Diurnal rhythms of plasma renin activity, atrial natriuretic peptide and arterial pressure during head-down bed rest in humans

Abstract The effects of prolonged head-down bed rest on the rhythms of several parameters (blood pressure, heart rate, haematocrit, plasma renin activity (PRA), atrial natriuretic peptide (ANP)) were assessed in six healthy men, aged 33 (SEM 2) years, who were submitted to bed rest for 28 days (D1-28). Systolic and diastolic blood pressure (BP_s and BP_d) and heart rate were measured at 0700 and 1900 hours; circulating PRA and ANP were determined from blood samples drawn at 0800, 1000, 1200, 1500, 1800 and 2200 hours before bed rest (D - 5), D1, 2, 7, 20, 27 during bed rest and post bed rest (D + 2). The BP_s was the lowest at 0700 hours and increased at 1900 hours. There was a significant difference between values during all the measurements. The BP_d and heart rate were lower at 0700 hours before and after bed rest and no significant difference appeared between these two values during the bed rest. The PRA and ANP concentrations were more stable during bed rest, and had not returned to original rhythmicity 2 days after bed rest. The mean daily concentration of ANP decreased during bed rest. It would seem from this study that changes occur in those rhythms during bed rest.

Key words Plasma renin activity · Atrial natriuretic peptide · Blood pressure · Heart rate

Introduction

Several studies have been devoted to a better understanding of cardiovascular adaptation to space flights (Leach et al. 1976). These studies have included haemodynamic and hormonal studies, but few investigations of rhythms can be found in the literature. However, the importance of changes in rhythms in true or simulated weightlessness has been underlined in some published works (Chavarri et al. 1977; Güell et al. 1983; Gharib et al. 1989). Several factors are probably involved in changes in circadian rhythms. Firstly, there is a reduction or an absence of gravity, an important environmental factor (see Fuller et al. 1989); secondly, space missions or bed-rest simulations have been conducted under conditions of confinement which may influence many psychological functions (Sandler 1982). The resulting instability of the circadian state will affect other physiological systems, circadian variations being a fundamental feature of many biological systems (sleep, endocrine and cardiovascular functions). No investigations of human circadian rhythms have been made during space operations. In bed-rest studies, changes in some circadian parameters (temperature, plasma cortisol and thyroxine, sodium and adrenaline excretion) have been observed (Vernikos-Danellis et al. 1972; Samel et al. 1993).

Since the early description of a circadian rhythm in plasma renin activity (PRA) in supine men which has been reported by Gordon et al. (1966), subsequent reports have generally confirmed that PRA varies diurnally in subjects receiving a normal Na⁺ diet, with peak secretion occurring during the early morning hours (Katz et al. 1975; Modlinger et al. 1976). Poirtaluppi et al. (1993) have found the existence of a causal relationship between the circadian rhythms of atrial natriuretic peptide (ANP) concentration and blood pressure. The existence of a circadian rhythm in ANP is still a matter of controversy. A diurnal variation in plasma ANP has been described in some studies (Poirtaluppi et al. 1993). Richards et al. (1987) have demonstrated that the significant changes observed reflect a subtle true intrinsic circadian rhythm. Follenius et al. (1992) have demonstrated the absence of an intrinsic
circadian rhythm in normal subjects. The present study was undertaken to examine.

1. The effect of continuous 28-day bed rest on the rhythms of circulating PRA and ANP
2. The changes in rhythmicity of systolic (BP_s) and diastolic blood pressure (BP_d) and heart rate during bed rest and
3. The relationship between the variation of arterial blood pressure and the rhythmicity of a humoral factor known to affect the cardiovascular system such as ANP.

**Methods**

Subjects

Six healthy normotensive men, with a mean age of 33.5 (SEM 2.2) years, mean height of 178 (SEM 0.9) cm and mean body mass of 77.6 (SEM 2.3) kg, who had passed a comprehensive medical examination, gave their informed consent to the experimental conditions after the details of the protocol were explained to them. This study was approved by an Ethics Committee (Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale Midi Pyrénées I Hôpital-Dieu Toulouse). Selection of the subjects was based on normal clinical investigation that comprised a detailed medical history, physical examination, general blood screening, and urine analyses. All the subjects were non-smokers, and none was taking medication at the time of the study.

