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Impact of hyperoxia and hypocapnia on neurological outcome in patients with aneurysmal subarachnoid haemorrhage

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Introduction: Aneurysmal subarachnoid hemorrhage (SAH) accounts for 80% of non-traumatic SAH and has higher morbidity and mortality. Hyperoxia and hypocapnia are associated with poor outcomes in critically ill patients with brain injuries or post-cardiac arrest status. Yet, the impact of hyperoxia and hypocapnia on neurological outcome in patients with aneurysmal SAH has not been well studied. In this study, we aim to evaluate their impact on neurological outcome in patients with aneurysmal SAH.

Methods: Patients with aneurysmal SAH admitted to Intensive Care Unit of a regional hospital in Hong Kong from January 2011 to December 2016 were included. Patients' demographics and comorbidities, clinical and radiological grading, blood gas, Glasgow Outcome Scale (GOS) at 3 months were recorded. Logistic regression analysis was performed to assess independent predictors for poor neurological outcome, i.e. GOS 1-3 at 3 months after initial insult.

Results: Among 244 patients with aneurysmal SAH, 50% (122 patients) had poor neurological outcome. They were older, had higher APACHE IV score, WFNS grading and Fisher grading scale, and lower GCS on day 1 and were more likely to have intracranial or intraventricular hemorrhage (ICH or IVH). Hyperoxia ($\text{PaO}_2 > 200$ mmHg) and hypocapnia ($\text{PaCO}_2 < 50$) (OR 5.172, 95% CI 2.348-11.393, $p = .055$ (OR 4.113, 95% CI 1.871-9.039, $p = .005$), and WFNS grade > 3 (OR 2.986, 95% CI 1.282-6.955, $p = 0.011$) independently predicted poor neurological outcome at 3 months.

Conclusion: Hyperoxia but not hypocapnia was associated with poor neurological outcomes at 3 months in patients with aneurysmal SAH.

Key words: Hyperoxia, hypocapnia, subarachnoid hemorrhage, neurology.

PYICU+ More Is Less: The Post-ICU Discharge Follow-up Programme

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Introduction: Intensive care unit (ICU) readmissions have been associated with increased length of hospital stay, mortality rate and healthcare spending. Though various critical care outreach programs have been developed and evaluated worldwide, none has been done in Hong Kong. Therefore, this study aimed to evaluate the effectiveness of a Post-ICU Discharge Follow-up Programme (PYICU+) on ICU readmissions and hospital mortality in ICU discharged patients with respiratory problems.

Methods: This study included prospective data collection for 26 months after the implementation of the PYICU+ since September 2015. The intervention group was then compared with the historical control group which was identified with the same inclusion and exclusion criteria for 26 months before the implementation of the programme. The PYICU+ included 3 daily follow-up visits at wards by an ICU Outreach Team to those ICU discharged patients at risk for respiratory problems. The ICU Outreach Team was led by a nurse consultant and supported by senior ICU doctors.

Results: A total of 612 subjects (the intervention group: 286, the control group: 326) were recruited. After the implementation of the PYICU+, only 8 early ICU readmissions in the intervention group were noted as compared to 38 early ICU readmissions in the historical control group. The reduction in the early ICU readmission within 72 hours was significant ($p < 0.001$), with an 89.8% reduction in the risk of early ICU readmission (OR 0.102, 95% CI 0.042, 0.248, $p < 0.001$).

There were also statistical significant reductions in the total ICU readmissions ($p = 0.001$); hospital mortality ($p = 0.021$) and 90 days mortality ($p = 0.001$) in the intervention group as compared to that of the control group.

Conclusion: This nurse-led PYICU+ is a newly developed programme (more) and proved to effectively reduce the early ICU readmission (less). The ICU outreach team continues the PYICU+ to the targeted patients so as to ensure patient safety and continuity of quality care during the critical transition period from ICU to general wards.

Key words: Post-ICU discharge follow-up, ICU readmission.

Effects of fluid balance on outcome of patients with aneurysmal subarachnoid haemorrhage

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Introduction: Aneurysmal subarachnoid hemorrhage (SAH) is a neurosurgical emergency that carries significant morbidities and mortality. Management includes bleeding control and supportive care to minimize secondary brain injuries. Fluid management in this group of patients remains a challenge. This study aims to determine whether early fluid balance can affect functional outcome.

