2 ratio increased, lung injury scores improved, pulmonary infiltrates decreased, the duration of mechanical ventilation was reduced to approximately 6 days, and mortality decreased from 70% to 15.4%. The only significant difference between responders and non-responders was the timing of treatment initiation. The average interval between deterioration of oxygenation (PaO_2/FiO_2 < 200 mmHg) and the first surfactant administration was 18 hours in responders compared with 36 hours in non-responders.

Dushianthan et al. (2023) administered natural bovine surfactant via inhalation using modern nebulizers to mechanically ventilated adults with COVID-19. In this randomized trial, no long-term survival benefit was observed. Nevertheless, other investigators [6, 9] have suggested that exogenous surfactant may represent a promising therapeutic option for COVID-19-associated respiratory failure. Multicenter studies [15] reported that early administration of bovine lung-derived surfactant (Surfactant-BL) was associated with reduced mortality and significantly improved oxygenation in patients with severe COVID-19.

Positive results were also reported with recombinant surfactant protein C-containing surfactant (Ventricute) [11]. However, other investigators [13] studying Ventricute in adults with severe ARDS failed to demonstrate significant clinical benefits. Although administration of the drug resulted in transient improvement in gas exchange during the first 24 hours, no statistically significant reduction in mortality or duration of mechanical ventilation was observed.

Overall, evidence supporting a mortality benefit from surfactant therapy in adult ARDS remains inconclusive [12]. Anzueto et al. (1996) conducted a large multicenter randomized controlled trial involving 725 adult patients with sepsis-associated ARDS who received continuous aerosolized administration of the synthetic surfactant Exosurf [16]. The treatment failed to improve oxygenation or reduce 30-day mortality.

Exosurf is a fully synthetic surfactant composed primarily of dipalmitoylphosphatidylcholine (DPPC) but lacking the critical surfactant proteins SP-B and SP-C. No significant advantages over placebo were observed. Mortality remained approximately 40% in both groups, while gas exchange, oxygenation indices, duration of mechanical ventilation, and the incidence of multiple organ failure were unchanged. These findings have been attributed to the absence of surfactant proteins and insufficient delivery of aerosolized surfactant to the alveolar space.

Similarly, a large meta-analysis by Meng et al. (2019), which included 11 randomized controlled trials involving 3,038 patients, demonstrated no significant clinical benefit of exogenous surfactant therapy in adults with ARDS-related respiratory failure [12].

Variability in surfactant formulations, dosage regimens, delivery methods, biological half-life, susceptibility to inactivation within the injured lung, and differences in biophysical properties may all contribute to the inconsistent results reported in clinical studies. Therefore, several authors have emphasized the need for further research aimed at developing optimized surfactant formulations and identifying the most effective timing, dosage, and administration techniques [4,11].

Targeted delivery of surfactant to affected lung regions appears to be essential for maximizing therapeutic efficacy. Furthermore, mechanical ventilation should be maintained using lung-protective strategies after surfactant administration, including low tidal volumes and adequate positive end-expiratory pressure (PEEP), in order to minimize surfactant degradation and inactivation [14]. Current evidence suggests that surfactant therapy is most effective when the underlying cause of respiratory failure has been adequately controlled or eliminated [14].

Pulmonary surfactant is a highly complex biological system consisting of multiple phospholipid classes, neutral lipids, cholesterol, and surfactant-associated proteins. Because of this complexity, it is extremely difficult to develop an exogenous surfactant preparation that fully reproduces the composition and function of native human surfactant. This may partly explain the inconsistent efficacy of animal-derived and synthetic surfactants in adult respiratory failure.

In the present study, administration of autologous surfactant obtained from the patient's own unaffected contralateral lung was associated with significant improvement in pulmonary mechanics, particularly lung compliance. Unlike commercially available exogenous surfactants, the autosurfactant used in this study preserved the native biochemical composition and surface-active properties of human surfactant. No adverse reactions attributable to autosurfactant administration were observed.

These findings suggest that autologous surfactant therapy may represent a promising approach for the management of acute postoperative respiratory failure. Nevertheless, larger controlled clinical studies are required to confirm its efficacy and safety.

Conclusions

Surfactant dysfunction appears to be an important factor in the development of acute postoperative respiratory failure following major thoracic surgery. Existing exogenous surfactant preparations have shown inconsistent efficacy in adult patients, which may be related to differences in biochemical composition, surface-active properties, delivery efficiency, and biological behavior compared with native human surfactant.

In the present study, administration of autologous surfactant obtained preoperatively from the patient's own unaffected contralateral lung was associated with significant improvements in pulmonary mechanics and oxygenation. Autosurfactant therapy resulted in increased tidal volume, improved lung compliance, and higher arterial oxygen saturation in patients with acute postoperative respiratory failure.

The proposed approach is innovative because it involves harvesting surfactant directly from the patient before surgery and administering this personalized biological preparation if postoperative respiratory failure develops. By preserving the native biochemical composition and surface-active properties of human surfactant, autosurfactant may represent a promising adjunctive treatment for acute postoperative respiratory failure.

Future studies should evaluate autosurfactant therapy in larger patient populations and include direct molecular assessment of surfactant phospholipids and surfactant-associated proteins to better elucidate the mechanisms underlying the observed clinical effects.

LIMITATIONS

This study has several limitations. First, the sample size was relatively small, which may limit the generalizability of the findings.Second, direct biochemical quantification of autosurfactant phospholipids and surfactant-associated proteins was not performed. Therefore, the mechanisms underlying the observed functional alterations can only be inferred indirectly. Future studies should include use autosurfactant in larger number of patients, direct molecular assessment of surfactant composition.

Declarations

Conflict of interest : The authors have no conflict of interest in recruiting the research material and writing this article.

Author Contributions

Adil A. Mustafin and Alua Sadriten: Conceptualization, data collection, investigation, formal analysis, statistical analysis, manuscript drafting, and interpretation of results.

Alibek Kh. Mustafin: Study design, supervision, methodology, critical revision of the manuscript and final approval of the submitted version.

Kulsara R. Rustemova**:** manuscript drafting, interpretation of results, critical revision of the manuscript, and final approval of the submitted version.

Ethical Approval: This study was approved by the Ethics

Committee of Astana Medical University (code: 3).

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Informed Consent: Written informed consent was obtained from all subjects.

Author Contribution

A.M. conceived, designed, and supervised the study, developed the methodology, performed the clinical procedures, interpreted the data, and critically revised the manuscript. Ad.M. contributed to patient management, data interpretation, and critical revision of the manuscript. K.R. contributed to study design, interpretation of the findings, manuscript editing, and scientific supervision. A.S. performed the literature review, statistical analysis, prepared the tables and figures, and drafted the manuscript. All authors reviewed and approved the final manuscript.

Data Availability

The datasets generated and analyzed during the current study are not publicly available because they contain confidential clinical data but are available from the corresponding author on reasonable request.

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