



# Molecular biomarkers associated with respiratory insufficiency in amyotrophic lateral sclerosis

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radio-telemetry recording of blood pressure (BP) and heart rate (HR), and in anaesthetised animals (induction: sodium pentobarbital, 60 mg/kg, ip; maintenance: 20% solution, v/v) with BP, ECG, HR, tracheal pressure, respiratory frequency (RF) and body temperature continuously monitored. Baro and chemoreflex were evaluated with phenylephrine (0.2 ml, 25 µg/ml; iv) and lobeline (0.2 ml, 25 µg/ml; iv), respectively. Behavioural changes were also evaluated through the elevated-plus maze, open-field and Y-maze tests. Immunohistochemistry and RT-PCR were executed to determine heart and brain inflammatory state. Serum biomarkers levels for organ dysfunction were also measured. Overall our results show a rise in BP and HR, and elevated RF due to increased chemoreflex sensitivity. 24 h following LPS injection, all groups have a significantly decreased baroreflex ( $p < 0.05$ ), however, 6 h post-injection, LPS12 show a statistically significant increase in baroreceptor reflex ( $p < 0.05$ ). At both time-points, the two LPS groups present an anxiety-like behaviour, associated with less locomotor/exploratory activity and highly significant cognitive impairment ( $p < .0001$ ). The autonomic evaluation of the anaesthetised LPS12 group results in an increase of the autonomic tone at 6 h post-LPS followed by a decrease at 24 h. The LPS6 group shows the opposite profile. Interestingly, conscious animals reveal a slightly different profile in both groups, with a continuous increase in autonomic tone for LPS12 and a decrease 24 h post-LPS in LPS6 group. The molecular studies show reactive astrogliosis and microgliosis, due to inflammatory processes in the hippocampus, as well as, an upregulation of pro-inflammatory factors in the heart and brain. Serum analysis yielded higher levels of biomarkers for renal and liver dysfunction ( $p < .05$ ) and pancreatic and neuromuscular injury ( $p < .05$ ), in the LPS12 group. Concluding, LPS administration induces strong modifications in both cardiac and neurological systems, during the early stages of the systemic inflammatory response. Being a good model for further pathophysiological and pharmacological studies related to Sepsis.

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## Molecular biomarkers associated with respiratory insufficiency in amyotrophic lateral sclerosis

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### ABSTRACT

Amyotrophic lateral sclerosis (ALS) is a devastating and fatal neurodegenerative disorder. Death typically occurs within 3–5 years after disease onset. The main cause of death in ALS is respiratory failure (RF). No effective treatment is available and no molecular biomarker related to respiratory outcome and to early ventilatory dysfunction was described so far. The club-cell protein (CC-16) is a biomarker associated with respiratory distress and lung inflammation.

The aim of this work is to test if CC-16 and IL-6 could be new biomarkers of ALS for early signs of respiratory insufficiency and disease progression. Additionally, we intend to study morphological and viscoelastic changes of the erythrocytes' membrane associating them with ALS patients' clinical profile.

Eighty-one ALS patients and 30 matched controls were included. Functional capacity and respiratory function (forced vital capacity) were evaluated. CC-16 and IL-6 were quantified by ELISA and multiplex technology, respectively. Morphological and viscoelastic properties of the erythrocytes were analysed by Atomic Force Microscopy (AFM).

CC-16 levels were significantly raised in ALS patients. In 17% of them, CC-16 level was above the upper cut-off value. On these patients, the risk of non-invasive ventilation was greater in the following 6 months and they tend to have higher mortality in the following 30 months. IL-6 values were not different in ALS population as compared with controls.

ALS patients have higher erythrocyte maximum height, area and volume, decreased erythrocyte membrane roughness and increased membrane stiffness than the control group. These results indicates abnormal erythrocyte structure and possible changes on membrane lipid composition on ALS patients.

We propose that increased CC-16 levels could be a marker of lung inflammatory response, associated with ventilatory insufficiency and related to impending respiratory failure, which are not fully predicted by conventional respiratory tests. Moreover, abnormalities in erythrocyte morphology may enhance the risk of tissue hypoxia.

