Chemoreflexes are important mechanisms for regulating ventilatory and cardiovascular function. The aim of this study was to determine the meaning of autonomic dysfunction for the pathophysiology and outcome in critical ill patients. For the determination of the chemoreflex sensitivity (ChRS), the ratio of the RR interval shift and the shift of oxygen partial pressure during a 5-min inhalation of oxygen with a nose mask was formed. Pathological chemoreflex sensitivity was predefined as a ChRS below 3.0 ms/mmHg. Out of the 27 critical ill patients included into the study, 17 had a sepsis and 10 a cardiogenic shock. In these patients, chemoreflex sensitivity was significantly reduced compared with a control group (sepsis: 2.1 ± 1.68, cardiogenic shock: 0.4 ± 0.27, controls: 5.0 ± 2.8 ms/mmHg; P<0.05 vs. sepsis or cardiogenic shock). There was a significant negative correlation (r=-0.6; P<0.01) between the chemoreflex sensitivity and the severity of illness described by the SOFA-score. We conclude that cardiac reflex mechanisms are changed toward increased sympathetic activity reflected by reduced chemoreflex sensitivity in critical ill patients. Moreover, there is a close negative correlation between the ChRS and the SOFA-score.

Key words: autonomic dysfunction, chemoreflex sensitivity, sepsis

INTRODUCTION

The autonomous nerve system enables the organism to adapt to stress and warrant organ perfusion and oxygenation. The sympathetic-vagal balance is maintained beyond several peripheral and central mechanisms, e.g., baro- and chemoreflex sensitivity or heart rate variability. Chemoreceptors are sensory receptors that are located in the glomus caroticum (1) and detect changes in blood
oxygenation. In response to oxygen stimulation, a neural impulse is sent to the cardiovascular center in the medulla, which leads to an RR interval increase via a feedback mechanism (2). It has been shown in a previous study that reduced chemoreflex sensitivity is a predictor for sudden cardiac death in patients with heart failure (3), but only few data exist concerning the meaning of autonomic dysfunction for the pathophysiology and outcome in critical ill patients.

In such patients, impairment of autonomic function might worsen the outcome possibly due to “loss of neural-humoral organ interaction” (4). Schmidt et al (5) have reported a reduced autonomic function in patients with multiple organ dysfunction syndromes. In the present study, we examined the chemoreflex sensitivity and its correlation to the sequential organ failure assessment score (SOFA) in critically ill patients with sepsis or cardiogenic shock.

PATIENTS AND METHODS

The study was approved by a local Ethics Committee and was performed in accordance with the guidelines set by the Declaration from Helsinki for Human Research.

Twenty seven critically ill patients (age 63.7 ± 8.2 yr, body mass index 27.8 ± 3.5 kg/m²; 20 males, 7 females), admitted to our intensive care unit, were included in the study. Seventeen (63%) of the 27 patients had sepsis and 10 (37%) had cardiogenic shock. The control group comprised 11 patients with unexplained syncope or paroxysmal supraventricular tachycardia without clinical signs of heart failure. Patients with atrial fibrillation, valvular prosthesis, undergoing valvular surgery, or pacemaker stimulation were excluded. Participants of the investigation were 29 to 75 years old (median 53.4 years). Arterial and venous blood samples were analysed by measuring the partial pressure of oxygen (PaO₂), partial pressure of carbon dioxide and pH using standard blood gas electrodes (ABL 300 radiometer, Copenhagen, Denmark).

In non-surgical intensive care patients Schumacher et al (6) developed a score which has been shown to have high sensitivity (98%) and specificity (96%) for detection of sepsis. Therefore, seven individual parameters were used: respiration rate, heart rate, body temperature, C-reactive protein, lactate, leukocytes, and thrombocytes. The highest point for each value of individual parameter is 3. This score shows a sharp significant distinction between septic and non-septic circulatory situation compared with invasive measurements of systemic vascular state. The severity of organ dysfunction was described according to the SOFA score (7).

