Critical Rounds Newsletter
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Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you **"Critical Rounds Newsletter"** which contain latest and interesting news in the field of Critical Care.

This issue contains:

1. Effect of therapeutic plasma exchange on concentrations of both tissue factor and tissue factor pathway inhibitor in septic shock

2. Evaluation of the features and prognostic significance of acute kidney injury in out-of-hospital cardiac arrest patients

3. Evaluation of the safety of physical rehabilitation for critically ill Patients

4. A Rare Case of Adult croup caused by influenza A virus

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Looking forward to your valuable feedback

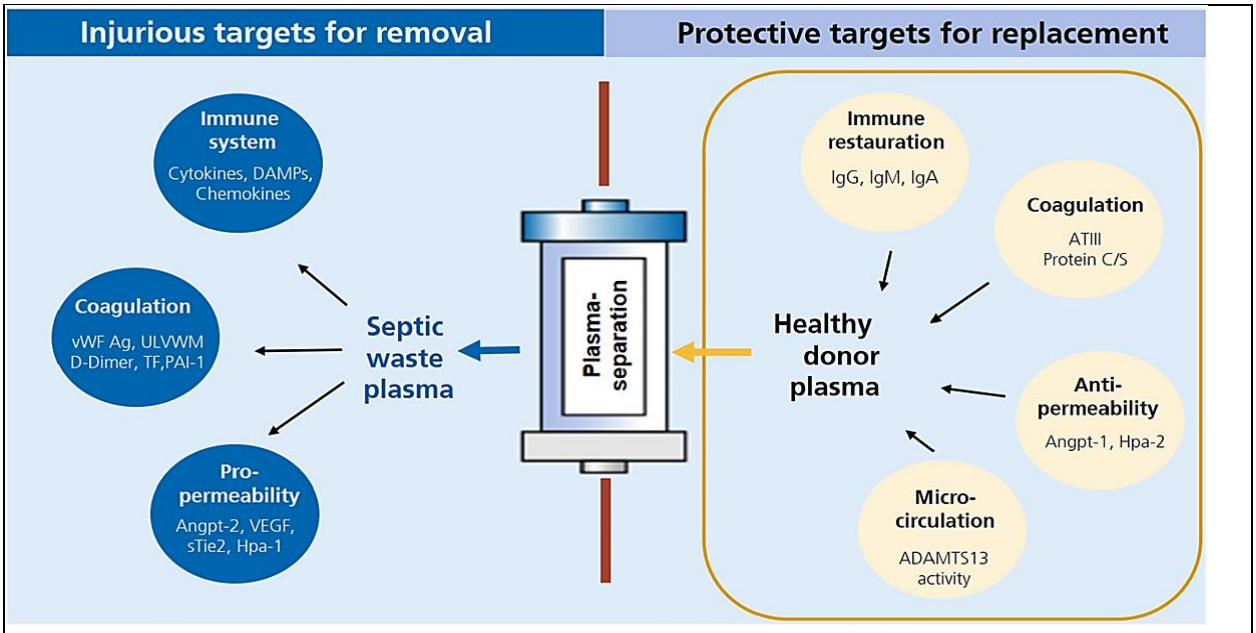
Best Regards,
Medical Team, Micro Labs Limited

Effect of therapeutic plasma exchange on concentrations of both tissue factor and tissue factor pathway inhibitor in septic shock

Introduction

Sepsis is a life-threatening organ malfunction induced by an abnormal host response to infection. Although the exact prevalence of sepsis is unclear, estimations show that it is a leading cause of mortality and serious illness globally. It was anticipated that sepsis would become more common, with increased public health and cost implications. The aging population with impaired immunity due to immunosenescence, as well as advances in immunomodulatory treatments for autoimmune diseases and cancer, and immune-suppressing therapies for solid-organ transplant recipients, make these populations more susceptible to infections.[1] Several treatment interventions targeting this host response have failed in studies thus far. Disseminated intravascular coagulation (DIC) and sepsis-induced coagulation (SIC) are intricate pathophysiological processes that may offer additional opportunities for interventional studies. Coagulopathy is a component of the pathological host response to infection in sepsis. Elevated plasma levels of tissue factor (TF) and tissue factor pathway inhibitor (TFPI) are linked to DIC, multi-organ failure, and higher mortality in sepsis. However, there are no treatments available currently that specifically target this axis.[2] So, this study examined how TPE affected the concentrations of TF and TFPI.

