GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 11 (368) ноябрь 2025

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

GEORGIAN MEDICAL NEWS
NO 11 (368) 2025

Содержание:

GEORGIAN MEDICAL NEWS
No 11 (368) 2025

SUCCESSFUL USE OF PROLONGED INHALATIONAL SURFACTANT THERAPY IN AN EXTREMELY SEVERE PATIENT WITH COVID-19-ASSOCIATED ARDS.

Marat Syzdykbayev[1], Bazar Tuleuov[2], Maksut Kazymov[3], Kulsara Rustemova[4], Gulshat Alimkhanova[5]*, Akzhunus Zheksenova[6], Rustem Kazangapov[7], Saltanat Khamzina[8], Saule Abdikazimova[8], Abzal Ismatov[9], Sanzhar Khalelov[10], Roman Khripunov[11].

[1]NJSC "Semey Medical University", Department of Anesthesiology and Reanimatology, Semey, Kazakhstan.

[2]Emergency hospital, Department of Surgery, Semey, Kazakhstan.

[3]NJSC "Semey Medical University", Department of General Medical Practice, Semey, Kazakhstan.

[4]Kokshetau State University named after Sh. Ualikhanov, State Scientific Research Institute of Life and Health Science, Department of Surgical Disciplines, Kokshetau, Kazakhstan.

[5]NJSC Scientific Center of Pediatrics and Pediatric Surgery, Department of Anesthesiology, Almaty, Kazakhstan.

[6]NJSC «Astana Medical University», Department of Surgery, Astana, Kazakhstan.

[7]Pavlodar Branch of Semey Medical University, Pavlodar, Kazakhstan.

[8]Kokshetau State University named after Sh. Ualikhanov, Higher School of Medicine, Department of Clinical Disciplines, Kokshetau, Kazakhstan.

[9]Hospital city, Department of Surgery, Astana, Kazakhstan.

[10]NJSC "Semey Medical University", Department maxillofacial surgery, Semey, Kazakhstan.

[11]East Kazakhstan Regional Specialized Medical Center, Department Anesthesiology and Reanimatology, Ust-Kamenogorsk, Kazakhstan.

Abstract.

Acute respiratory distress syndrome (ARDS) is a severe complication of COVID-19. During the pathogenesis of ARDS, a deficiency of alveolar surfactant could lead to severe hypoxemia. This report demonstrates that exogenous surfactant administration improves the overall clinical condition, reduces severe hypoxemia, and enhances the P/F ratio, thereby preventing the multiple organ dysfunction syndrome (MODS) that usually follows hypoxemia. In our experience, inhalational administration of surfactant preparations for one week was the key to successful treatment and recovery of extremely severe patients who would otherwise have had an unfavorable prognosis.

Key words. ARDS, COVID-19, MODS, Surfactant.

Introduction.

The COVID-19-related ARDS is accompanied by damage to the alveolar type II cells, the main source of lung surfactant [1,2]. Surfactant deficiency due to alveolar type II cell damage leads to atelectasis and bilateral infiltration in the inferior lobes of the lungs, further aggravating the disease severity [3].

Alveolar surfactant plays a protective role in the lungs, providing a “first line of defense” against infections [4]. The existing data show that surfactant deficiency is often accompanied by a reduction of clearance from many bacterial and viral infections, including group B *streptococcus* [5,6], *Pseudomonas aeruginosa* [7], and respiratory syncytial virus [8]. Surfactant possesses a direct anti-bacterial activity against *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter aerogenes* [9] and an antifungal activity against *Histoplasma capsulatum* [10].

At the beginning of the COVID-19 pandemic, there was virtually no experience with surfactant preparations. Later, many studies reported the successful use of surfactant preparations in treating COVID-19 [1,11-15]. Here, we present our experience treating a patient with severe COVID-19-related ARDS using a complex therapy consisting of inhalational administration of an exogenous surfactant preparation and supportive medications.

Case Report.

