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CIRCADIAN RHYTHMS OF THE ACID-BASE BALANCE AND BLOOD GAS COMPOSITION

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Any biological system, according to the law of structural-functional temporal discreteness, embodies time [3], and knowledge of the temporal characteristics of biological processes is an essential condition for the establishment of criteria of the physiological norm [6].

This paper describes a study of circadian fluctuations in the acid-base balance system and in the blood gas composition, and the use of cosinor analysis to investigate the parameters of the cirdadian rhythms in normal man.

EXPERIMENTAL METHODS

Twenty healthy volunteers aged 20-26 years were investigated at 3 and 9 a.m. and 3 and 9 p.m., corresponding to the four different parts of the 24-h period (night, morning, afternoon, evening), in the spring (March). All subjects confirmed to a standard program of daily activity, a standard diet, and a natural alternation of day and night. They slept from 11 p.m. until 7 a.m. Samples of capillary blood were taken from the finger to measure the following parameters with the aid of appropriate electrodes by the direct method: true pH (pH_t), partial pressure of carbon dioxide (pCO_2), and partial pressure of oxygen (pO_2). The measurements were made on the OP-210/3 biological microanalyzer (Radelkis, Hungary). The metabolic pH (pH_{met}), the actual bicarbonate (AB), standard bicarbonate (SB), buffer bases (BB), base excess (BE), and degree of oxygenation of hemoglobin (HbO_2) were determined by Severinghaus' method, based on the Siggaard–Andersen linearized nomogram [7]. The blood hemoglobin concentration was measured by a photocolorimetric method [1]. The numerical results were subjected to statistical analysis by computer by the Student–Fisher method and the cosinor program [8], which revealed the parameters of the circadian rhythms at a 95% level of significance: mesors, mean levels for the 24-h period; calculated acrophases, peaks of the maximum relative to the beginning of the 24-h period (midnight); and amplitudes. To

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TABLE 1. Time Course of Parameters of Acid-Base Balance and Blood Gas Composition $(\bar{X} \pm S_{\bar{x}})$ during 24-h Period

Parameter	Clock time			
	3 a.m.	9 a.m.	3 p.m.	9 p.m.
pH_t	7,399±0,008	7,410±0,005	7,454±0,010	7,425±0,006
pH_{met}	7,397±0,011	7,372±0,010	7,405±0,012	7,391±0,011
AB (mmoles/liter)	23,8±0,76	21,7±0,75	23,4±0,83	22,8±0,85
SB (mmoles/liter)	24,6±0,66	23,2±0,58	25,3±0,77	24,2±0,69
BB (mmoles/liter)	46,1±0,89	44,0±0,79	46,8±1,00	45,5±0,93
BE (mmoles/liter)	—1,88±2,12	—2,47±1,10	—2,30±2,81	—2,11±2,07
pCO_2 (mm Hg)	41,0±1,29	35,6±1,05	34,4±0,60	36,0±1,02
pO_2 (mm Hg)	76,2±2,55	71,8±1,88	71,6±2,52	67,6±0,77
HbO_2, %	94,9±0,46	94,5±0,37	94,8±0,51	93,9±0,21
Hb	8,49±0,26	8,80±0,14	9,17±0,24	8,61±0,11

Note. Shift of buffer bases (BE) toward deficiency (—BE) or excess (+BE) shown by arithmetic mean values.

TABLE 2. Parameters of Circadian Rhythms of Values of Acid-Base Balance and Blood Gas Composition

Parameter	Parameter of rhythms		
	mesor $(\bar{X} \pm S_{\bar{x}})$	amplitude	acrophase
pH_t	7,422±0,008	0,026 (0,018—0,033)	16.05 (15.08—17.30)
pH_{met}	7,391±0,006	0,017 (0,010—0,024)	19.40 (16.54—22.39)
AB (mmoles/liter)	22,9±0,40	1,48 (0,80—2,22)	22.55 (21.06—02.37)
SB (mmoles/liter)	24,3±0,35	0,96 (0,60—1,30)	18.45 (16.28—21.11)
BB (mmoles/liter)	45,6±0,46	1,29 (0,80—1,80)	19.03 (16.38—21.27)
pCO_2 (mm Hg)	36,7±0,63	3,30 (2,60—4,10)	02.47 (01.14—04.06)
pO_2 (mm Hg)	71,8±1,10	2,56 (1,65—3,50)	04.39 (02.52—07.00)
HbO_2, %	94,5±0,20	0,69 (0,42—1,00)	08.07 (05.40—10.38)
Hb	8,76±0,10	0,29 (0,24—0,34)	14.16 (13.24—15.16)

Note. Mesors and amplitudes expressed in corresponding units of measurement, acrophases in hours before the full stop, minutes after the full stop; 95% confidence intervals shown between parentheses. Times here are expressed according to the 24-h clock.

assess correlation between individual parameters in the course of the 24-h cycle, coefficients of linear (parametric) correlation of temporal series and coefficients of nonparametric rank correlation (according to Spearman [4]) were calculated by computer.