Methods: We retrospectively reviewed 140 patients with SAH admitted to intensive care unit (ICU) of Pamela Youde Nethersole Eastern Hospital between January 2011 to December 2016. Data on patients demographics and clinical characteristics were collected, including cumulative 4 days fluid balance, age, mean arterial pressure, maximum glucose, Acute Physiology and Chronic Health Evaluation (APACHE) IV score, Glasgow Coma Scale (GCS), modified Fisher scale, WFNS (World Federation of Neurosurgical Societies) grade, presence of vasospasm and surgical or endovascular management of the aneurysm. The primary outcome was Glasgow Outcome Scale (GOS) at 3 months with GOS 1 to 3 classified as poor outcome and GOS 4 to 5 as good outcome. Secondary outcomes were ventilator days, hospital and ICU length of stay (LOS).

Results: One hundred and forty patients were included in the analysis. The median age was 55.5 years. Twenty (14.3%) patients had died. The cumulative 4 days fluid balance was associated with poor outcome in the univariate analysis ($p=0.002$). In the logistic regression analysis, it is not independently associated with poor outcome. Age, APACHE IV score, and modified Fisher scale 4 were independent predictors of poor outcome. The cumulative 4 days fluid balance was not associated with secondary outcomes: ICU LOS (Spearman's rho correlation coefficient, $r=0.152$, $p=0.073$), hospital LOS ($r=0.126$, $p=0.137$) and ventilator days ($r=0.252$, $p=0.003$).

Conclusion: In this cohort of patients, age, APACHE IV, and modified Fisher scale 4 were independent predictors of poor functional outcome in patients with SAH.

Key words: Subarachnoid hemorrhage, fluid balance, outcome.

Effect of earplugs and eye masks on sleep quality and delirium in intensive care patients

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Introduction: Sleep problems are common in intensive care patients. It could affect the cognitive function of patients, increase their anxiety and lead to delirium. Sedative and hypnotic drugs have side effects. Complementary therapies are becoming increasingly important to reduce disorders by stimulating sensory perception and creating relaxing effects. To evaluate the effect of earplugs and eye masks on sleep quality and delirium in intensive care patients.

Methods: The relevant randomized controlled trials (RCTs) about the effect of earplugs and eye masks on sleep quality and delirium in intensive care patients were searched in PubMed, MEDLINE, CINAHL, The Cochrane Library-central, CNKI, WANGFANG, CBM from start date to March 2018.

Results: 20 RCTs were included, totally 1364 participants. The results of meta-analysis showed that earplugs and eye masks significantly reduced the incidence of delirium [RR = 0.52, 95% CI (0.41,0.66), p 0.01], improved sleep quality of intensive care patients [SMD=1.43, 95% CI (0.92, 1.93), p 0.05].

Conclusion: The current evidence indicates that earplugs and eye masks is beneficial to the incidence of delirium and sleep quality. No evidence to support earplugs and eye masks are efficacious in improving the sleep time. Due to the limited quantity and quality of included studies, more high quality studies are needed to verify the above conclusion.

Key words: Meta analysis.

Clinical predictors and outcomes of *Escherichia coli* bacteremia in critically ill patients in a regional hospital in Hong Kong

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Introduction: *Escherichia coli* (EC) is one of the most common bloodstream infections and carries a significant mortality rate. International studies have shown that age, antibiotic resistance and choice of empirical antibiotics affect the prognosis of patients with EC bacteremia. However, there is scarce local data to evaluate on the prognostic factors for EC bacteremia in Hong Kong. Our study aimed to evaluate the clinical predictors and outcomes of EC bacteremia in critically ill patients admitted to Intensive Care Unit (ICU) in a regional hospital in Hong Kong.

Methods: The study is a retrospective analysis of patients with EC bacteremia admitted to the Department of ICU of Pamela Youde Nethersole Eastern Hospital (PYNEH), from 1/1/2009 to 30/12/2017 (8 years). Patients' demographics, past medical histories, clinical parameters, microbiological data, drug prescriptions, and supportive treatments were analyzed.

Results: Among 380 patients, 30-day non-survivors were older ($p=0.016$), more likely to present with respiratory sepsis ($p=0.001$) and require renal replacement therapy and mechanical ventilation during ICU stay ($p=0.001$) (HR=6.129; 95% CI=3.271-11.485; $p=0.001$), respiratory sepsis (HR=4.366; 95% CI=2.147-8.878; $p=0.001$), liver cirrhosis (HR=3.007; 95% CI=1.685-5.365; $p=0.001$), albumin ≥ 24 g/L (HR=2.999; 95% CI=1.597-5.632; $p=0.001$), liver cirrhosis (HR=2.632, CI=1.051-6.591, $p=0.039$), albumin ≥ 24 g/L (HR=2.291; 95% CI=1.229-4.270; $p=0.009$) and interventional radiological (IR) procedures or operative interventions (HR=0.358; 95% CI=0.188-0.679; $p=0.002$) were independent risk factors for 30-day mortality.