A 47-year-old woman with a medical history of arterial hypertension, obesity, and impaired glucose tolerance was admitted to the hospital after one week of dyspnea at rest, fever, dry cough, and generalized weakness. On admission, the patient was febrile (39.2 °C) and disoriented, with an oxygen saturation of 34%. Arterial blood gas analysis revealed a partial pressure of oxygen (PaO_2) of 40 mm Hg and a PaO_2/FiO_2 (P/F) ratio of 40 (Figure 1A & B). The P/F ratio, calculated as the ratio of partial arterial oxygen tension (PaO_2) to the fraction of inspired oxygen (FiO_2), is a key indicator of the degree of hypoxemia and pulmonary gas exchange efficiency. Normal values range from approximately 300 to 500 mm Hg; values below 300 mm Hg indicate impaired gas exchange, and those below 200 mm Hg correspond to severe hypoxemia. The P/F ratio, primarily used to assess the severity of acute respiratory distress syndrome (ARDS), provides valuable information about the extent of respiratory dysfunction.

A nasopharyngeal swab tested positive for SARS-CoV-2 by PCR, and chest radiography demonstrated bilateral pulmonary opacities.

Prior to admission, the patient had been treated at home with Rotacef, dexamethasone, nadroparin calcium (Fraxiparine), and budesonide (Pulmicort). Following emergency care, including support of vital functions and non-invasive ventilation with 100% oxygen, arterial PaO_2 and the P/F ratio improved, reaching 62 mm Hg and 62, respectively, by the second day of hospitalization (Figure 1A & B).

Despite complex treatment, including prone positioning and administration of the drugs listed in Table 1, the P/F ratio—an important parameter for assessing disease severity and predicting ARDS progression—did not improve further. After extensive team discussions and consultations, it was decided

Table 1. *The complex treatment schedule.*

Drugs	**Dosage and route of administration**
Anticoagulants - Heparin (Hepasan)	 20,000 un/24 h
Antibiotics - amoxicillin/clavulanic acid **(**Amoxiclant) - Levofloxacin	 1.2g, IV, 3 times/24h 100ml, IV drip, 2 times/24h
Corticosteroids - Methylprednisolone **(**Metipred)	 250mg, IV drip, 1 time/24h
Ascorbic acid 5% solution	6ml, IV
Interleukine-6 antagonist - Tocilizumab (Actemra)	 20ml (400mg), IV drip
Immunoglobulins - Human Normal Immunoglobulin (Kiovig)	 100 ml, IV drip, 1 time/24h
Correction of arterial hypertension - Isosorbide dinitrate - Valsartan (Valmac)	 10ml, IV drip, 1 time/24h 90 mg, *per os*, 1 time/day
Diuretics - Spironolactone (Aldaron) - Furosemide (Lasix)	 100mg, *per os*, 1 time/24h 4ml, IV, 1-2 times/24h
Correction of hyperglycemia - Human insulin (Actrapid)	 2 IU, subcutaneous, 3 times/24h
Antifungal - Mycophenolate mofetil **(**Mycosan)	 100ml, IV drip, 1 time/24h

to administer a surfactant preparation with the specific aim of improving the P/F ratio.

On the third day of hospitalization, the inhalational exogenous surfactant preparation Curosurf® (poractant alfa) was administered 3 times a day. The PaO_2 and P/F ratio improved significantly and reached the values of 82 mm Hg and 82, respectively (Figure 1A & B). The patient complained of a sore throat and difficulty tolerating the treatment. Some decrease in oxygen saturation was observed immediately after an inhalation; however, 20 – 30 min following the inhalation, the saturation reached 100%.

On the fourth day of hospitalization, we administered another surfactant preparation – Surfactant BL (Biosurf, Russia), inhalational, 3 times a day. The medication was well tolerated by the patient, without any adverse effects. The PaO_2 value increased significantly up to 156 mm Hg (Figure 1A); the fraction of inspired oxygen (FiO_2) reduced to 90%. P/F ratio has reached the value of 173 (Figure 1B).