RESULTS

Data on the circadian rhythm of the parameters of the acid-base balance and blood gas composition are given in Table 1. Parameters of the circadian rhythms are given in Table 2. The highest pH was observed at 3 p.m. (7.454), the lowest at 3 a.m. (7.399) ($P < 0.001$). The calculated acrophase of pH_t was 4:05 p.m. (3:08 p.m. to 5:30 p.m.). In parentheses, here and later in the text, 95% confidence intervals are given after values of the acrophases. This arrangement of the pH_t acrophase is evidence that the hydrogen ion concentration in the blood was low during the afternoon, and the acid-base balance was shifted toward alkalosis, which was most marked between 3:08 p.m. and 5:30 p.m. At night the hydrogen ion concentration, on the other hand, was high and the acid-base balance shifted toward acidosis.

Acrophases of pH_{met}, standard bicarbonate (SB) and buffer bases (BB) were approximately within the same time interval as the acrophase of pH_t, with a small shift toward later times (Table 2). The acrophase of actual bicarbonate (AB) was shifted to 10:55 p.m. (9:06 p.m. to 2:37 a.m.). All parameters of the acid-base state during the circadian cycle were synchronized and positive correlation existed between them. For example, coefficients of parametric and rank (in parentheses) correlation between pH_t and pH_{met}, AB, SB, and BB were 0.66 (0.61), 0.52 (0.49), 0.66 (0.59), and 0.67 (0.60) respectively.

The partial pressure of CO_2 in the blood was highest at night (at 3 a.,.) and exceeded the minimal level of pCO_2 by 19.1% at 3 p.m. ($p < 0.001$). The partial pressure of oxygen also was maximal at 3 a.m., when it was 12.7% higher (P 0.01) than the minimal value, observed at 9 p.m. (Table 1). The rise in pCO_2 at night was evidently due to reduction of ventilation of the lungs during sleep [5]. The rise of pO_2 can be linked with a decrease in O_2 uptake from the capillary blood by the tissue cells at night [2]. The increased ventilation of the lungs in the afternoon [5] and the increased oxygen uptake in the evening [2], on the other hand, lead to the fall in pCO_2 and pO_2 observed at this time. The acrophases of pCO_2 and pO_2 were synchronized (the internal acrophase between them was 1:52 a.m.), and they were out of phase with the acrophase of pH_t (Table 2). The internal acrophase between pCO_2 and pH_t was 10 h 42 min, and that between pO_2 and pH_t was 12 h 39 min. The arrangement of the acrophases of pCO_2 and pH_t suggests that the nocturnal fall and dirunal rise of pH are due to a relative excess of pO_2 in the blood at night compared with by day. Evidence of the presence of negative correlations between pCO_2 and pH during the 24-h cycle also was given by the coefficients of parametric (–0.47) and rank (–0.59) correlation.

Oxygenation of hemoglobin took place most intensively in the morning, and the acrophase of HbO_2 was 8:07 a.m. (5:40 to 10:38 a.m.). The concentration of hemoglobin, the main protein buffer of the blood, was highest in the afternoon: acrophase at 2:16 p.m. (1:24 p.m. to 3:16 p.m.) (Table 2). Very close position correlation was found between HbO_2 and pO_2 during the 24-h period: The coefficient of parametric correlation was 0.93 and of rank correlation 0.94. Less close but significant correlation between the time series for HbO_2 and hemoglobin was found: The coefficient of parametric correlation was 0.30 and of rank correlation 0.37.

All the parameters of acid-base balance and blood gas composition studied in this investigation thus undergo significant, rhythmic, and interconnected fluctuations during the 24-h cycle; they are integrated into a definite circadian temporal organization, knowledge of whose parameters is essential for an objective and accurate assessment of the results of experimental and clinical investigations.

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