Abstract 9

Korresponderende forfatter  Marco Bo Hansen
Email  marcobhansen@gmail.com
Afdeling  Anæstesi- og Operationsklinikken, HovedOrtoCentret, afd. 4231
Hospital/institution  Rigshospitalet
Medforfattere  Lars Simon Rasmussen, Mattias Svensson, Bhavya Chakrakodi, Trond Bruun, Martin Bruun Madsen, Anders Perner, Peter Garred, INFECT Study Group, Ole Hyldegaard and Anna Norrby-Teglund
Titel  The association between cytokine response and disease severity in patients with necrotising soft tissue infection: a multicentre, prospective, observational study

Introduction
Early diagnosis and assessment of necrotising soft tissue infection (NSTI) can be challenging. Analysis of inflammatory markers could provide important information about disease severity and guide decision making. However, prospective studies on plasma inflammatory markers in NSTI are limited. For this purpose, we investigated the association between plasma cytokine levels and the Laboratory Risk Indicator for Necrotising Fasciitis (LRINEC) score, disease severity and mortality in patients with NSTI. We hypothesized that high cytokine levels upon hospital admission were associated with a high LRINEC score, high SAPS II and SOFA scores, presence of septic shock and β-haemolytic streptococcal infection, treatment of renal replacement therapy (RRT), amputation and 30-day mortality.

Methods
This multicentre, prospective, observational study of 159 patients with NSTI was conducted between February 2013 and November 2015 in five Scandinavian ICUs. Plasma samples were taken upon hospital admission and analysed for interleukin-1β (IL-1β), IL-6, IL-10 and tumor necrosis factor-α (TNF-α). The severity of NSTI was assessed by the LRINEC score, SAPS II, SOFA score, septic shock, β-haemolytic streptococcal infection, RRT and amputation.

Results
A LRINEC score ≥ 6 was seen in 116 (73%) patients. We found no significant difference in baseline cytokine levels according to a LRINEC score above or below 6 (IL-1β: 3.0 vs. 1.3; IL-6: 607 vs. 289; IL-10: 38.4 vs. 38.8; TNF-α: 15.1 vs. 7.8 pg/mL, P > 0.05), but IL-6 level had the strongest association to SAPS II (Rho = 0.41) and SOFA-score (Rho = 0.51), P < 0.0001. Patients with septic shock and patients receiving RRT had higher levels of all cytokines (P < 0.01 and P < 0.05, respectively). Patients with streptococcal infection and those undergoing amputation had higher levels of IL-6, IL-10 and TNF-α (Fig. 1). There was no difference in mortality between patients with a LRINEC score above or below 6, but 30-day mortality was correlated to high baseline levels of all cytokines (unadjusted analysis). In the adjusted analysis, the association was the strongest for IL-1β (OR 3.86 [95% CI, 1.43-10.40], P = 0.008) and IL-10 (OR 4.80 [95% CI, 1.67-13.78], P = 0.004).

Conclusion
We found no significant association between LRINEC score and cytokine levels on admission. IL-6 was consistently associated with disease severity, whereas IL-1β and IL-10 had the strongest association with 30-day mortality.

ClinicalTrials.gov: NCT01790698.
URL: https://clinicaltrials.gov/ct2/show/NCT01790698?term=NCT01790698&rank=1
Introduction
Sleep and wakefulness are interconnected stages, regulated by mechanisms in the basal brain. Disturbed sleep may cause prolonged ICU stay, increased morbidity and mortality. Several studies reveal pathological sleep patterns in critically ill patients. Critically ill patients in the busy environment of an ICU are exposed to disturbances, such as the high level of noise and light, procedures, mechanical ventilation and medication.

We aimed to determine if improving the ICU environment would lead to better sleep quality, assessed by polysomnography (PSG), in critically ill mechanically ventilated patients.
Methods
The night-intervention ‘Quiet routine’ protocol included procedures directed towards improving the ICU environment between 10 pm and 6 am. Noise levels during control and intervention nights were recorded. Patients on mechanical ventilation and able to give consent were randomized to the intervention on the first or the second night of the study. We monitored sleep by PSG. The standard, American Academy of Sleep Medicine (AASM), sleep scoring criteria were insufficient for the assessment of PSGs. AASM classification was extended by criteria, suggested by Watson et al.1 The PSGs were assessed by an expert in sleep medicine.