Higher baseline TF (and TFPI) plasma concentrations may predict treatment response and could guide predictive enrichment strategies in future clinical trials.



Plasma exchange in septic shock

Methods:

This post-hoc biobank analysis included 51 patients with early (shock onset <24 h) and severe (norepinephrine dose >0.4 µg/kg/min) septic shock, receiving either standard of care treatment (SOC, n=14) or SOC + one single TPE (n=37). Plasma concentrations of TF and TFPI were evaluated at 6 hours following study admission. TPE's effect on TF and TFPI concentrations was assessed and compared to those of SOC patients. Baseline TF and TFPI concentrations were utilized to predict clinical responsiveness to adjunctive TPE, as evidenced by a reduction in lactate concentrations throughout the first 24 hours after inclusion in the trial.

Results

Seventy-two percent of patients were male, with a median age of 54 (IQR 42-60). The lungs and abdomen were the most common sites of infection, with the causative pathogen identified in approximately 75% of cases. TPE significantly reduced circulating concentrations of TF and TFPI, while SOC group showed no difference. Within 6 hours, the relative change in TF was +14 (-0.8 to +30.4) % (p=0.089) in the SOC and −18.3 (−32.6 to −2.2) % (p<0.001) in the TPE group. Likewise, the relative change in TFPI was +14.4 (−2.3 to +30.9) % (p=0.076) in the SOC group and −20 (−32.8 to −7.9) % (p<0.001) in the TPE group (between group p=0.022) (Figure 1). The ratio of TF to TFPI remained constant in both the SOC and TPE groups. SOC patients had greater TF and TFPI concentrations at baseline, which led to an increase in lactate levels over the first 24 hours. Patients undergoing TPE showed consistent reductions in lactate concentrations across all degrees of baseline TF and TFPI increases. In a multivariate mixed-effects model, higher baseline TF (p=0.003) and TFPI (p=0.053) levels resulted in stronger longitudinal lactate concentration reduction effects in the TPE group.

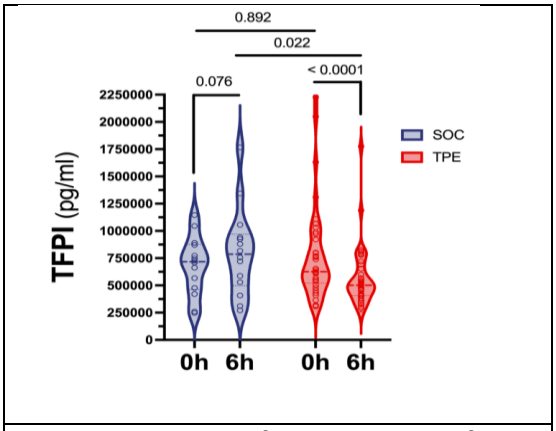


Figure 1. Impact of TPE on tissue factor pathway inhibitor concentrations.

Discussion

This post-hoc study of a prospective observational trial and a bicentric RCT evaluated the impact of TPE on TF and TFPI in septic shock patients. Higher baseline TF (and TFPI) levels were associated with sustained lactate reduction in the TPE group but not in the SOC group within the first 24 hours of study enrolment. The association between high TF levels and the effectiveness of TPE in decreasing lactate has a convincing pathophysiologic explanation.[2] Elevated levels of TF, a powerful coagulation initiator, have been linked to sepsis-related coagulopathy and microvascular changes.[3]

Conclusion

Adjunctive TPE in septic shock significantly reduces TF and TFPI levels, potentially contributing to early hemodynamic recovery in patients. Higher baseline TF (and TFPI) plasma concentrations may predict treatment response and could inform predictive enrichment tactics in future clinical trials.