During the following day, the inhalation of Surfactant BL was reduced to 1-2 times a day. The PaO_2 and P/F ratio values decreased (128 mm Hg and 142, respectively; Figure 1A & B), while the FiO_2 was maintained at about 90%. Overall, the inhalational therapy with the exogenous surfactant preparations was conducted for 7 days, one day with the Curosurf®, and 6 days with the Surfactant BL. Following this period of treatment, a slow increase in PaO_2 and P/F ratio values was observed (Figure 1A & B).

We emphasize that before treatment with surfactant preparations, the patient exhibited early signs of MODS, including oliguria (300–1000 ml/24h), mild elevations in blood urea and creatinine levels, signs of coagulopathy, and increased alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels.

The complex therapy described above led to the following improvements: normalization of urine output up to 1800 ml/24 h and a decrease in blood levels of ALT, AST, urea, and creatinine (Figure 2).

A similar trend was also observed with the blood level of C-reactive protein (CRP). Initially, the blood CRP was greater than 200 mg/ml (Figure 3A, 210.2 mg/ml at “Day 1” and 207.2 mg/ml at “Day 2”, respectively), then decreased (Figure 3A, 0 mg/ml at “Day 4” and 26.7 mg/ml at “Day 5”, respectively). The blood level of the D-dimer was about 1300 ng/ml at Day 1, then increased transiently to 2600 ng/ml at “Day 4”, then decreased to 1900 ng/ml at “Day 5” (Figure 3B).

All the medications listed above were administered from the first day of hospitalization; however, significant improvement in respiratory signs occurred after the beginning of the inhalational administration of surfactant preparations. In particular, the above-mentioned respiratory signs included: a reduction in oxygen supply fraction to 90%; increased breathing; decreased wheezing, and disappearance of crepitus on auscultation. The patient noticed an improvement in general well-being and increased appetite.

After three weeks in the hospital, the oxygen saturation reached 97%, while the oxygen supply fraction was reduced to 70%. The blood levels of ALT, AST, urea, and creatinine were normalized. The patient became more active and spent more time sitting on the bed.

Finally, the patient was discharged after 54 days of treatment in our hospital. The patient spent most of this time in the intensive care unit. Upon discharge, rehabilitation therapy was recommended.

Discussion.

Severe hypoxia in COVID-19 patients underlies the development of multiple organ failure, and subsequently, an

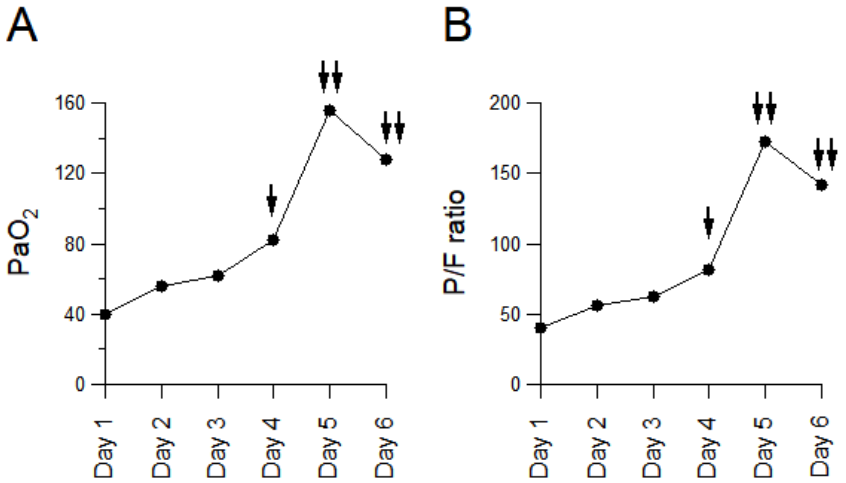

Figure 1. *The partial pressure of oxygen (PaO_2) and P/F ratio during the first 6 days upon admission to the hospital. The single arrow indicates the inhalational administration of Curosurf® (poractant alfa) surfactant preparation. Two arrows indicate the inhalational administration of Surfactant BL preparation.*