Results
We included 19 patients. Two patients were excluded due to deterioration. Sound level analysis showed insignificant effect of the intervention on noise reduction (p=0.3). Analysis of the overnight PSGs revealed that approximately 60% of the patients had only pathologic patterns.

Discussion
The application of PSG in critically ill patients is limited due to technical difficulties and challenges with the analysis. Foreman et al.2 used PSG for evaluation of the effect of earplugs and eye masks, and melatonin treatment on sleep quality in neurological ICU. The authors found that 65% of the PSGs were unscorable in accordance to standard criteria. Ten out of the 12 participants in the mentioned study had altered sensorium. Although all the patients in our study were awake and without delirium at inclusion, only 38% of all the recorded epochs could be scored according to AASM standard.

Conclusions
Characteristics of normal sleep were absent in many of the PSGs in these critically ill patients. Watson’s sleep scoring classification for critically ill patients was found useful for scoring PSGs. We were not able to reduce noise levels in the ICU and did not find any association between the environmental intervention and the presence of normal sleep characteristics in the PSG.

References
Introduction

Over 30,000 patients are annually admitted to Danish Intensive Care Units (ICUs). Effectiveness of treatment has increased and the overall survival rate is now above 80%. Consequently, the period after ICU discharge has gained increasing attention and follow-up interventions have become more common. These interventions have given name to the concept of ‘aftercare’. Aftercare includes both early in-hospital rehabilitation initiated after ICU discharge and rehabilitation after hospital discharge.

This study aims to investigate aftercare activities in Denmark after ICU treatment.

Method

We conducted an electronic questionnaire survey that was distributed by e-mail to the heads of ICUs at 31 general ICUs, excluding specialized ICUs (cardiothoracic surgery, neurosurgery, pediatrics, neonatology, and postoperative wards). The questionnaire was divided into the following 4 sections: early aftercare, late aftercare, future development, and demographics.

Results

Data were collected from June 1st – July 29th 2016. The response rate was 30 out of 31 (97%). Overall, 26 of 30 ICUs (87%; CI 75-99) offered aftercare. Nine out of 29 (31%; CI 14-48) ICUs offered both early and late aftercare. Eight out of 29 (28%; CI 11-44) ICUs offered only early aftercare and 8 out of 29 (28%; CI 11-44) offered only late aftercare. One ICU did not complete the questionnaire, but had early aftercare. Eligibility criteria for aftercare were mostly based on ICU length of stay or was an individual clinician-based decision.

Early aftercare:
All 18 teams involved a nurse visit, and 12 teams also involved a doctor. Most common activities were management of respiration, tracheostomy care, and nutrition.

Late aftercare:
All 17 teams involved a nurse visit, and 9 teams also involved a doctor. The most common intervention was review of ICU diaries.

Discussion

Our study found that 87% of general ICUs offered some, but varying level of aftercare. Comparing our results to the latest Danish study from 2011 [1], that reported an aftercare intervention in 8 out of 48 (17%) ICUs, our results reflect an increased focus on, and follow up after ICU admission for critical illness.

Conclusion

Eighty-seven percent of Danish ICUs offer aftercare to their patients. Selection of patients for follow up and type of interventions vary greatly between hospitals.


Abstract 3

Korresponderende forfatter Yuliya Boyko
Email yuliya.boyko@rsyd.dk
Afdeling Anaesthesiologisk-Intensiv afdeling V
Hospital/institution Odense Universitetshospital
Medforsfattere René Holst; Poul Jennum; Helle Oerding; Miki Nikolic; Palle Toft
Titel Melatonin secretion pattern in critically ill patients

Introduction

Abnormal circadian and sleep homeostasis are present in critically ill patients. Limited data suggest that this may be associated with morbidity and mortality. We aimed to analyze melatonin secretion and polysomnography (PSG) in conscious critically ill patients on mechanical ventilation with and without remifentanil analgosedation.

