# Influence of posture on haemodynamics, sodium and hormonal homeostasis in cirrhotic patients with and without ascites

I. Colle[1], D. Schoors[2], H. Van Vlierberghe[1], G. Van Maele[3], M. De Vos[1], H. Reynaert[4]

(1) Department of Gastroenterology-Hepatology, University Hospital Ghent (UZ-Gent), Ghent, Belgium ; (2) Department of Cardiology, University Hospital Free University Brussels (AZ-VUB), Brussels, Belgium ; (3) Department of Medical statistics, University Hospital Ghent (UZ-Gent), Ghent, Belgium ; (4) Department of Gastroenterology-Hepatology, University Hospital Free University Brussels (AZ-VUB), Brussels, Belgium.

## Abstract

***Background / Aims :*** **Previous studies in preascitic cirrhosis demonstrated sodium retention during upright posture and sodium hyperexcretion during bed-rest. In patients with ascites, sodium excretion and creatinine clearance decreased during upright posture. Head-down tilting (HDT) accentuated the natriuretic effect of bed-rest in short term studies. The aim of this study was to evaluate the effects of prolonged change in posture on sodium homeostasis and on haemodynamics in cirrhotic patients.**

***Methods :*** **Eighteen cirrhotic patients (9 with, 9 without ascites), were studied during 12 h upright, supine and HDT position (-10°). During each position, 12 h urine collections were performed and blood samples were obtained before and after change in position. Non-invasive systemic hemodynamic measurements were performed.**

***Results :*** **There was no significant difference between HDT and supine position in both ascitic and preascitic groups for urinary volume, fractional sodium excretion, creatinine clearance, urinary and plasma hormones and hemodynamics. Urinary volume (in supine and HDT) and fractional sodium excretion (in supine) were significantly higher and urinary noradrenaline and plasma renin (in supine and HDT) significantly lower in the preascitic group compared with the ascitic patients. Cardiac output and heart rate decreased after 12 h supine and HDT, suggesting a deactivation of sympatic nervous system and catecholamines.**

***Conclusion :*** **Our results demonstrate that prolonged HDT had no advantage over normal bed-rest in both patient groups. Possibly, a short-term beneficial effect of HDT was lost after several hours.** (Acta gastroenterol. belg., **2003**, 66, **206-212**).

**Key words** : liver cirrhosis, ascites, preascitic, sodium excretion, posture, head-down-tilting, supine, hemodynamics, hormones.

## 1. Introduction

The clinical course of patients with cirrhosis is often complicated by the occurrence of ascites and peripheral oedema. Intrahepatic sinusoidal hypertension and a reduction of effective arterial blood volume, caused by peripheral arteriolar vasodilatation, presence of arteriovenous shunts, sequestration of blood in the splanchnic vascular system and portosystemic collaterals, are the main causes of sodium retention (1-4). In the preascitic stage, sodium and water retention are adequate to normalise effective plasma volume and to return renin-angiotensin-aldosterone system, noradrenaline and vasopressin to normal values, thus leading to normalisation of sodium and water excretion (1,2). With progression of liver disease, the increase in plasma volume becomes insufficient to maintain adequate circulatory homeostasis and continued renal sodium and water retention results in the formation of ascites (1-3,5).

In patients with preascitic cirrhosis, head-out water immersion, a manoeuvre that has been shown to redistribute extra-vascular fluid into the central intra-vascular compartment, caused exaggerated sodium excretion (6). In cirrhotic patients with ascites, head-out water immersion during 2 to 3 hours caused a marked natriuresis in some patients, but not in others (7,8).

Although less pronounced than head-out water immersion, altered posture also results in changes of central blood volume. The haemodynamic consequences of head-down-tilting (HDT) are very similar to those of head-out water immersion. In analogy with head-out water immersion studies, - 6° HDT further increased right atrial pressure by 135% (9), increased ANP (10), increased urinary volume, creatinine clearance and fractional excretion of sodium (FENa) (11) and decreased plasma renin (PR), plasma aldosterone (PA) and catecholamines during –10° HDT (9,12) as compared with supine position in normal subjects. These results suggest that head-out water immersion and HDT could have beneficial effects on haemodynamics and natriuresis as compared with supine position in cirrhotic patients. In cirrhotic patients, central blood volume decreased by 16% during sitting, whereas it increased by 8% during –12° head-down tilting as compared to recumbency (13). In addition, changes in sodium excretion occurred during changes in position. Moreover, in well compensated cirrhotics, standing induced an aldosterone-dependent sodium retention and prolonged bed-rest (24 h) caused hypernatriuresis through enhanced atrial natriuretic peptide (ANP) release as well as plasma aldosterone suppression (14,15). Excessive central redistribution of an expanded blood volume resulting in changes in ANP, plasma renin (PR) and circulating catecholamines is probably the explanation for this phenomenon (16).

