ICU

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Paediatrics

Quality improvement in the PICU – a primer for intensivists, *N. Mehta*

PICU Up! A multicomponent early mobility intervention for critically ill children, *S. Kudchadkar*

PICU-acquired complications: the new marker of the quality of care, *K. Choong*

Caring for children in the PICU - from novel technology to family-centred care: new challenges for old needs, *E. Esteban, I. Jordan, F. José Cambra*

Virtual reality experience in the PICU, *M. Malakooti*

PLUS

Seven steps to design, procure, implement and maintain a Clinical Information System for your intensive care unit, *T. Kyprianou*

Respiratory physiotherapy in critically ill patients, *V. Comellini, S.Nava, A. Artigas*

A structural approach for diagnosing weaning failure - a case from a specialised weaning centre, *T. Frenzel, L. Roesthuis, J. van der Hoeven*

Vitamin D deficiency in ICU patients, *G. Martucci, K. Amrein, J. Ney*

Noise in the intensive care unit: where does it come from and what can you do about it? *J. Darbyshire*

Keeping the Person in Personalised Medicine, *M. Abrams*

European guidelines on the management of traumatic induced bleeding, *R. Rossaint*

Can Goal-Directed Therapy solve the economic burden of postsurgical complications? *W. Habenbacher*

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Use of sedation and controlled paralysis in ICU patients with ARDS

According to a National Institutes of Health sponsored clinical trial that was conducted at several North American hospitals and was led by clinician-scientists at the University of Pittsburgh and University of Colorado schools of medicine, reversibly paralysing and sedating hospitalised patients with severe breathing problems does not prove improve patient outcomes in a large majority of cases. Findings were presented at the American Thoracic Society's Annual Meeting and are published in the New England Journal of Medicine.

This trial was conducted to settle an ongoing debate within the critical care medicine community as to whether it is better to paralyse and sedate patients in acute respiratory distress or to avoid heavy sedation to improve the patient's recovery. According to senior author Derek Angus, Chair of PITT's Department of Critical Care Medicine, this issue has always been a dilemma for clinicians since many well-done clinical studies show that temporarily paralysing patients to improve mechanical breathing could save lives. But it is not possible to paralyse a patient without heavy sedation. As per the findings of the trial, sedation results in worse recovery, hence providing the answer to this long-standing debate that sedation with intermittent short-term paralysis is as good as deep sedation with continuous paralysis.

The trial - Re-evaluation Of Systemic Early neuromuscular blockade (ROSE) is the first of the National Heart, Lung, and Blood Institute's (NHLBI) Prevention & Early Treatment of Acute Lung Injury (PETAL) Network. The network conducts clinical trials designed to prevent diseases or treat patients who are at risk for acute lung injury or acute respiratory distress syndrome (ARDS). One of the key areas of emphasis for the PETAL Network is early detection, and that is why every member institute of this network is required to include critical care, emergency medicine, acute care or trauma principal investigators. This is to ensure that critical issues are recognised and triaged, and the odds of patient recovery are improved before they even get to the intensive care unit.

> **"sedation with intermittent short-term paralysis is as good as deep sedation with continuous paralysis"**

The ROSE trial has already enrolled 1006 patients in 48 US and Canadian hospitals. The patients were enrolled within hours after the onset of moderate to severe ARDS. Half of the patient population was given a 48-hour continuous neuromuscular blockade and heavy sedation while the other half was given light sedation. Study clinicians had the option of giving a small dose of neuromuscular blockade that would wear off within an hour to ease respiratory intubation.

James Kiley, Director of the Division of Lung Diseases at the NHLBI, explains that the PETAL network wants to conduct trials that would help answer these important questions. The results of these trials can help clinicians make decisions early on so that they can provide better care for patients with ARDS.

The idea for the ROSE trial originated because of findings from another trial in 2010 that reported reduced mortality with neuromuscular blockade. All participants in that French trial were heavy sedated, whether they received the neuromuscular blockade or not. But in North America, clinicians have been trying to stay away from heavy sedation as it is associated with cardiovascular complications, delirium, and increased difficulty weaning patients from mechanical ventilation.

