Attenuated autonomic function in multiple organ dysfunction syndrome across three age groups

Hendrik Schmidt1*, Ursula Müller-Werdan1, Thomas Hoffmann1, Darrel P. Francis2, Massimo F. Piepoli2, Mathias Rauchhaus1, Roland Prondzinsky1, Harald Lopnow1, Michael Buerke1, Dirk Hoyer3 and Karl Werdan1

1 Martin Luther University, Halle-Wittenberg, Germany
2 National Heart and Lung Institute, London, UK
3 Institute of Pathophysiology and Pathobiochemistry, Biomagnetic Center, Department of Neurology, Friedrich Schiller University, Jena, Germany

Abstract

Multiple organ dysfunction syndrome (MODS) is the failure of several organs after a trigger event. The mortality is high, at up to 70%. We hypothesize that autonomic dysfunction may substantially contribute to the development of MODS and speculate that there is an age dependence of autonomic dysfunction in MODS. A total of 90 consecutively admitted MODS patients were assigned to this study. Three variables of autonomic function were analyzed: heart rate variability (HRV), baroreflex sensitivity (BRS) and chemoreflex sensitivity (CRS). The patient cohort was divided into three age groups. The main finding was that BRS, CRS and almost all indices of HRV were attenuated in comparison to normal range data and there was no age dependence for HRV. In conclusion, autonomic dysfunction in MODS is attenuated. The influence of MODS on autonomic function overwhelms the age dependence of autonomic function observed in healthy subjects.

Keywords: age; baroreflex sensitivity; chemoreflex sensitivity; heart rate variability; multiple organ dysfunction syndrome.

Introduction

Multiple organ dysfunction syndrome (MODS) is the sequential failure of several organs following a trigger event, commonly sepsis, but also cardiogenic shock or pneumonia. Despite advances in the treatment of sepsis as the main trigger of MODS [7], mortality remains high and treatment in the intensive care unit (ICU) is expensive [2]. MODS is characterized by activation of the innate immunity, resulting in inappropriate release of inflammatory mediators leading to cell damage of parenchymal organs and to inflammatory, metabolic and neuroendocrine disturbances [4]. Since autonomic dysfunction forms part of the severe systemic inflammatory response syndrome, disturbances of the neurally mediated organ interactions in sepsis and in non-infectious inflammatory response syndrome may well contribute to the development of MODS [4]. A basic feature of the healthy human body is continuous communication between all vital organs through signals of the autonomic nervous system. Godin and Buchman [4] proposed a concept of an “uncoupling” of these neurally mediated organ interactions in MODS and sepsis: bacterial toxins and sepsis mediators can potently alter neural reflexes and cytokine pathways and thus cause a defect in interorgan communication, thereby advancing single organ dysfunction into MODS.

Heart rate variability (HRV), baroreflex sensitivity and chemoreflex sensitivity are tools to characterize autonomic function and cardiorespiratory interactions in MODS patients [4]. To date there are data describing a reduction in HRV that is correlated with the severity of illness in septic patients, in critically ill patients with head injuries, and in pediatric patients [3, 14, 16]. However, there are no data concerning the impact of other components of autonomic dysfunction, such as the impairment of baro- and chemoreflexes, on the development of MODS [3, 14, 16].

The aim of the present study was to detect whether autonomic dysfunction is equally pronounced in young, middle-aged and older patients.

Materials and methods

This prospective study was approved by the local Ethics Committee of the Medical Faculty of the Martin-Luther-University, Halle-Wittenberg.

Patients

We enrolled 90 MODS patients consecutively admitted to the medical intensive care unit at the University Department of Medicine I/III, Martin Luther University Halle-Wittenberg, during a study period of 24 months. Five patients were excluded due to the quantity of artifacts in the Holter ECG.
Study protocol

Measurements of autonomic function (HRV, baroreflex sensitivity, and chemoreflex sensitivity) were performed within 48 h of patient admission to the ICU.

HRV All patients were studied at the bedside in the supine position. Continuous 24-h ECG recordings were obtained using Holter recorders (DMS, Dateline, NV, USA; MTM multiteched GmbH, Huenfelden-Dauborn, Germany; and Ela Med, Munich, Germany). Recordings were analyzed by a blinded research Holter technician using a standard software package (DMS, Dateline, NV, USA) and standard Holter analysis techniques for labeling beats and artifacts. All artifacts and ectopic beats were removed and the resulting missing data were replaced by interpolation between the three preceding and the three successive intervals. A second independent observer (cardiologist) edited and double-checked the recordings, reanalyzed the data and confirmed the results with those of the research Holter technician. Only recordings with ≥20 h of usable data were included in the analysis. The sampling rate of the ECG acquisition was 256 Hz. HRV analysis was carried out according to the Task Force guidelines [1]. The frequency domain indices were calculated from the power spectra for heart-period time series (by fast-Fourier transformation, FFT) expressed in ms²/Hz according to the Task Force standards [1].