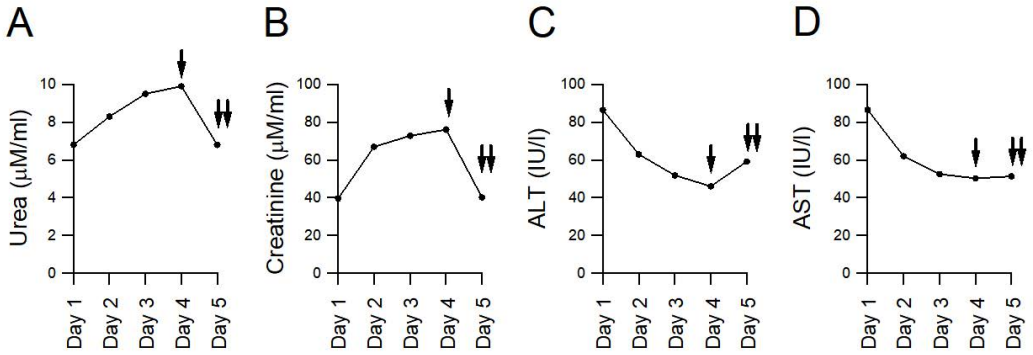

Figure 2. *Blood levels of urea, creatinine, ALT, and AST during the first 5 days upon admission to the hospital. The single arrow indicates the inhalational administration of Curosurf® (poractant alfa) surfactant preparation. Two arrows indicate the inhalational administration of Surfactant BL preparation.*

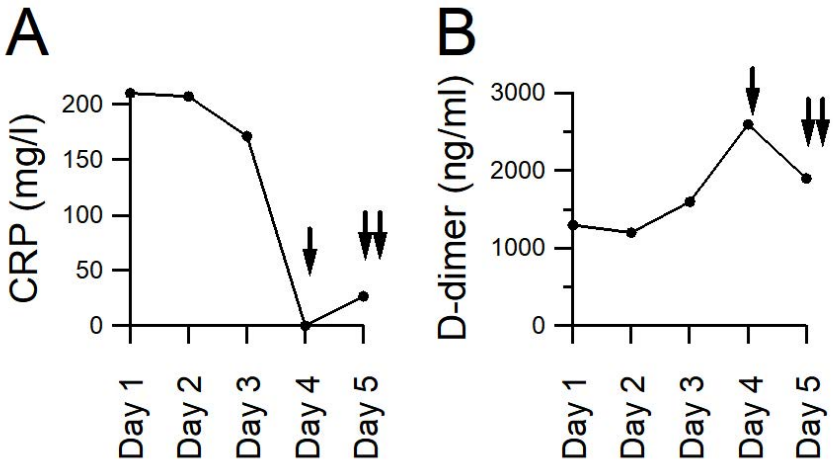

Figure 3. *Blood levels of CRP and D-dimer during the first 5 days upon admission to the hospital. The single arrow indicates the inhalational administration of Curosurf® (poractant alfa) surfactant preparation. Two arrows indicate the inhalational administration of Surfactant BL preparation.*

unfavorable outcome [16]. Our patient has some signs of the beginning stage of MODS. Her condition is compatible with the previously published cases in which severe coronavirus disease complicated by hypoxemia and dyspnea progressed to ARDS [1]. Besides the lungs, COVID-19 is also related to damage to other organs, such as the liver, kidneys, heart, gastrointestinal, hematological, and nervous systems [3,17,18]. In these cases, a high mortality rate and induction of multiple organ failure were observed [17,18]. In 17% of the patients with severe COVID-19, the ARDS could develop as early as one week after the onset of the disease, and the condition of 65% of the patients worsens, and these patients usually die due to the incidence of MODS [18,19]. The reported incidence of ARDS varies between 15.6% and 31%, much higher than other organ damage [20]. It has been shown that the ARDS occurrence is closely correlated with older age groups (i.e., more common in people over 65), as well as with arterial hypertension and diabetes mellitus [21]. Our patient had arterial hypertension, obesity, and newly diagnosed diabetes mellitus and, therefore, was at risk of ARDS development.