Determination of chemoreflex sensitivity

For the determination of the chemoreflex sensitivity RR intervals and venous oxygen partial pressure (PvO₂) were measured before and after the inhalation of oxygen via a nose mask. Oxygen was inhaled over a period of 5 min (6 l/min) in the supine body position. In mechanically ventilated patients (n=16) inspired oxygen fraction (FiO₂) was increased. All patients were isolated in a quiet room in order to prevent external influences on the autonomic nerve system. Medication was not changed during the measurement of chemoreflex sensitivity. Chemosensitivity was calculated as a difference in RR intervals (ms) divided by a difference in the PvO₂ (mmHg). According to previous studies in healthy volunteers, the chemosensitivity ratio below 3 ms/mmHg was considered to be pathological (8).
Statistical analysis

Statistical Package for Social Sciences (SPSS 11.0 for Windows, Munich Germany) was used for data evaluation. Correlation coefficients were generated with the Spearman test. Significant difference between groups was assumed at the level of error < 5%.

RESULTS

All participants of our study had documented sinus rhythm. No significant differences in regard to diabetes mellitus, arterial hypertension, and chronic obstructive pulmonary disease could be observed among the groups diabetes: 5 (29%) in sepsis, 4 (40%) in cardiogenic shock, and 4 (36%) in controls; hypertension: 7 (41%) in sepsis, 5 (50%) in cardiogenic shock, and 4 (36%) in controls; COPD: 4 (23%) in sepsis, 2 (20%) in cardiac shock, and 2 (18%) in controls]. The chemoreflex sensitivity was significantly reduced in patients with sepsis and cardiogenic shock compared with the control group (Fig. 1). Moreover, we found a significant negative correlation (r=-0.6; P<0.01) between the chemoreflex sensitivity and the severity of illness described by the SOFA score.

DISCUSSION

Oxygen breathing causes a decrease in heart rate and a comparable rate-dependant decrease in cardiac output in healthy volunteers (9). Furthermore, systemic resistance and blood pressure increase during oxygen breathing. Our data suggest that this physiological response to changes in oxygenation is diminished in critically ill patients, who show reduced chemoreflex sensitivity.

Fig. 1. Chemoreflex sensitivity in critically ill patients compared with the control group. *P<0.05 and **P<0.01 for the differences from the control group.
This loss of variability might be a consequence of advanced disease, a hypothesis first offered by Godin and Buchman (4) in 1996.

Chemoreflex sensitivity is an indicator of the autonomic tone and reflects the interaction of sympathetic and parasympathetic neural pathways. Reduced variability of the autonomic nervous system is correlated with a poor prognosis (10). In the present study we found a close correlation of the ChRS and the SOFA score. This may indicate a good prognostic value of these parameters. On the other hand, Schmidt et al (11) found that chemoreflex sensitivity is influenced by mechanical ventilation with fixed minute ventilation in 20 healthy volunteers. They suggest that ventilation causes major disturbances in the measurement of cardiac chemoreflex sensitivity.

In summary, we found that cardiac reflex mechanisms are changed toward increased sympathetic activity in critically ill patients. Furthermore, we found a close negative correlation between the SOFA score and the chemoreflex sensitivity. Whether the hyperoxic ChRS might be a tool in risk stratification in patients with sepsis or cardiogenic shock has to be investigated in larger prospective trials.

Conflicts of interest: The authors had no conflicts of interest to declare in relation to this article.

REFERENCES


11. Schmidt H, Opitz H, Peschel T *et al.* The cardiac chemoreflex sensitivity measurement is impaired by respiration. *Int Care Med* 1998; 24: 164.

Received: June 20, 2008.
Accepted: August 20, 2008.

Author’s address: Per Otto Schueller, Division of Cardiology, Department of Medicine, Pneumology and Angiology, University Hospital, Moorenstr. 5, 40225 Düsseldorf, Germany; phone: +49 211 8118800, fax: +49 211 8118858; e-mail: schueller@med.uni-duesseldorf.de