Baroreflex sensitivity The baroreflex phenylephrine method was performed in accordance with the standard method originally described by Smyth et al. [15] using invasive blood pressure measurement of a study-independent arterial line. The baroreflex test was performed on 48 of the 85 patients.

Chemoreflex sensitivity Measurement of this variable was recently described in detail [13]. Briefly, all patients underwent a three-phase protocol, with each phase taking 5 min. During phase 1, all patients were breathing a predefined inspiratory oxygen fraction (FiO₂). In phase 2, FiO₂ was increased by 1/3 for 5 min or 5 l O₂/min was given to non-ventilated patients via a nose tube to increase arterial oxygen pressure appropriately. In phase 3, FiO₂ was adjusted to the predefined FiO₂ of phase 1 to decrease arterial oxygen tension to baseline levels. At the end of each phase, blood samples were drawn for blood gas analysis and measured immediately by routine hospital analysis (Radiometer®, ABL 330, Copenhagen, Denmark). A 12-lead ECG (standard lead with a prominent R wave) was recorded continuously. The chemoreflex sensitivity was calculated as the regression slope of arterial oxygen tension to RR interval [13]. This test was performed on 61 of the 85 patients.

Age To evaluate the age dependence of the autonomic indices assessed, the study population of patients (24–96 years) was divided into three subcohorts: younger (<40 years, n = 9), middle-aged (40–60 years, n = 31) and older patients (>60 years, n = 45) as described by Pikkujämsä et al. [9].

Statistical analysis

Numerical data are presented as mean±SD, except when indicated otherwise. The Kolmogorov-Smirnov test was used to test for normal distribution, and, if required, data were log-transformed. One-way ANOVA with the Scheffe post hoc procedure was used for intergroup comparisons. All data were analyzed using commercial software (SPSS, SPSS Inc., Chicago, IL, USA version 11.0 and Statview 5.0, SAS Institute Inc., Cary, NC, USA).

Results

Autonomic dysfunction in MODS patients

The APACHE II score of the MODS patients enrolled into the study was 27.7±8.0 and the sepsis score according to Elebute and Stoner 13.5±5.6 [12]. Out of the 85 enrolled patients, 62% had septic MODS and 62% were sedated. All HRV variables assessed (SDNN, SDANN, pNN50, TP, LF, HF, VLF), except RMSSD, and the barore- and chemoreflex sensitivities were significantly lower in MODS patients [12].

Figure 1 illustrates an example of attenuated HRV of a MODS patient and a healthy subject.

Autonomic function of MODS patients and age

Across the three age groups (group 1: <40 years, n = 9; group 2: 40–60 years, n = 31; and group 3: >60 years, n = 45), illness severity and sepsis scores were comparable (APACHE II score 27.9±9.9, 25.5±7.6 and 27.4±8.0 for groups 1, 2 and 3, respectively; p = 0.1). HRV variables were not significantly different between the groups (SDNN 51.3±25.2, 62.6±32.9 and 55.2±30.4 ms for groups 1, 2 and 3, respectively, p = 0.5; SDANN 48.8±23.9, 55.3±31.5 and 48.2±29.7 ms, p = 0.6; pNN50 1.1±2.3%, 6.5±11.5% and 4.5±6.2%, p = 0.2; rMSSD 12.1±12.3, 32.3±35.0 and 26.0±20.9, p = 0.1; TP 195.2±245.6, 797.4±1445.3 and 577.1±1515.7 ms², p = 0.5; LF 29.7±49.8, 121.1±224.8 and 154.8±525.5 ms², p = 0.7; HF 31.3±34.0, 124.3±299.0 and 120.3±274.3 ms², p = 0.6; VLF 37.8±78.8, 300.1±929.8 and 149.9±488.3 ms², p = 0.5; LF/HF 1.7±0.8, 1.2±1.1 and 1.0±0.8, p = 0.2; CRS 0.7±0.7, 0.5±0.4 and 0.5±0.3 ms/mm Hg, p = 0.8).

Baroreflex sensitivity declined with age: 1.5±1.7, 2.4±1.7 and 0.9±0.7 ms/mm Hg for groups 1, 2 and 3, respectively (p = 0.002 for group 2 vs. group 3).

Discussion

This study provides clinical evidence that autonomic dysfunction is equally pronounced in young, middle-aged and older MODS patients, with the exception of baroreflex sensitivity, which was more blunted in older patients.

Autonomic dysfunction in ICU relevant disorders

In cardiology, a reduction in HRV is a predictor of mortality and fatal arrhythmic events after myocardial infarc-
The chemoreflex sensitivity in healthy subjects. In our study, age seemed to play no significant role [13].

Our results suggest that the decrease in autonomic function can mainly be attributed to the severity of disease, which masks potential age effects. Hopefully, autonomic function may recover after effective treatment of MODS not only in younger, but also in elderly patients [11].

References

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