Methods

Eight conscious critically ill patients on mechanical ventilation were included. Blood-melatonin samples were taken every 4th hour, and PSG was recorded during a 48-hour study period. PSGs were analyzed in accordance with American Academy of Sleep Medicine criteria if sleep patterns were identified; otherwise, Watson’s classification was applied1. As remifentanil analgosedation was periodically administered during the study, the effect of remifentanil on melatonin and sleep pattern was assessed.
Results
Melatonin secretion pattern in these critically ill patients followed a phase-delayed diurnal curve with acrophase in serum at 4.30 am and nadir at 4.30 pm (fig.1). We did not observe any effect of remifentanil on melatonin secretion pattern. We found the risk of having atypical sleep compared to normal sleep being significantly lower (p=0.000) under remifentanil analgesedation, though REM-sleep was only observed during the nonsedation period.

Discussion
In line with findings by Gehlbach et al.2, we observed phase-delayed diurnal variation of melatonin secretion in our patients. Evening light exposure in ICU due to procedures could probably explain phase-delay.
The effect of remifentanil on melatonin secretion has only been studied in healthy participants. We found no effect of remifentanil analgesedation on melatonin secretion pattern in our patients. Small doses of remifentanil possibly explain missing effect of remifentanil on melatonin secretion.
The association of remifentanil with the presence of atypical /normal sleep characteristics in PSG in critically ill patients has not yet been studied. We found remifentanil to be associated with lower risk for atypical sleep compared with normal sleep. The etiology of this finding is unclear and needs further investigation.

Conclusion
We found preserved but phase-delayed diurnal pattern of melatonin secretion in these critically ill patients on mechanical ventilation. Remifentanil did not have any effect on melatonin secretion pattern, but was associated with lower risk of atypical sleep pattern compared with normal sleep. REM sleep was only seen in the PSG recordings without remifentanil.

References

Abstract 5
Korresponderende forfatter Helene Korvenius Nedergaard
Email helene.korvenius.nedergaard@rsyd.dk
Afdeling Anaesthesiologisk afdeling
Hospital/institution Sygehus Lillebælt, Kolding
Medforfattere Trine Haberlandt (anaesthesiologisk afdeling, Sygehus Lillebælt, Kolding), Hanne Irene Jensen (anaesthesiologisk afdeling, Sygehus Lillebælt, Kolding), Palle Toft (anaesthesiologisk-intensiv afdeling V, Odense Universitetshospital)
Titel Pressure ulcers in critically ill patients – preventable by non-sedation? A substudy of the NONSEDA-trial

Introduction
Pressure ulcers increase the risk of serious infection and are associated with higher mortality and longer stay in the ICU [1]. Pa-
Patients on mechanical ventilation are often sedated, leading to sustained periods of immobility. Clinical experience suggests that nonsedated patients are easier mobilized and change position in bed more often. We therefore hypothesize that nonsedation might prevent pressure ulcers.

Methods
Retrospective data on patients included in the NONSEDA trial, at the Kolding trial site, per May 1, 2016. In the NONSEDA-trial patients are randomised to standard care (sedation with a daily wake up) or nonsedation during mechanical ventilation. Whether a patient is sedated cannot be blinded. However, the ICU-nurses performing the clinical assessment were unaware that we investigated pressure ulcers. All data were extracted before the patient’s randomization status was revealed. If we encountered difficulties ascertaining whether an ulcer was ICU-acquired or present at admission, we chose worst-case scenario and assumed that the ulcer was ICU-acquired. The primary outcome was total number of pressure ulcers acquired in the ICU, described by grade (I-IV) and localization.

Results
We identified 65 pressure ulcers in 150 patients. There were no significant differences between groups regarding sex, age, BMI, APACHE II or SAPS II. There were 34 grade 1 pressure ulcers (sedated: 18, nonsedated: 16), 29 grade 2 ulcers (sedated: 17, nonsedated: 12) and 2 grade 3 ulcers (sedated: 1, nonsedated: 1), with no significant difference between groups. Concerning localization, we grouped results into three: sacrum, heels and caused by equipment (for example from nostril from oxygen catheter). The localization of the ulcers were significantly different (p=0.04): sacrum (sedated: 36%, nonsedated: 21%), heels (sedated: 33%, nonsedated: 17%), from equipment (sedated: 31%, nonsedated: 62%).