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Evaluation of the features and prognostic significance of acute kidney injury in out-of-hospital cardiac arrest patients

Introduction

Acute kidney injury (AKI) is a serious clinical renal syndrome that can be caused by ischemia, nephrotoxic drugs, oxidative stress, inflammation, or urinary tract blockage. It has a high incidence and mortality rate. Epidemiological studies indicated that the incidence of acute kidney injury (AKI) among general inpatients was 5%, whereas severe patients have a mortality rate of over 50%.[1] Around 40% of patients resuscitated from out-of-hospital cardiac arrest (OHCA) experience AKI, which was linked to poor short- and long-term survival. In addition, patients with pre-existing kidney impairment before an OHCA incident have a higher 90-day death rate. Post-resuscitation care can prevent additional renal deterioration and improve outcomes.[2] So, this study aimed to identify AKI characteristics based on the Kidney Disease Improving Global Outcomes (KDIGO) classification, as well as the prognostic significance of AKI severity in a defined OHCA population enrolled in the Blood Pressure and Oxygenation Targets After OHCA trial.

Acute kidney injury (AKI) patients, with or without continuous kidney replacement therapy (CKRT), showed lower 1-year survival than non-AKI patients.

Methods

This was a randomized trial that included 789 OHCA patients with a presumed cardiac etiology and prolonged return of spontaneous circulation (ROSC). The study comprised 759 patients with no prior dialysis-dependent renal illness who survived at least 48 hours. AKI was classified according to the kidney disease: improving global outcome (KDIGO) classification, and patients were categorized into three groups according to the degree of AKI development and the requirement for continuous kidney replacement therapy (CKRT): no AKI, AKI no CKRT, and AKI CKRT. The primary outcome was overall survival within 365 days after OHCA in the AKI group. Adjusted Cox proportional hazard models were used to compare overall survival within 365 days among the three groups.

Results

This study included 759 patients and according to the KDIGO definition, 254 patients (33.5%) developed AKI, with 77 requiring CKRT and 177 not required for CKRT. AKI-CKRT patients experienced longer time-to-ROSC and greater metabolic disturbances upon hospital admission. The severity of kidney impairment reduced overall survival after OHCA within 365 days.

According to an adjusted Cox regression analysis, AKI was significantly linked to a lower overall survival rate up to 365 days, with similar hazard ratios compared to no AKI (HR 1.75, 95% CI 1.13–2.70 vs. HR 1.76, 95% CI 1.30–2.39). AKI patients had significantly lower weighted mean values of MAP up to ICU Day 5, with a decreasing trend as severity increased. (Figure 1). According to Kaplan-Meier survival estimates, patients with no AKI had a 74% overall survival rate until 365 days after hospital admission, 55% with AKI and no CKRT, and 43% with AKI-CKRT.