The lungs are typically the first organs affected in patients who progress to multiple organ dysfunction syndrome (MODS), with initial pulmonary impairment preceding cardiac, renal, and hepatic dysfunction [22,23]. Therefore, preventing the occurrence of MODS by supporting lung function is particularly important, as early pulmonary impairment can trigger subsequent multi-organ failure. From this perspective, we suggest that administration of exogenous pulmonary surfactant may have played a central role in the observed improvement of our patient, likely promoting expansion of alveoli not affected by fibrosis. This alveolar recruitment may have contributed to reduced hypoxia and increased arterial oxygen partial pressure and P/F ratio [19], thereby lowering the risk of MODS.

The complex therapy, which included surfactant along with antibiotics, anticoagulants, corticosteroids, immunoglobulins, and other agents, was associated with normalization of urine output and reductions in ALT, AST, urea, and creatinine, reflecting overall clinical improvement. The marked decrease in CRP levels may be attributed to tocilizumab, an anti-IL-6 monoclonal antibody, which blocks IL-6 signaling and reduces hepatic synthesis of inflammation- and coagulation-related proteins [24-27]. A transient, "paradoxical" increase in D-dimer levels on the fourth day, also reported in severe COVID-19 cases [28,29], may result from partial inhibition of IL-6–mediated inflammatory activity [29], insufficient to prevent the release of the pro-thrombotic peptide α-defensin from neutrophils, thereby accelerating coagulation and causing elevated D-dimer levels [30].

Conclusion.

To summarize, we report that the complex therapy, which included the prolonged use of surfactant preparations in the intensive care of ARDS secondary to COVID-19 pneumonia, improved arterial oxygen tension (PaO_2) and the PaO_2/FiO_2 (P/F) ratio. The patient, admitted with severe ARDS and a P/F ratio of approximately 40, recovered following this therapy, despite the generally unfavourable prognosis associated with the presence of concomitant severe diseases.

REFERENCES

1. Heching M, Lev S, Shitenberg D, et al. Surfactant for the Treatment of ARDS in a Patient With COVID-19. Chest. 2021;160:e9-e12.
2. Takano H. Pulmonary surfactant itself must be a strong defender against SARS-CoV-2. Med Hypotheses. 2020;144:110020.
3. Gurka DP, Balk RA. Acute respiratory failure. Critical Care Medicine: Elsevier. 2008:773-94.
4. Ghosh S, Das S, Mondal R, et al. A review on the effect of COVID-19 in type 2 asthma and its management. Int Immunopharmacol. 2021;91:107309.
5. LeVine AM, Bruno MD, Huelsman KM, et al. Surfactant protein A-deficient mice are susceptible to group B streptococcal infection. J Immunol. 1997;158:4336-40.
6. LeVine AM, Kurak KE, Wright JR, et al. Surfactant protein-A binds group B streptococcus enhancing phagocytosis and clearance from lungs of surfactant protein-A-deficient mice. Am J Respir Cell Mol Biol. 1999;20:279-86.
7. LeVine AM, Kurak KE, Bruno MD, et al. Surfactant protein-A-deficient mice are susceptible to Pseudomonas aeruginosa infection. Am J Respir Cell Mol Biol. 1998;19:700-8.
8. LeVine AM, Gwozdz J, Stark J, et al. Surfactant protein-A enhances respiratory syncytial virus clearance in vivo. J Clin Invest. 1999;103:1015-21.
9. Wu H, Kuzmenko A, Wan S, et al. Surfactant proteins A and D inhibit the growth of Gram-negative bacteria by increasing membrane permeability. J Clin Invest. 2003;111:1589-602.
10. McCormack FX, Gibbons R, Ward SR, et al. Macrophage-independent fungicidal action of the pulmonary collectins. J Biol Chem. 2003;278:36250-6.
11. Ahmed S, Akter MS, Roy K, et al. Role of Surfactant for the Treatment of Alveolar Cells against Coronavirus (Covid-19). Annual Research & Review in Biology. 2020;35:34-9.
12. Bautin AE AS, Seyliev AA SM, Merzhoeva Z, et al. Inhalation surfactant therapy in the integrated treatment of severe COVID-19 pneumonia. Tuberculosis and Lung Diseases. 2020;98.
13. Mirastschijski U, Dembinski R, Maedler K. Lung Surfactant for Pulmonary Barrier Restoration in Patients With COVID-19 Pneumonia. Front Med (Lausanne). 2020;7:254.
14. Piva S, DiBlasi RM, Slee AE, et al. Surfactant therapy for COVID-19 related ARDS: a retrospective case-control pilot study. Respir Res. 2021;22:20.
15. Pramod K, Kotta S, Jijith US, et al. Surfactant-based prophylaxis and therapy against COVID-19: A possibility. Med Hypotheses. 2020;143:110081.
16. Singer M. Management of multiple organ failure: guidelines but no hard-and-fast rules. J Antimicrob Chemother. 1998;41:103-12.
17. Gupta A, Madhavan MV, Sehgal K, et al. Extrapulmonary manifestations of COVID-19. Nat Med. 2020;26:1017-32.
18. Chen J, Qi T, Liu L, et al. Clinical progression of patients with COVID-19 in Shanghai, China. J Infect. 2020;80:e1-e6.
19. Radermacher P, Maggiore SM, Mercat A. Fifty Years of Research in ARDS. Gas Exchange in Acute Respiratory Distress Syndrome. Am J Respir Crit Care Med. 2017;196:964-84.