In cirrhotic patients with ascites, sitting induced not only sodium retention, but also decreased renal function and increased plasma aldosterone, renin and noradrena-

Correspondence address : Dr. Isabelle Colle, Dept. Hepato-Gastroenterology, University Hospital Ghent 1K12 IE, De Pintelaan 185, 9000 Gent, Belgium. E-mail : Isabelle.Colle@rug.ac.be.

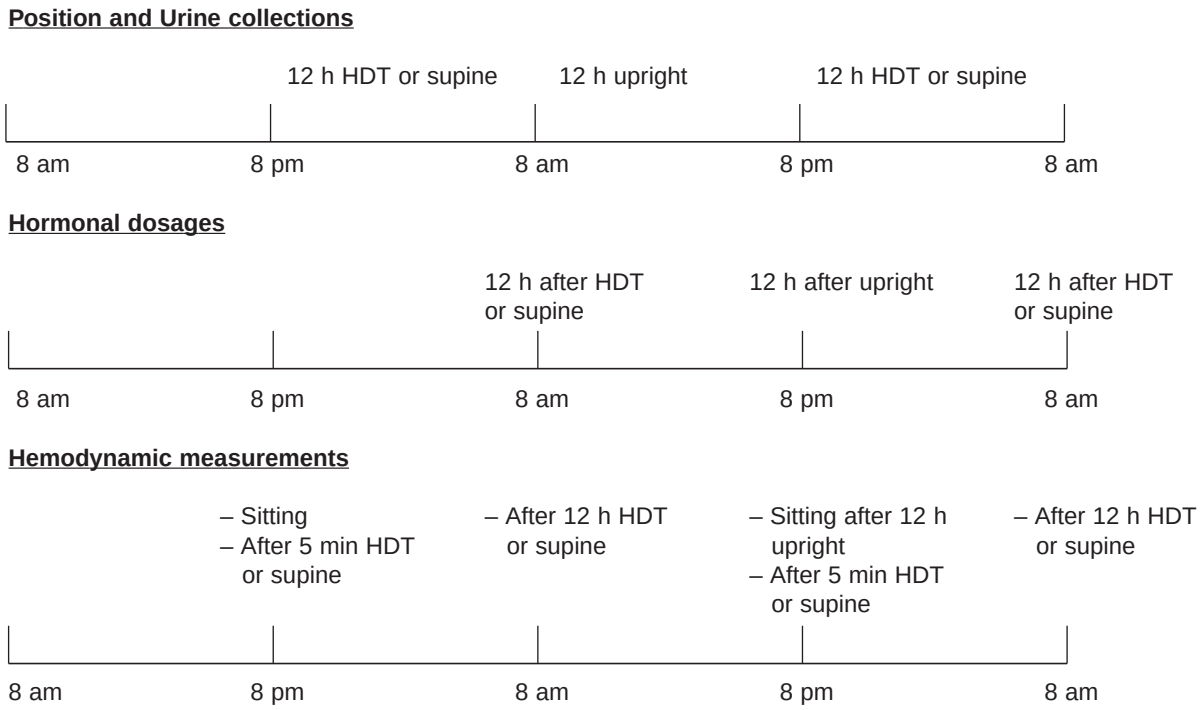


Fig. 1. — Design of the study

line levels (17). A 2 h recumbency did however, not significantly increase sodium excretion in these patients (18).

Sodium excretion was more pronounced during 2 h HDT than during recumbency and upright posture in both normal controls and patients with fluid retention (11,19). As compared with recumbency, HDT caused a significant increase of central venous blood volume, central venous pressure and atrial natriuretic factor in normal subjects and in patients with cirrhosis, whereas PR, PA and circulating catecholamines significantly decreased (13). One could therefore expect that HDT induces a more pronounced increase of sodium excretion than normal bed-rest in cirrhotic patients (11).