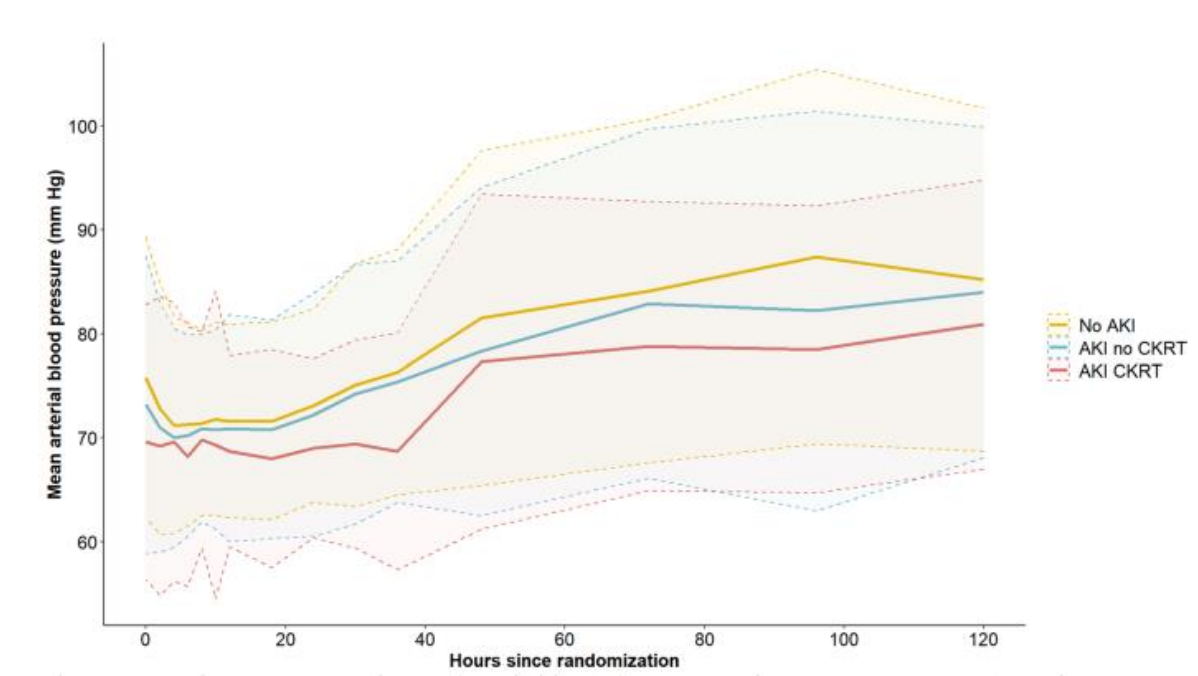

Figure 1. Mean arterial pressure. Mean arterial pressure (±SD) across time for three groups: no AKI, AKI without CKRT, and AKI with CKRT.

Discussion

The 1-year overall survival was shorter for patients with AKI than for those without AKI, regardless of whether they had CKRT or not. In this study, 30% of patients who had AKI received CKRT treatment. Also, it was found that patients who were resuscitated after OHCA and developed AKI, regardless of CKRT commencement, had lower 1-year overall survival rates than non-AKI patients.[2] A previous study found that AKI complicates care for 40% of cardiac arrest survivors and was linked with significantly higher short- and long-term mortality.[3]

Conclusion

Individuals with AKI, regardless of when CKRT was started, had a lower one-year overall survival rate than non-AKI patients among comatose patients who had been resuscitated after OHCA. This association remained statistically significant even after accounting for additional peri-arrest risk variables.

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Evaluation of the safety of physical rehabilitation for critically ill Patients

Introduction

The risk assessment tool can help clinicians determine when to begin rehabilitation for patients on vasoactive medications.

Patients in intensive care units (ICUs) are physically rehabilitated or mobilized to avoid problems and improve patient outcomes.[1] ICU-acquired weakness, or ICU-AW, is a typical neuromuscular consequence of critical illness. Early mobilization of critically sick patients is a potential intervention to decrease the frequency and severity of ICU-AW. Early mobility has been shown in studies to minimize ICU and hospital stays, reduce mechanical ventilation time, increase long-term functional independence, and reduce mortality rates.[2] Physical therapy has minimal adverse event rates. However, a recent study suggested that delivering a greater dosage at an earlier time point may be less safe and may not improve outcomes. The evaluation of ICU physical rehabilitation safety data was limited due to differences in how studies define adverse event outcomes. When administering vasoactive medicines to critically sick patients, it was important to assess their cardiovascular capacity to ensure their safety during physical activity. So, this study aimed to develop a consensus among clinicians and patients on the definition of an adverse event during adult physical rehabilitation in an ICU and also, to determine expert consensus among clinicians on the characteristics of adult ICU patients receiving vasoactive drugs who have a low or high risk of adverse events during physical rehabilitation, as well as those who are not suited to rehabilitation.