Discussion
We found no significant difference in the incidence of pressure ulcers. The vast majority of the ulcers identified were grade 1 and 2 were, reflecting the great awareness on pressure ulcers in Denmark and in this particular ICU. This awareness is reflected in the relatively high number of grade 1 pressure ulcers, which also covers “pressure traces”, describing a condition before grade 1.

A difference in the localization of pressure ulcers was found. The sedated patients mainly had ulcers in the classic localizations, sacrum and heels. The non-sedated mainly had ulcers related to various equipment. Considering the long-term prognosis, ulcers deriving from equipment are most likely easier to relieve and must be expected to heal faster.

This substudy is planned to include 200 patients. We expect to reach this number in November 2016. When data on all patients are available, analyses will be updated.

Reference

Abstract A
Korresponderende forfatter  Johan Larsson
Email  johanlarsson923@gmail.com
Afdeling  Anæstesiologisk afdeling
Hospital/institution  Nordsjællands Hospital Hillerød
Medforfattere  Theis Skovsgaard Itenov, Morten Heiberg Bestle
Titel  Risk prediction models for mortality in patients with ventilator-associated pneumonia: A systematic review and meta-analysis

Introduction
Ventilator-associated pneumonia (VAP) is a common and serious complication in patients requiring mechanical ventilation in the intensive care unit (ICU). A precise instrument to stratify the severity among patients with VAP is warranted to reduce heterogeneity in clinical trials, better define the disease and ultimately improve clinical therapy [1]. The aim of this study was to identify models used to predict mortality in VAP patients and assess their prognostic accuracy.

Methods
PUBMED and EMBASE were searched in February 2016. We included studies in English that evaluated models ability to predict the risk of mortality in unselected patients with VAP. The reported mortality with the longest follow up was used in the meta-analysis. Prognostic accuracy was measured with the area under the receiver operator characteristic curve (AUC).

Results
We identified 19 articles studying 7 different models’ ability to predict mortality in VAP patients. The models were APACHE II (9 studies, n=1398), CPIS (4 studies, n=303), IBMP-10 (3 studies, n=406), VAP PIRO (2 studies, n=589), SOFA (7 studies, n=1019),
SAPS II (6 studies, n=1043) and APACHE III (1 study, n=198). APACHE II had the highest pooled AUC (95% confidence intervals), 0.72 (0.64-0.80) and CPIS had the lowest pooled AUC, 0.64 (0.55-0.72).

Discussion
We identified 7 models that have been evaluated for their ability to predict mortality in patients with VAP. Of these, APACHE II was the most studied model. IMBP-10 and VAP PIRO are designed to predict mortality in VAP patients and are based on few variables. They have shown promising results in their original studies, which could not be reproduced in the validation studies. SAPS II and SOFA score have been studied in combination with the biomarkers Procalcitonin and Midregional pro-atrial natriuretic peptide, which improved the predictive accuracy [2]. It is possible, that the simpler prediction models could benefit from the biomarkers at VAP onset, making them more precise in predicting death.

Conclusion
Many models have been evaluated for their ability to predict mortality in patients with VAP. The models had nearly equal predictive accuracies, although some models are more complex and time consuming.


---

Abstract 28

Korresponderende forfatter: Signe Voigt Lauridsen
Email: signevoigt@gmail.com

Aim
To describe coagulation in ICH patients at admission and during the first 24 hours after symptom onset. Our hypothesis was that ICH patients had a systemic activated coagulation at admission compared to 24 hours after symptom onset.

Methods
The Study was approved by the Regional Committee System. Patients diagnosed with ICH were enrolled prospectively at Aarhus University Hospital. Blood samples were obtained at time of arrival to hospital as well as 6 and 24 hours after symptom onset (+/-2 hours). Conventional coagulation tests were measured. ROTEM® analyses were performed using the standard assays EXTEM, INTEM, FIBTEM and HEPTEM. Thrombin generation was quantified by Calibrated Automated Thrombogram®. Reference interval for ROTEM (figure 1 and 2) were obtained from Department of Clinical Biochemistry, Aarhus University Hospital. All results are reported as median (interquartile range), except for age.