Taken together, several lines of evidence indicate that changes in posture may decrease sodium and water retention through a central redistribution of the expanded blood volume, resulting in downregulation of the renin-angiotensin-aldosterone system and adrenergic system and increased ANP levels.

The aim of this study was to evaluate the effects of prolonged (12 h) bed-rest as compared with –10° HDT, on sodium excretion in cirrhotic patients with and without ascites. Furthermore, the effects of posture on systemic hemodynamics and on hormones involved in sodium homeostasis were examined.

## 2. Patients and methods

### 2.1. *Patients*

Eighteen patients with liver cirrhosis were studied. Nine patients (7 males and 2 females) had tense ascites : their age ranged from 38 to 79 years (mean 56 years) ; 6 patients had alcoholic and 3 had postnecrotic cirrhosis. According to the Child-Pugh (20) classification, 2 of them were class B and 7 class C. Nine patients (4 males and 5 females) had no ascites : their age ranged from 38 to 66 years (mean 53 years) ; 8 patients had alcoholic and 1 had postnecrotic cirrhosis. Four patients were classified as Child-Pugh class A, 3 as Child-Pugh class B and 2 as Child-Pugh class C. Patients with ascites had a significantly higher Child-Pugh score (10.6 ± 1.5 versus 7.4 ± 1.7 ; $P = 0.002$) than patients without ascites.

All patients had biopsy-proven cirrhosis. The presence or absence of ascites was confirmed by ultrasound. Patients with compensated cirrhosis, never had ascites before. Patients with a recent (< 6 weeks) overt gastrointestinal bleeding, malignancy, heart failure or cardiomyopathy, arterial hypertension, diabetes, renal insufficiency, neuropathy or acute hepatitis were not included in the study. Patients in whom recently a large volume paracentesis was performed were also excluded. Diuretics, ACE-inhibitors, beta-blockers, non-steroidal anti-inflammatory drugs or corticosteroids were withdrawn at least one week prior to the start of the study. The study protocol was designed and performed according to the principles of the Declaration of Helsinki, and informed consent was obtained from each patient.

### 2.2. *Study protocol* (Fig. 1)

All subjects included in the study were admitted in the hospital and received a controlled 52 mmol sodium diet which was initiated three days before the start of the study. All subjects were randomised by stratification to be either first in supine or -10° HDT position from 8 p.m. till 8 a.m. Patients were not allowed to leave their

bed. At 8 a.m. the patients adopted the upright position (standing, sitting and walking but no recumbency) till 8 p.m. At 8 p.m. the second day, all patients remained in bed in the other position than the previous night (supine or HDT) (Fig. 1).

At 8 p.m., 8 a.m. and 8 p.m., 12 h urine collections for volume, sodium, creatinine, noradrenaline and adrenaline were started. Blood samples for creatinine, plasma aldosterone (PA), plasma renin (PR) and Atrial natriuretic peptide (ANP) were obtained before and after each urine collection (Fig. 1).

Haemodynamic measurements were made at 8 p.m., 8 a.m., 8 p.m. and 8 a.m. (Fig. 1). A non-invasive cardiac output monitor (Bomed, Hegelbach Medical, Brussels, Belgium) based on changes in bioimpedance was installed, by placing 8 electrodes in a frontal plane, as described earlier (21,22). The electrodes for each measurement were positioned identically in each patient, to minimize inaccuracy, as a 1cm difference in localisation of the electrode can result in a 10% change in stroke volume. The distance between the inner electrodes is obtained from a manufacturer-supplied nomogram based on sex, height and weight. In ascitic patients, the distance between the inner electrodes is probably overestimated. Heart rate (beats per minute, bpm) and cardiac output (CO, l/min) were measured. Cardiac index (CI) was calculated by the formula : CI (l/min.m$^2$) = CO / BSA (body surface area). Blood pressure was measured by a standard mercury sphygmomanometer. The mean arterial blood pressure (MAP) was calculated by the formula : MAP (mmHg) = [2 × diastolic blood pressure + systolic blood pressure] / 3.