Conclusion: Disease severity, respiratory sepsis, use of steroid, age and liver cirrhosis are important predictors for 30-day mortality in critically ill patients with EC bacteremia, while IR procedures or operative interventions is associated with lower 30-day mortality.

Key words: *Escherichia coli* bacteremia.

Analysis of trends in usage of neuromuscular blockers in intensive units of South Korea: a retrospective nationwide population study

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Introduction: Neuromuscular blockade, as an adjuvant therapy in the ventilatory and medical management of common critical illnesses, has an important but increasingly controversial role in the delivery of 21st century care in the modern intensive care unit (ICU). We analyzed the current aspects of the use of neuromuscular blockers in ICUs nationally based on data from the Health Insurance Review of Assessment Service (HIRA) in South Korea.

Methods: We performed a retrospective review of the data available in the HIRA database. We defined 779,985 patients who were admitted to the ICU from January 1, 2010 to December 31, 2014. Descriptive statistics were calculated to analyze the type and frequency of neuromuscular blockers used in the ICU, using drug codes related with neuromuscular blockers commonly prescribed in ICU.

Results: A total of 283,631 patients (30.59%) underwent mechanical ventilation among a total of 779,985 ICU admitted patients. The mean age at admission in ICU was 63.89 years, and 460,673 patients (59.06%) were male. The most commonly used neuromuscular blocker was vecuronium in all patients admitted to ICU. The usage rate of vecuronium decreased, whereas the usage rate of rocuronium and cisatracurium increased (Table 1). Between 2010 and 2014, pancuronium and succinylcholine were not prescribed in Korea. Among all patients admitted ICU, 61.20% were admitted to tertiary general hospital. The higher grade of the hospital was associated with higher rate of neuromuscular blockers usage (Table 2).

Conclusion: It is clear that a large gap still exists between published evidence/guidelines and actual intensivist practice. Even when guidelines based on high-quality evidence are available, it is clear that wide variation in clinical practice exists. However, the trend of drug usage is changing to keep with the guidelines which recommend minimizing or interrupting sedation, reducing immobility.

Key words: Neuromuscular blockers.

Variability of antibiotic trough concentrations in critically ill patients receiving renal replacement therapy: A pragmatic, multi-national observational study

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Introduction: Achieving appropriate blood antibiotic concentrations is important to optimise the treatment of sepsis and improve mortality. We tested the hypothesis that the prescription of renal replacement therapy (RRT), and antibiotics in ICU is highly variable, and resultant antibiotic blood concentrations are unlikely to consistently meet appropriate therapeutic targets.

Methods: Prospective, observational, multi-national, pharmacokinetic study in 26 intensive care units. Antibiotic dosing and RRT prescription were determined by individual unit protocols. Patient demographic, RRT and clinical data and trough antibiotic concentrations of meropenem, piperacillin-tazobactam, vancomycin, and linezolid were evaluated. Beta lactam therapeutic target concentrations were established; high (4xMIC) and low (1xMIC) for common gram-negative bacteria in ICU. Vancomycin target concentrations were; high (≥ 20 mg/L) and low (≥ 15 mg/L), according to current guidelines.

Results: 384 patients were enrolled from 26 ICUs. Patients received meropenem (n=187); piperacillin (n=160); tazobactam (n=101); vancomycin (n=60); and linezolid (n=6), providing 514 trough concentrations. Linezolid trough concentrations were not evaluated because of small numbers. We observed a wide variability in patient illness severity, antibiotic dosing regimens prescribed for all antibiotics, as well as in the modality and prescribing practices for RRT. A wide range of trough concentrations was observed (Figure 1). Trough concentrations failed to meet higher and lower therapeutic targets in 26%, 36%, 72%, and 4%, 4%, and 55% of patient samples for meropenem, piperacillin and vancomycin, respectively.

Conclusion: Current antibiotic dosing and RRT prescribing practices result in antibiotic concentrations that fail to meet therapeutic targets in many patients. Individualised antibiotic dosing, using algorithms derived from an understanding of PK and practice variability, supported by therapeutic drug monitoring, are needed to improve the adequacy and consistency of blood antibiotic concentrations in critically ill patients requiring RRT.