Experiment procedure

The subjects remained in a special hospital unit (CHU Rangueil, Toulouse) for a total of 39 days, including 7 ambulatory control days when the subjects equilibrated to the standardized diet, 28 days of bed rest (D1-28), and 4 days of post-bed rest recovery. The volunteers were put on a controlled diet of 140 mmol Na^-1 and 70 mmol K^+^-1 throughout the study. The room temperature was maintained at 21°C-22°C and room lighting was on between 0700 and 2300 hours. No records were kept on sleep or day-time naps but the subjects declared that they slept approximately from 2300 to 0600 hours; day-time naps were restricted. Fluid intake was measured. Body mass was measured daily in the morning, before breakfast. Heart rate, BP_s, and BP_d were measured (Dynamap R 1846, SX/SXP, Critikon) twice daily (700 and 1900 hours). Lunch was at 1200 hours and dinner at 1900 hours immediately after the blood sampling. The experiments were conducted during November and December.

During the bed rest period, the subjects remained head-down (−6°) without interruption: all testing, showering, voiding and defaecation functions were done in the head-down position. They were allowed to use one pillow and to raise themselves on one elbow to eat.

Hormone studies

A catheter was inserted into an antecubital vein 1 h before the first blood sampling of the day. A 15-ml blood sample was drawn for each sampling (D − 5, D1, D2, D7, D20, D27 and D + 2) at 0800, 1000, 1200, 1500, 1800 and 2200 hours in heparin tubes. All tubes of blood were stored on ice until centrifugation (4°C, 10 min, 3000 rpm) and then plasma was frozen at −80°C. The measurements (D − 5, D + 2) were made after 1-h rest in a seated position, because we have demonstrated previously that the seated position is the best control for the head down position (Gharib et al. 1988).

Microhaematocrit was measured using heparin microhaematocrit tubes spun for 6 min at 11 500 rpm. We assayed the plasma ANP and PRA. The ANP (99–126) radio-immunooassay was made after extraction with octadecylsilyl cartridges (Sep-Pack) (Gauquelin and Gharib 1990). The antibodies were a gift of the Clinical Research Institute of Montreal. The intra- and interassay coefficients of variation were 6.8% and 16.8%, respectively. The PRA was measured with antibodies raised in the laboratory (pH 7.4, incubation 16 h), intra- and interassay coefficients of variation were 1% and 2.5%, respectively, and sensitivity was 20ng.l^-1.min^-1 (Vincent et al. 1972).

**Results**

BP_s, BP_d and heart rate

Fig. 1 shows that before, during and after bed rest, BP_s was lower at 700 hours [116.5 (SEM 0.5) mmHg] than at 1900 hours [125.7 (SEM 0.5) mmHg]. There was a significant difference (P < 0.05) between these two values during the whole study. The BP_d and heart rate were lower at 700 hours than at 1900 hours before and after bed rest (P < 0.05) and did not differ significantly during the bed-rest period. Bed rest caused greater tachycardia, accompanied by hypotension and syncopal symptoms. A significant increase (P < 0.05) in the difference between BP_s and BP_d occurred during bed rest.

Haematocrit

As shown in Fig. 2 during bed rest, we found a decrease in plasma volume (−11.2%) whereas the haematocrit (Hct) was increased. For Hct, no significant rhythmicity (P > 0.05) was observed throughout the bed-rest period because of large interindividual differences in the occurrence of the daily Hct peak.

PRA and ANP

Figures 3 and 4 show the PRA and the ANP rhythms at various time intervals during the study. A significant (P < 0.05) variation with minimal values occurring at 0800 hours for PRA and at 1200 hours for ANP was observed during the ambulatory prebed-rest control period. Analysis of variance demonstrated that the peak value was significantly different from all other times.