### 2.3. *Determinations*

Urinary parameters

Urine was collected for 12 h in a polyethylene container containing 20 ml of 6 mmol HCl. Urinary sodium levels were determined by flame photometry (IL 943, Instrumentation laboratory SpA, Milano, Italy) and expressed as urinary sodium / urinary creatinine ratio. Urinary creatinine was assayed by the kinetic Jaffé method on a RA-1000 autoanalyser (Technicon, New York, NY, USA). Creatinine clearance was calculated by the formula : [urinary volume × urinary creatinine] / [plasma creatinine]. Fractional excretion of sodium (FENa) was defined as [urinary sodium × plasma creatinine × 100%] divided by [plasma sodium × urinary creatinine]. Urinary noradrenaline and adrenaline were measured as described earlier (23).

Blood parameters

Blood samples for sodium and creatinine were obtained in 5 ml tubes with heparin and automatically processed by a Kodak Ektechem XR 700 (Clinical products division, Kodak Co, Rochester, NY, USA). Blood samples for PA and PR were collected in EDTA-tubes and rapidly centrifuged at room temperature. Samples were stored at -20°C for a maximum of 8 weeks. Plasma aldosterone was assayed with a RIA-kit made by the RIA-lab of the Hospital of the Free University of Brussels. The sensitivity of this assay is 2 ng/l, the inter-assay coefficient of variation is < 13% and normal values are 12-125 ng/l after rest and 70-295 ng/l after activity. Active renin was measured with a commercially available radio immunoassay (RIA)-kit (Renin Active Pasteur CT 79970, ERIA Diagnostics Pasteur, Marnes la Coquette, France). The sensitivity of this assay is 1.5 ng/l, the inter-assay coefficient of variation is < 13.9%, the intra-assay coefficient is < 6.5% and the normal values are 10-30 ng/l after rest and 10-65 ng/l after activity. Blood samples for ANP were collected in EDTA-tubes on crushed ice, rapidly centrifuged in a cooled centrifuge and stored at a temperature of -80°C for a maximum of 8 weeks. A commercially available RIA-kit was used to determine ANP (Nichols-Institute, Diagnostics BV, Wijchen, The Netherlands). The sensitivity of this assay is 11 ng/l, the inter-assay variate coefficient is < 5.5%, the intra-assay coefficient is < 7.7% and the normal values are 25-111 ng/l. Blood samples for ADH were collected in EDTA-tubes on crushed ice, rapidly centrifuged in a cooled centrifuge and stored at a temperature of -80°C for a maximum of 8 weeks. A commercially available RIA-kit was used to determine ADH (Incstar Corporation, Stillwater, Minnesota, USA). The sensitivity of this assay is 2.5 ng/l, the inter-assay variation coefficient is < 11%, the intra-assay coefficient is < 5% and the normal values are 0-2 ng/l if the plasma osmolality is under 285 mosmol/kg $H_2O$ and between 2-12 ng/l if the plasma osmolality is above 285 mosmol/kg $H_2O$.

Statistical analysis

Results are expressed as mean ± standard deviation (SD). To evaluate statistical significance of differences within groups, the Wilcoxon matched-pairs signed-rank test was used. Differences observed between groups were analysed using the Mann-Whitney U-test. *P* values < 0.05 are considered to be statistically significant.

As results of upright position during the day can not be compared with HDT or supine during the night because of day-night rhythm variations (fluid intake is different during day and night, sympathic nervous system is more activated during day than during night, whereas parasympathic nervous system overwhelms at night), we compared only HDT versus supine position both performed during the night. For the haemodynamic results, we compared also upright position just before lying down with HDT and supine after 12 h.

## 3. Results

### *3.1. Side effects*

No side effects were observed during the study and all patients tolerated the procedure well.

Table 1. — **Posture dependent changes in hemodynamic parameters in patients without and with ascites. Wilcoxon rank-test (P < 0.05) for upright versus supine 12 h, upright versus head-down tilting (hdt)12 h and supine 12 h versus hdt 12 h**