Findings from the ROSE trial show that patients who received the neuromuscular blockade and were highly sedated developed more cardiovascular issues while in the hospital. However, no significant difference was found in mortality between the two groups at three months, six months, or 12 months follow-up.

The study has completed enrolment ahead of schedule, and it is believed that findings will soon be available for healthcare providers, which could result in rapid implementation of enhanced care for ARDS patients. Derek Angus has said that so far, the results suggest that avoiding paralysis and deep sedation is the best practice for most patients who are hospitalised for breathing problems. But future trials will have to test whether there is a subpopulation of patients with ARDS who could still benefit from neuromuscular blockade. ■

Reference

Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome. The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network. New England Journal of Medicine.

New recommendations for stroke systems of care - American Stroke Association policy statement

Approximately 7.2 million Americans 20 years or older have had a stroke. Nearly 800,000 people in the U.S. have a new or recurrent stroke each year. A stroke occurs every 40 seconds in the U.S., and someone dies of a stroke every four minutes.

According to a policy statement published by the American Stroke Association, and published in the journal Stroke, improvements in stroke systems of care are imperative to ensure advancement in the treatment and care of stroke patients and to improve patient outcomes. The statement was released during the National Emergency Medical Services (EMS) Week. Over the last decade, stroke systems have seen vast improvements in the availability of endovascular therapy, neurocritical care, and stroke centre certification. The use of telestroke and mobile stroke units have further improved access for stroke patients to alteplase, a lifesaving, clot-busting drug.

As Opeolu Adeoye, the chair of the writing group for the statement and associate professor of emergency medicine and neurosurgery at the University of Cincinnati points out, there have been monumental advancements in acute stroke care over the last 14 years. The concept of a comprehensive stroke system of care has evolved. This new policy statement reflects the progress that has been made so far and highlights what still needs to be done to maximise patient outcomes.

As per the statement, if more than one intravenous alteplase-capable hospital is within reach, EMS should consider additional travel time of up to 15 minutes to reach a hospital that is capable of performing endovascular thrombectomy for patients who have had a severe stroke. Both these treatments, intravenous alteplase, and endovascular thrombectomy, should be administered as soon as possible to be effective. However, not every hospital can deliver these services. As Adeoye points out, getting to the hospital quickly is important for patients with a large vessel blockade, but so is getting to the right hospital.

The new policy statement from the American Stroke Association also addresses disparities in care among racial and ethnical minorities, who are less likely to use EMS and who also have the lowest awareness of the causes and symptoms of stroke.

> "getting to the hospital quickly is important for patients, but so is getting to the right hospital"

This lack of knowledge, especially among the Hispanic and black population, can hamper timely stroke care. That is why the American Stroke Association has emphasised on the importance of implementing public education programmes that focus on stroke systems and highlights the importance of seeking emergency care by calling 9-1-1 if stroke symptoms are observed.

Other recommendations include:

- Implementation of local and regional public education initiatives to increase awareness of symptoms with an emphasis on high-risk populations.
- The need for EMS leaders, governmental agencies, medical authorities, and local experts to work together and to adopt consistent and standardised triage protocols to rapidly identify patients with a known or suspected stroke.
- For certified stroke centres to provide help to stroke survivors to reduce the risk of subsequent strokes, as per the guidelines for secondary prevention.
- To design a stroke system that provides comprehensive post-stroke care, including primary care and specialised stroke services including physical, occupational, speech, and/or other therapies needed at time of discharge.
- To enact policies to standardise the organisation of stroke care, to lower barriers to seeking emergency care for stroke, to ensure that stroke patients receive care at the right hospital at the right time, and to facilitate access to secondary prevention of rehabilitation and recovery resources after stroke.

Overall, the goal of these recommendations is to create optimised stroke systems of care. The American Heart Association's Get With The Guidelines - Stroke at U.S. Hospitals have been associated with an 8% reduction in mortality at one year and improved functional outcome at the time of discharge.

Reference

Adeoye, O et al. (2019) Recommendations for the establishment of stroke systems of care: a 2019 update: a policy statement from the American Stroke Association. Stroke.