Results
Forty-one patients were enrolled with a mean age of 62 years (range 27-95 years), 66 % were women. At admission, Median Glasgow Coma Score (GCS) was 13 (9-15), National Institutes of Health Stroke Scale (NIHSS) score was 16 (7-20) and median APACHEII score was 15 (11-21). Thirty days mortality was 17%. Conventional coagulation tests showed elevated fibrin D-dimer at 1.2 mg/ml (0.6 – 2.0 mg/ml, reference interval: <0.5 mg/ml) at admission, and 1.1 (0.4 – 2.0) (p= 0.07) at 24 hours. Eighty-two percent were outside reference interval at admission. ROTEM® parameters demonstrated a subtle hypercoagulable state in the acute phase and 24 hours after symptom onset. EXTEM maximum clot firmness (MCF) was elevated both at admission (67 mm (62-70 mm)) and after 24 hours (66 mm (63-69 mm))
(p = 0.2), with 60% outside reference interval at admission. FIBTEM MCF was elevated both at admission (21 mm (16-26)) and after 24 hours (21 mm (17-23)) (p= 0.7), with 55% outside reference interval (Figure 1 and 2). Thrombin generation results were within reference interval except for time to peak, which at admission was (5.9 min (5.1- 7.0 min)) compared to 24 hours (6.4 min (5.9 - 7.7)) (p = 0.2), with 59% outside reference interval.

Conclusions
ROTEM® and conventional coagulation tests indicated a subtle systemic hypercoagulable state in ICH patients in the acute phase and up to 24 hours after symptom onset. The subtle systemic hypercoagulable state did not change significantly within 24 hours after admission. The present results support new evidence that a hypercoagulable state occurs following an acute ICH.

Reference
Abstract

Korresponderende forfatter: Sofie Højlund
Email: sofie.hojlund@gmail.com
Afdeling: Klinik for allergi UA-816GE
Hospital/institution: Dansk Anaesthesia Allergi Center, Gentofte Hospital
Titel: Low incidence of biphasic allergic reactions in patients admitted to intensive care following anaphylaxis

Background
Biphasic allergic reactions (BAR) are reported in the literature to occur in 1-23% of allergic reactions. This apparent risk of a recurrence of the allergic symptoms leads to increased observation time in patients admitted to hospital following anaphylaxis. There is currently no consensus on the optimal observation time in anaphylaxis guidelines worldwide. Patients admitted to intensive care following anaphylaxis may be postulated to have had more severe reactions and potentially a higher risk of a BAR; however this has never been investigated.

The purpose of this study was to examine incidence, triggers, symptoms and treatment of BAR, in patients admitted following anaphylaxis to intensive care units (ICUs) in the Capital Region of Copenhagen.

Method
Records of all patients admitted to five ICUs in the period 2011-2014 with the diagnoses: “Anaphylaxis without specification” or “Anaphylaxis by correct drug administration” were reviewed for data on the initial allergic reaction, which led to intensive care admission. Only patients with a clinical reaction fulfilling internationally accepted criteria for anaphylaxis (1) were included. Records from ICU were then reviewed to identify potential BAR defined as renewed allergy symptoms occurring 1-78 hours after initial symptoms had resolved, without further exposure to the potential trigger.

Results
A total of 83 cases of anaphylaxis leading to hospitalization in one of five ICUs were identified. Drugs were the most common trigger (70%) with antibiotics accounting for 45%. Skin symptoms were present in 83% of cases, followed by circulatory (58%), and respiratory (54%) symptoms. Respectively 98% and 96% were treated with antihistamines and steroids, however, only 80% were treated with adrenaline. Only ten cases presented at least one symptom after the initial allergic reaction. Of these, three were possible and one was a probable BAR giving a total incidence of 4.8% (1.2% if only including the probable reaction). All cases were mild with skin symptoms only, and occurred on average 14 hours after the initial reactions.

Discussion
This study finds that the incidence of BAR in patients admitted to ICU following anaphylaxis is lower than suggested in the literature. None of the identified reactions were severe and all responded to treatment with antihistamines and steroids. This implies a need for an evaluation of recommended observation times after anaphylaxis, for which there is currently no consensus. Also, further studies identifying potential risk factors for rare BAR are needed.

Conclusion
The findings in this study implies that the incidence of BAR may be overestimated in the literature.