Amyotrophic lateral sclerosis (ALS) is a devastating and fatal neurodegenerative disorder. Death typically occurs within 3–5 years after disease onset. Respiratory failure (RF) is the main cause of death. No effective treatment and no molecular biomarker related to respiratory outcome and to early ventilatory dysfunction are available. The club-cell protein (CC-16) is a biomarker associated with respiratory distress and lung inflammation.

The aim of this work is to test if CC-16 and IL-6 could be new biomarkers of ALS for early signs of respiratory insufficiency and disease progression. Additionally, we intend to study morphological and viscoelastic changes of the erythrocytes' membrane associating them with ALS patients' clinical profile.

Functional capacity and respiratory function (forced vital capacity) were evaluated in 81 ALS patients and 30 matched controls. CC-16 and IL-6 were quantified by ELISA and Multiplex-technology, respectively. Morphological and viscoelastic properties of the erythrocytes were analysed by Atomic Force Microscopy (AFM).

A significant negative correlation was found between [IL-6] and PhrAMPL, but not with ALSFRS-R or disease duration. CC-16 levels were significantly raised in ALS patients. In 17% of them, CC-16 level was above the upper cut-off value. On these patients, the risk of non-invasive ventilation was greater in the following 6 months and they tend to have higher mortality. ALS patients have higher erythrocyte maximum height, area, volume, decreased erythrocyte membrane roughness and increased membrane stiffness.

These results indicate that abnormal erythrocyte structure and possible changes on membrane lipid composition on ALS patients. Our results show that IL-6 levels are not dependent on the duration or severity of the disease, however, IL-6 may provide a marker of respiratory dysfunction in ALS. We propose that increased CC-16 levels could be a marker of lung inflammatory response, associated with ventilatory insufficiency and related to impending RF, which are not fully predicted by conventional respiratory tests. Moreover, abnormalities in erythrocyte morphology may enhance the risk of tissue hypoxia.

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## Nursing communication handover in emergency department

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### ABSTRACT

**Introduction:** Effective communication in the transition of care is fundamental to improve patient safety and contribute to the reduction of adverse events [1]. A study carried out in 2014, in fifty-five hospital units in Portugal, under the “Evaluation of Patient Safety Culture in Hospitals”, concluded that patient safety culture is not yet widely acknowledged as a priority for health professionals [2], and that 70% of adverse health events occur due to communication failures among health professionals during the transition of care. Ineffective communication can be found in different health contexts, being more frequent during the transition of care, when it is essential to manage situations quickly and effectively. The peri-operative period, the ICU and emergency department are examples of contexts where communication processes are complex and prone to errors.

**Objective:** To know nurses' opinion about the transition of care in the emergency department, as well as their knowledge on the patient safety.

**Materials and Methods:** This is a descriptive and exploratory study with a quantitative approach. Non-probabilistic and convenience sample. This study intends to answer the following research questions: What is the opinion of the emergency department nurses about the time of transition of care during shift change? Do nurses know the guidelines for patient safety in the care transition?

A questionnaire was used as a data collection instrument. It consists of three parts: a first part on sample characterisation; a second part that seeks to know the opinion of nurses about the transition of care in the change of shift; and a third part, with the objective of assessing nurses' knowledge on patient's safety. The questionnaire was applied during the month of January 2019.

**Results:** Of the total of seventy questionnaires delivered fifty were returned, with a response rate of 67.57%. The sample is essentially composed of women (82%), with a mean age of 33.46 years. They have on average 10.67 years as nurses and 7.29 years as nurses in the emergency department. With regard to nurses' opinion on the transition of care during shift change, four domains were found, namely: Positive aspects of the nursing care transition moment; Negative aspects of the nursing care transition moment; Patient evaluation at the moment of nursing care transition; and management of the information obtained during the nursing care transition. Regarding nurses' knowledge on patient safety, three areas were identified: Knowledge of the guidelines on effective communication in the transition of care; Benefits of using a standard tool in the transition of care, and training in the area of patient safety.

**Discussion and conclusions:** Nurses feel that there are a number of factors that interfere with the transition of care; there is irrelevant information that is transmitted in the moment of transition of care and the ISBAR methodology contributes to decision-making and critical thinking. It is important to promote team training in the area of patient safety. Nurses have the legal obligation to ensure continuity of care through effective communication, using existing resources, namely the ISBAR tool.