Methods

This was an international, three-stage Delphi analysis, conducted to (a) define adverse events in a general ICU population and (b) determine which risks should be considered before physical rehabilitation for patients taking vasoactive medications. A multinational group of critical care specialists and clinical researchers participated. Former ICU patients and their families assisted in defining adverse events. Round one was an open round where people suggested what to include. In round two, participants assessed their agreement with these proposals on a five-point Likert scale, with a 70% consensus agreement criterion utilized. Round three involved re-rating recommendations that did not reach a consensus and reviewing anonymous participant ratings from round two.

Results

Twenty-four multi-professional ICU clinicians and clinical researchers from 10 countries spanning five continents were recruited. The average period of ICU experience was 18 years (standard deviation 8), and 61% had publications on ICU rehabilitation. Five previous ICU patients and one family were selected to define adverse events. The Delphi procedure had a 97% response rate. After reaching a consensus on 54 adverse occurrences, an adverse event instrument was developed based on their findings. Only one event ('a large amount of chest secretions') was accepted by the majority of patients/relatives, with 72.4% voting for exclusion and 66.7% voting to include (Table 1). Second, consensus was established on 50 risk variables for patients using vasoactive medications that should be assessed before physical rehabilitation.

Adverse event	Participant ratings (%)		
	Strongly disagree + disagree	Undecided	Agree + strongly agree
Events that reached consensus after round 2			
Large amounts of chest secretions			
All participants	72.4	10.3	17.2
Clinicians	87.0	8.7	4.3
Patients	16.7	16.7	66.7
Events that reached consensus after round 3			
Any respiratory deterioration			
All participants	82.8	0	17.2
Clinicians	95.7	0	4.3
Patients	33.3	0	66.7
Undecided events after round 3 (with round 3 ratings)			
Any cardiovascular deterioration			
All participants	65.5	3.4	31.0
Clinicians	78.3	0	21.7
Patients	16.7	16.7	66.7
Dizziness due to cardiovascular deterioration			
All participants	68.9	24.1	6.8
Clinicians	78.2	17.4	4.3
Patients	33.3	50.0	16.7
Any unplanned movement of any indwelling devices, lines, tubes or drains			
All participants	51.7	10.3	37.9
Clinicians	60.9	8.7	30.4
Patients	16.7	16.7	66.7
Increased pain			
All participants	69.0	6.9	24.1
Clinicians	78.3	0	21.7
Patients	33.3	33.3	33.3
Agitation			
All participants	62.1	0	37.9
Clinicians	69.6	0	30.4
Patients	33.3	0	66.7
Patient distress			
All participants	51.7	6.9	41.3
Clinicians	65.2	4.3	30.4
Patients	0	16.7	83.3
Bearing weight inappropriately on an injured leg			
All participants	41.4	10.3	48.2
Clinicians	52.2	8.7	39.1
Patients	0	16.7	83.3
Increase in patient hallucinations			
All participants	58.6	3.4	37.9
Clinicians	69.6	4.3	26.1
Patients	16.7	0	83.3

All participants: n = 29. Clinicians: n = 23. Patients: n = 6

Table 1: Adverse events where the majority of patients' evaluations deviate from the group average

Discussion

In this study, international group of ICU doctors, clinician researchers, and former ICU patients consented on an adverse event tool to assess the safety of physical rehabilitation for patients in critical care.[1] A Previous study found that there was not a significant effect of rehabilitation on safety.[3] In contrast, the biggest ICU rehabilitation trial showed that increase in adverse events when intense rehabilitation was compared to normal care.[4]

Conclusion

The adverse event tool can be used in physical rehabilitation studies to ensure consistent safety assessments. The risk assessment tool can help clinicians determine when to start rehabilitation for patients on vasoactive medicines.

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A Rare Case of Adult croup caused by influenza A virus

Introduction

Croup is a respiratory disease that affects approximately 3% of children aged six months to three years. Fever and/or acute respiratory disease account for 7% of annual hospital admissions in children under five years old. Croup is an upper respiratory blockage caused by enlargement in the larynx, trachea, and bronchi, leading to inspiratory stridor and barking cough.[1] Laryngotracheitis is the most prevalent and unique manifestation of the condition. Further, Influenza is an acute respiratory disease caused by influenza type A and B viruses. It can cause mild to severe sickness and outbreaks throughout the winter season.[2] This is a rare case in which influenza A virus (IAV) causes croup in an adult patient.