| | Upright versus supine | P-value | Upright versus hdt | P-value | Supine versus hdt | P-value |
|---|---|---|---|---|---|---|
| Cardiac index (l/min/m²) | | | | | | |
| No ascites | 4.20 ± 1.64 vs 3.26 ± 0.98 | **0.01** | 4.20 ± 1.64 vs 3.33 ± 1.27 | **0.007** | 3.26 ± 0.98 vs 3.33 ± 1.27 | 0.78 |
| Ascites | 5.91 ± 3.33 vs 4.43 ± 1.83 | **0.02** | 5.91 ± 3.33 vs 4.61 ± 1.92 | **0.03** | 4.43 ± 1.83 vs 4.61 ± 1.92 | 0.37 |
| Mean arterial pressure (mmHg) | | | | | | |
| No ascites | 100 ± 12 vs 94 ± 13 | **0.03** | 100 ± 12 vs 95 ± 17 | 0.09 | 94 ± 13 vs 95 ± 17 | 0.91 |
| Ascites | 92 ± 13 vs 88 ± 10 | 0.17 | 92 ± 13 vs 88 ± 9 | 0.44 | 88 ± 10 vs 88 ± 9 | 0.74 |
| Heart rate (bpm) | | | | | | |
| No ascites | 88 ± 18 vs 78 ± 14 | **0.02** | 88 ± 18 vs 79 ± 14 | **0.02** | 78 ± 14 vs 79 ± 14 | 0.73 |
| Ascites | 97 ± 12 vs 84 ± 9 | **0.01** | 97 ± 12 vs 88 ± 11 | **0.008** | 84 ± 9 vs 88 ± 11 | 0.08 |

Table 2. — **Results (mean ± SD) of 12 h urine collections in 9 patients without and 9 patients with ascites during upright posture, supine and head-down tilting (HDT) position**
**Urinary volume (ml/gram urinary creatinine), Urinary noradrenaline excretion (mg/gram urinary creatinine), Urinary adrenaline excretion (mg/gram urinary creatinine)**
**Significance between the non-ascites and ascites group is given when P < 0.05 (Mann-Whitney U-test)**

| | No ascites | Ascites | P |
|---|---|---|---|
| Urinary Volume (ml/g cr) | | | |
| Upright | 970 ± 347 | 739 ± 396 | 0.24 |
| Supine | 2323 ± 716 | 1064 ± 695 | **0.002** |
| HDT | 2179 ± 1117 | 1242 ±635 | **0.05** |
| Creatine Clearance (ml/min) | | | |
| Upright | 88 ± 47 | 54 ± 36 | 0.17 |
| Supine | 77 ± 26 | 106 ± 104 | 0.93 |
| HDT | 85 ± 55 | 80 ± 83 | 0.49 |
| Fractional sodium excretion (%) | | | |
| Upright | 0.11 ± 0.13 | 0.17 ± 0.23 | 0.48 |
| Supine | 0.39 ± 0.31 | 0.17 ± 0.20 | **0.05** |
| HDT | 0.30 ± 0.17 | 0.22 ± 0.26 | 0.19 |
| Urinary noradrenaline (µg/g cr) | | | |
| Upright | 54 ± 34 | 82 ± 37 | 0.07 |
| Supine | 35 ± 24 | 60 ± 23 | **0.04** |
| HDT | 41 ± 41 | 76 ± 35 | **0.03** |
| Urinary adrenaline (µg/g cr) | | | |
| Upright | 9.9 ± 7.4 | 12.8 ± 6.8 | 0.38 |
| Supine | 5.0 ± 2.9 | 10.0 ± 6.8 | 0.06 |
| HDT | 6.1 ± 5.2 | 8.7 ± 5.8 | 0.34 |

### 3.2. *Comparison of Supine versus HDT position*

#### 3.2.1. Haemodynamic parameters (Table 1) :

In this study, CI, MAP and HR were not different between HDT and supine position in both preascitic and ascitic patients.

In patients without ascites, CI and HR decreased significantly after supine and after HDT as compared with the standing position (4.20 ± 1.64 l/min/m² and 88 ± 18 bpm, respectively). Moreover, a significant decrease in MAP was found after supine position, but not after HDT.

In patients with ascites, CI and heart rate decreased significantly after supine and after HDT as compared with the upright position. No significant change in MAP between the 3 positions was found in the ascites group.

#### 3.2.2. Urinary analysis (Table 2) :

In both the preascitic and ascitic group, urinary volume, creatinine clearance, FENa, urinary noradrenaline and adrenaline were not different between HDT and supine position.

#### 3.2.3. Plasma hormones (Table 3) :

No statistical difference was observed for PR, PA, ADH, ANP and ANP/PA between HDT and supine position in both patient groups.