Key words: Pharmacokinetics, antibiotic dosing, meropenem, piperacillin, vancomycin.

Impact of appropriate empirical antibiotics on clinical outcome in *Klebsiella pneumoniae* bacteraemia in the intensive care unit

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Introduction: *Klebsiella pneumoniae* (KP) is a common Gram-negative bacterium causing a myriad of infections such as pneumonia, urinary tract infection and other nosocomial infections. Treatment options have been reduced due to the emergence of multi-drug resistant strains worldwide. On the other hand, inappropriate empirical antibiotics in septic shock are associated with poor outcome. In this study, we aim to evaluate the impact of appropriate empirical antibiotics on outcomes in KP bacteraemia in critical care setting.

Methods: Adults admitted to intensive care unit of a regional hospital in Hong Kong with KP bacteraemia from January 2009 to June 2017 were retrospectively reviewed. Demographics, antibiotics, microbiology and outcomes were analyzed. Cox regression analysis was performed to determine independent predictors for 90-day mortality and logistic regression analysis was used to identify independent predictors for patients to have received inappropriate empirical antibiotics.

Results: During the study period, a total of 205 patients with KP bacteraemia were identified, in which 148 received appropriate empirical antibiotics (72.2%) while 57 did not (27.8%). Inappropriate or no empirical antibiotics was associated with significantly higher 90-days mortality (HR 3.419; 95% CI 2.12-5.51; p 0.001). Other independent predictors include: concomitant congestive heart failure (HR 2.395; 95% CI 1.18-4.83; p=0.015), medical patients (HR 2.390; 95% CI 1.40-4.07; p=0.001), higher total SOFA score (HR 1.097; 95% CI 1.05-1.14; p 0.001). Patients with chronic kidney disease (CKD) or end stage renal failure (ESRF) (OR 4.802, p=0.006), infection caused by ESBL or carbapenem resistance strain (OR 4.339, p=0.003), patients who were mechanically ventilated (OR 4.066, p=0.001) were more likely to have received inappropriate empirical antibiotics.

Conclusion: Appropriate antibiotics improve mortality of patients with KP bacteraemia. Patients with pre-existing CKD/ESRF, infection by ESBL or carbapenem resistance strain and mechanically ventilated patients are more likely to have received inappropriate antimicrobials treatment.

Key words: Sepsis, bacteraemia, antibiotics.

Preconditioning with netrin-1 in acute myocardial infarction model of rat improves systolic and diastolic left ventricular dysfunction

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Introduction: Left ventricular (LV) diastolic function does not recover from ischemia/reperfusion (IR) injury like acute myocardial infarction (MI) compared with systolic function and is important to surgical outcome under any type of anesthesia. Netrin-1 is known to improve IR injury at acute MI rat model. To evaluate the improvement of diastolic LV dysfunction as well as systolic function by preconditioning with netrin-1 after acute MI rat model, we examined the changes of echocardiographic parameters and compared with them before and after MI using netrin-1.

Methods: Male, 8-to 9-week-old, Sprague-Dawley rats with a mean body weight of 277.40 ± 9.48 g were anesthetized with pentobarbital (65 mg/kg IP) under intubation and positive pressure ventilation. The acute MI model had the ligation of left coronary artery under heart exposure through 4-5th intercostal space then closed. Another group of rat underwent sham ligation without tightening the suture around the coronary artery. After 30 minutes of ischemia, netrin-1 (5 mcg/kg) was slowly injected into MI group but vehicle (normal saline) into another MI group via tail vein. Using Vevo2100, echocardiographic studies were performed before surgery and after 120 minutes of reperfusion. Echocardiographic parameters matched systolic function with fractional shortening (FS) and ejection fraction (EF), but diastolic function with E' and E/E' ratio.

Results: MI-vehicle group had significantly attenuated FS, EF and E' compared with sham, while MI-netrin group had significant reduction in attenuation of them compared with MI-vehicle group. MI-vehicle group had significantly increased E/E' ratio compared with MI-vehicle group, while MI-netrin group had significant reduction in increase of it.

Conclusion: Preconditioning with netrin-1 makes meaningful improvement of systolic dysfunction with significant increase with FS and EF after acute MI. Also it helps E' recovery for LV diastolic function and E/E' ratio for left atrial pressure which means diastolic functional recovery.

Key words: Myocardial infarction, diastolic dysfunction, preconditioning.