Croup is a common respiratory disease during childhood and extremely rare in adulthood, caused by influenza A. Unlike croup in pediatric patients, it is a serious condition that affects the patient's outcome and prognosis.

Case Presentation:

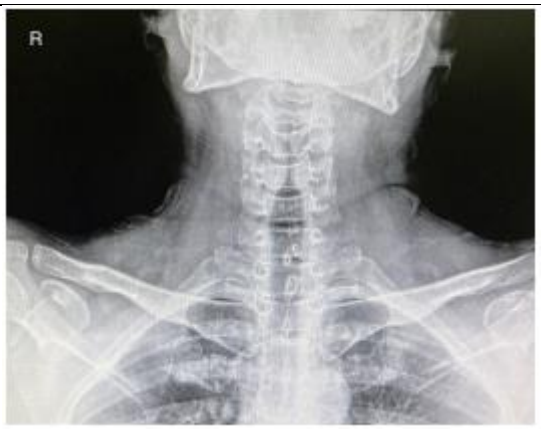

Figure 1. Constriction of the upper trachea, similar to the "steeple sign" seen on AP radiographs. AP, anteroposterior.

A 35-year-old male presented to the emergency room agitated with fever, "barking" cough, and worsening dyspnea over the previous 12 hours. Medical history was essential in seeking medical assessment 72 hours earlier after being involved in an uncomplicated motor vehicle accident. He stated that he hasn't had the seasonal influenza vaccine since 2020. His vital signs at admission were as follows: temperature of 37.8 °C, oxygen saturation of 95% on room air with no signs of cyanosis, respiratory rate of 26 breaths per minute, heart rate of 112 beats per minute with regular rhythm, and blood pressure of 110/70 mmHg. The physical examination confirmed the utilization of supplementary respiratory muscles and the presence of biphasic stridor while at rest. On chest radiograph, it showed upper tracheal constriction, which was consistent with the so-called steeple sign (Figure 1). A white blood cell count of 14.40 (reference range: 4–10) $\times 10^3/mm^3$ was significant according to laboratory tests. A quick molecular test on a nasopharyngeal swab revealed that it contained IAV. A diagnosis of IAV-related croup was made. Since there are no set dosages or standards for treating adult croup (AC), treatment began with a single dose of dexamethasone (8 mg) administered intravenously. Nebulized racemic epinephrine and humidified oxygen were also administered. Additionally, oseltamivir 75 mg orally twice daily for five days was prescribed as part of the influenza A treatment. For careful observation, the patient was admitted to the intensive care unit (ICU). Following the delivery of racemic epinephrine, the patient's stridor resolved within minutes, and over the next three hours, their breathing ability returned. The patient was moved from the intensive care unit to the usual nursing floor after a 24-hour control chest X-ray revealed that the subglottic constriction had resolved. After his symptoms completely subsided on the third day, the patient was discharged, and a follow-up appointment was set for the following week, during which he continued to be asymptomatic.

Discussion

Croup is commonly seen in pediatric patients, with a higher prevalence in children between the ages of 6 months and 3 years but extremely rare in adulthood. In the present case, a 35-year-old man presented with croup, which is very rare in adults.[2] Croup rates among children under the age of two who visited emergency rooms between 1999 and 2005 ranged from 30.9 to 49.6 per 1000 visits. The incidence is highest in the second year of life, with the majority of cases occurring between the ages of three months and three years. Moreover, unlike croup in children, it is a devastating condition that impacts the outcomes and prognoses of adult patients.[3]

Conclusion

Influenza A-induced croup in adults is a rare clinical condition. So, it is crucial for early diagnosis and treatment. Unlike croup in children, it is a serious disease that affects patients' outcomes and prognoses in adults.

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