20. Li X, Ma X. Acute respiratory failure in COVID-19: is it "typical" ARDS? Crit Care. 2020;24:198.
21. Wu C, Chen X, Cai Y, et al. Risk Factors Associated with Acute Respiratory Distress Syndrome and Death in Patients with Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med. 2020;180:934-43.
22. Ciesla DJ, Moore EE, Johnson JL, et al. The role of the lung in postinjury multiple organ failure. Surgery. 2005;138:749-57.
23. Ramirez M. Multiple organ dysfunction syndrome. Curr Probl Pediatr Adolesc Health Care. 2013;43:273-7.
24. Okuda Y. Review of tocilizumab in the treatment of rheumatoid arthritis. Biologics. 2008;2:75-82.
25. Hashimoto S, Yoshizaki K, Uno K, et al. Prompt Reduction in CRP, IL-6, IFN-gamma, IP-10, and MCP-1 and a Relatively Low Basal Ratio of Ferritin/CRP Is Possibly Associated with the Efficacy of Tocilizumab Monotherapy in Severely to Critically Ill Patients With COVID-19. Front Med (Lausanne). 2021;8:734838.
26. Di Nisio M, Potere N, Candeloro M, et al. Interleukin-6 receptor blockade with subcutaneous tocilizumab improves coagulation activity in patients with COVID-19. Eur J Intern Med. 2021;83:34-8.
27. Gualtierotti R, Ingegnoli F, Boscolo M, et al. Tocilizumab Effects on Coagulation Factor XIII in Patients with Rheumatoid Arthritis. Adv Ther. 2019;36:3494-502.
28. Griffin DO, Jensen A, Khan M, et al. Pulmonary Embolism and Increased Levels of d-Dimer in Patients with Coronavirus Disease. Emerg Infect Dis. 2020;26:1941-3.
29. Toniati P, Piva S, Cattalini M, et al. Tocilizumab for the treatment of severe COVID-19 pneumonia with hyperinflammatory syndrome and acute respiratory failure: A single center study of 100 patients in Brescia, Italy. Autoimmun Rev. 2020;19:102568.
30. Abdeen S, Abu-Fanne R, Bdeir K, et al. Divergent impacts of tocilizumab and colchicine in COVID-19-associated coagulopathy: the role of alpha-defensins. Br J Haematol. 2022;196:923-7.