Cocoon bed aims to lower ICU delirium

The intensive care unit environment can be extremely stressful, even if they provide some of the best care in the world. It is believed that a patient in the ICU has their sleep interrupted approximately every three minutes either through noise, lights, or medical intervention. Up to 80% of patients in the ICU suffer from some form of delirium, and nearly 30% develop post-traumatic stress disorder.

In order to improve the treatment of patients in the ICU and to lower the rates of delirium, Brisbane's Prince Charles Hospital Foundation has designed the world's first hospital bed that is being called the "Intensive Care Cocoon." The cocoon features noise-cancelling technology that removes the incessant beeping of monitoring equipment from the patient's head. It also stimulates day and night, and allows patients to view a live video of their home so that they can talk to their family members and their pets.

As Prof. John Fraser, the director of the Critical Care Research Group at Prince Charles Hospital in Brisbane points out, a stay in the ICU can seem like the worst jet-lag ever, and while patients with critical conditions are treated in the ICU, there are environmental factors that often worsen mortality, increase time in hospital and overall frighten people. He highlights the fact that the risk of mortality at six months increases by 300% in patients with delirium.

Patients have been known to suffer from anxiety during their ICU stay and from PTSD after. For some, the ICU can be the scariest place they've ever seen. It is thus evident that there is a need to address this issue and to focus on improving the patient experience in the ICU.

The Prince Charles Hospital Foundation plans to build two prototypes of the beds if it is able to raise $1 million in donation. These beds might be expensive to build, but if rolled out across hospitals, it is believed that they can make intensive care cheaper in the long run and can reduce the length of time patients stay in the ICU.

Reference

The Common Good. People Powering Medical Discoveries. An initiative of the Prince Charles Hospital Foundation.

Big Data and subtypes of sepsis

Results of a study conducted by the University of Pittsburgh School of Medicine suggests that sepsis is not one condition, but many conditions that could benefit from different treatments. The findings are published in JAMA and were presented at the American Thoracic Society's Annual Meeting.

Sepsis is the number one killer of hospitalised patients and is a life-threatening condition that arises when the body's response to infection begins to injure its own tissues and organs. It has been over a decade, and no major breakthroughs have happened in the treatment of sepsis. The only improvement observed so far is the enforcement of the "one-size-fits-all" approach for prompt treatment, highlights Christopher Seymour, associate professor in Pitt's Department of Critical Care Medicine and member of Pitt's Clinical Research Investigation and Systems Modeling of Acute Illness Center. But as he explains, these protocols ignore the fact that all sepsis patients are not the same. It is a condition that kills nearly 6 million people annually, and using a one-size-fits-all approach is unacceptable for such a huge threat to patients.

By seeing sepsis as several different conditions, and with varying clinical characteristics, it may be possible to discover and test therapies that are tailored to treat the different subtypes of sepsis.

The "Sepsis ENdotyping in Emergency Care" (SENECA) project, funded by the National Institutes of Health (NIH), has used computer algorithms to analyse 29 clinical variables found in the electronic health records of more than 20,000 patients who had sepsis within six hours of hospital arrival. Patients were clustered into four distinct sepsis types, which include:

1. Alpha - found to be the most common (33%) and with the least organ dysfunction and lowest in-hospital death rate at 2%.
2. Beta - found in approximately 27% of patients; mostly elderly patients with the most chronic illness and kidney dysfunction.
3. Gamma - almost the same frequency as beta; but associated with greater inflammation and pulmonary dysfunction.
4. Delta - least common at around 13%; most deadly type, often associated with liver dysfunction and shock; showed highest in-hospital death rate at 32%.

After studying another 43,000 sepsis patients, the UPMC team confirmed these findings. These findings were then applied to recently completed international clinical trials that tested different therapies for sepsis. None of these trials had anything significant to report. However, results might have been different if the trial participants had been classified on the basis of these four subtypes. For example, early goal-directed therapy (EGDT) was not found to have any benefit following a five-year study, but when the UPMC team re-examined the results, they found that it could have benefitted the Alpha type of sepsis patients but would result in worse outcomes for the Delta subtype.

