Abstract

Introduction

Subarachnoid hemorrhage (SAH) is a life-threatening medical emergency that, in addition to primary central nervous system damage, leads to the development of numerous systemic complications. One of the most significant clinical problems in patients treated in the Intensive Care Unit (ICU) is acute respiratory failure (ARF), which significantly worsens the prognosis. The pathogenesis of gas exchange impairment in this group of patients is complex and biphasic. In the early period, excessive activation of the sympathetic nervous system plays a dominant role, leading to pulmonary microcirculation disturbances and secondary myocardial injury, resulting in the development of a cardiogenic phenotype of ARF. In the later phase of hospitalization, due to the need for prolonged mechanical ventilation, infectious complications become significantly important, primarily ventilator-associated pneumonia (VAP). The aim of the dissertation was to comprehensively evaluate the pathomechanisms of ARF in SAH patients, with particular emphasis on the usefulness of metanephrine concentration in a 24-hour urine collection in differentiating the respiratory failure phenotype, as well as assessing the incidence and etiology of VAP.

Material and methods

To achieve these objectives, two independent studies were conducted in a reference, multidisciplinary ICU. The first, a prospective pilot study (2022–2023), which included 18 patients with SAH and early ARF, defined as a decrease in the oxygenation index below 300 mmHg within the first 48 hours of admission. In this group, the concentration of metanephrine in a 24-hour urine collection was measured, and serum inflammatory markers, including interleukin-6, were analyzed to precisely differentiate between the cardiogenic and non-cardiogenic phenotypes of ARF. The second stage was a retrospective study (2019–2021, n=58), assessed the incidence of VAP based on standardized CDC epidemiological criteria, analyzing clinical parameters, and the results of microbiological tests of respiratory tract samples.

Results

In the prospective study, it was proven that patients with a cardiogenic mechanism of ARF were characterized by significantly deeper hypoxemia (median oxygenation index: 190 vs. 296 mmHg; $p < 0.05$) and an almost four times higher concentration of metanephrine in the

24-hour urine collection on admission (median: 249 vs. 63.5 ng/mL; p = 0.007) compared to the group without a cardiogenic component. The non-cardiogenic phenotype, on the other hand, was characterized by significantly higher concentrations of inflammatory markers, including interleukin-6 (median: 34 vs. 8.3 pg/mL; p = 0.013). Furthermore, in the group with the cardiogenic ARF phenotype, a perfect negative and statistically significant correlation was demonstrated between metanephrine concentration and OI on the first day of observation (R = -1.0; p < 0.001). A perfect positive and statistically significant correlation was also observed between metanephrine concentration and serum lactate concentration on the second and third days of treatment (R = 1.0; p < 0.001). The retrospective analysis showed that VAP developed in 19% of the evaluated patients (9 out of 47 patients), and the median time to diagnosis was 3.5 days (IQR: 3–4.5). The occurrence of VAP was associated with a higher risk of ICU death (OR = 1.69; 95% CI: 0.38–7.57) and higher in-hospital mortality (OR = 2.29; 95% CI: 0.43–12.24); notably, none of the patients diagnosed with VAP in the studied sample was successfully weaned from mechanical ventilation. At the same time, it was found that even cases of early-onset ventilator-associated pneumonia (EO-VAP) could be caused by multidrug-resistant (MDR) pathogens.

Conclusions

Measurement of metanephrine concentration in a 24-hour urine collection is a useful biomarker for differentiating between cardiogenic and non-cardiogenic ARF phenotypes. In the later period of therapy, VAP constitutes a critical challenge that significantly worsens the prognosis. The obtained results indicate the necessity of implementing personalized therapeutic strategies that consider the dynamically changing ARF phenotype and strict monitoring of infectious risk in neurocritically ill patients.

Keywords: subarachnoid hemorrhage, acute respiratory failure, metanephrine, mechanical ventilation, ventilator-associated pneumonia