If you think about it logically, the theory of sepsis subtypes makes perfect sense. Just like all breast cancer patients do not receive the same treatment (as some breast cancers can be more invasive and require aggressive treatment), the same is true for sepsis. There is thus a need to find therapies that apply to specific types of sepsis and then design clinical trials to test those therapies.

Reference

Seymour CW et al. (2019) Derivation, Validation, and Potential Treatment Implications of Novel Clinical Phenotypes for Sepsis. JAMA.

Sedation with dexmedetomidine in critically ill patients

Dexmedetomidine is used to sedate patients while maintaining a certain degree of sustainability. The use of dexmedetomidine is known to reduce the duration of mechanical ventilation and delirium among patients in the intensive care unit (ICU). However, its use as the sole sedative agent in patients undergoing mechanical ventilation has not been studied extensively.

An open-label, randomised trial was conducted with 4000 critically ill adults who had been undergoing ventilation for less than 12 hours in the ICU. These patients were expected to receive ventilator support for longer than the next calendar day. Patients either received dexmedetomidine as the sole sedative or usual care with propofol, midazolam, or other sedatives. The primary outcome of the trial was the rate of death from any cause at 90 days and the target range of sedation-scores on the Richmond Agitation and Sedation Scale was -2 to +1 (lightly sedated to restless).

As per the results of the trial, the primary outcome event occurred in 566 of 1948 patients in the dexmedetomidine group, and in 569 of 1956 patients in the usual-care group. In order to achieve the required level of sedation, patients in the dexmedetomidine group received supplemental propofol, midazolam, or both during the first two days after randomisation, while the same drugs were administered as primary sedatives in the usual-care group. It was observed that the incidence of bradycardia and hypotension was more common in the dexmedetomidine group.

> **"patients undergoing mechanical ventilation in the ICU and who received dexmedetomidine for sedation had a similar rate of death at 90 days compared to the usual-care group"**

Findings from this trial suggest that patients undergoing mechanical ventilation in the ICU and who received dexmedetomidine for sedation had a similar rate of death at 90 days compared to the usual-care group. The dexmedetomidine group needed supplemental sedatives to achieve the required level of sedation. Overall, the dexmedetomidine group reported more adverse events compared to the usual-care group.

Reference

Shehabi Y et al. (2019) Early Sedation with Dexmedetomidine in Critically Ill Patients. New England Journal of Medicine.

Use of opioids in the ICU not linked to continued prescriptions

According to a new study, opioids prescribed in the intensive care unit (ICU) do not drive risks for continued use or prescriptions. The findings were presented at the American Thoracic Society (ATS) 2019 International Meeting in Dallas, TX.

Opiate abuse is a major healthcare issue. In the U.S., opioid-related deaths have increased more than three-fold from 2000 to 2016. The use of opioids in the ICU have to follow guidelines that are adjusted to a standard based on necessary opiate exposure only. This applies to parenteral opioids and oral opioids.

The study was conducted with 3102 opiate-naive patients admitted from 2016-2017. 45% of these patients received opioids in the ICU and were exposed according to their prescription. As a general profile, opioid-receiving patients were younger, with greater weight, height, APACHE scores, and greater lengths of stay in both the hospital and the ICU. The primary outcome of the study was opioid prescriptions within 1-year post-discharge.

Study investigators from the Cleveland Clinic and Duke University Medical Center shared the findings that patients who were prescribed opioids in the ICU did not report an increase in the risk of continued opioid prescription at 1 year after discharge. These findings thus support the guideline set by the Society of Critical Care Medicine regarding the management of pain, agitation, and delirium.

Healthcare providers should continue to address pain optimally and should manage patients in the ICU by using the comprehensive bundle to provide comfort as well as prevent delirium.

Reference

Chen A et al. (2019) Use of Opioids in the Medical Intensive Care Unit Is Not Associated with Outpatient Opiate Use. ATS International Conference. Available from abstractsonline.com/pp8/#!/5789/presentation/26085