### 3.3. *Differences between patients with and without ascites*

#### 3.3.1. Haemodynamic parameters (Table 1) :

Heart rate, MAP and CI were not significantly different between patients with and without ascites. However, a trend towards a higher CI and HR and a lower MAP was observed in the ascites group compared with the preascitic groups in the 3 positions.

#### 3.3.2. Urinary analysis (Table 2)

In upright posture, we did not find significant differences in urinary volume, creatinine clearance, FENa, urinary noradrenaline and adrenaline excretion between patients with and without ascites.

Table 3. — **Results (mean ± SD) of neurohumoral parameters in cirrhotic patients without and with ascites after 12 hours of upright posture, 12 hours in supine position and 12 hours in head-down tilting (HDT) position Significance between the non-ascites and ascites group is given when P < 0.05 (Mann-Whitney U-test)**

| | No ascites | Ascites | P |
|---|---|---|---|
| Plasma Renin Activity (ng/l) | | | |
| After upright posture | 106.0 ± 230.9 | 300.9 ± 401.9 | **0.02** |
| After supine posture | 47.9 ± 113.5 | 131.5 ± 181.5 | **0.006** |
| After HDT | 65.8 ± 173.4 | 126.9 ± 173.6 | **0.006** |
| Plasma Aldosterone (ng/l) | | | |
| After upright posture | 414.9 ± 653.6 | 628.8 ± 527.4 | 0.32 |
| After supine posture | 229.8 ± 426.8 | 324.2 ± 270.8 | 0.09 |
| After HDT | 235.7 ± 470.8 | 320.8 ± 260.0 | **0.03** |
| Antidiuretic hormone (ng/l) | | | |
| After upright posture | 0.95 ± 0.29 | 1.01 ± 0.47 | 0.96 |
| After supine posture | 0.86 ± 0.24 | 1.11 ± 0.78 | 1 |
| After HDT | 0.78 ± 0.19 | 0.89 ± 0.27 | 0.61 |
| Atrial natriuretic peptide (ng/l) | | | |
| After upright posture | 179.1 ± 75.9 | 252.0 ± 118.3 | 0.17 |
| After supine posture | 210.9 ± 91.9 | 266.6 ± 138.5 | 0.43 |
| After HDT | 214.8 ± 107.5 | 292.8 ± 155.2 | 0.28 |
| ANP/aldosterone | | | |
| After upright posture | 1.2 ± 1.3 | 1.8 ± 3.1 | 0.53 |
| After supine posture | 2.4 ± 1.6 | 1.7 ± 2.0 | 0.23 |
| After HDT | 3.2 ± 2.6 | 1.8 ± 2.3 | 0.27 |

The ascitic group had a lower increase in urinary volume as compared with the non-ascitic group (after supine 1064 ± 695 vs. 2323 ± 716 ml/g cr ; $P = 0.002$ and after HDT 1242 ± 635 versus 2179 ± 1117 ml/g cr ; $P = 0.05$). The patients with ascites had a lower increase in FENa as compared with the patients without ascites (after supine 0.17 ± 0.23% versus 0.39 ± 0.31% ; $P = 0.05$). The ascitic group had also a significantly lower decrease in urinary noradrenaline (after supine 60 ± 23 versus 35 ± 24 µg/g cr ; $P = 0.04$ and after HDT 76 ± 35 versus 41 ± 41 µg/g cr ; $P = 0.03$) as compared with the non-ascitic group.

3.3.3. Plasma hormones (Table 3) :

Plasma renin was higher in the ascitic group compared with the non-ascitic group in the 3 positions. PA, ADH and ANP tended to be higher and ANP/PA tended to be lower in the ascites group compared with the non-ascites group in the 3 positions.

## 4. Discussion

The present study is the first in which prolonged (12 h) – 10° HDT is compared with supine position (12 h) in patients with cirrhosis. To our knowledge only one short-term study (10 minutes in HDT) of 4 cirrhotic patients was performed by Henriksen *et al.*, and showed an increase in central blood volume of 8% (13). One preliminary study, presented in abstract form in 8 cirrhotic patients with ascites showed a significant increase in urinary volume and FENa and a decrease in PR and PA after 12 h HDT as compared with supine position (19).

In contrast to the short-term studies, we did not observe any significant differences for urinary sodium and volume excretion, PR, PA, ANP and haemodynamics between prolonged HDT and supine in both ascitic and preascitic patients. A possible explanation for this discrepancy is that differences only occur shortly after change in posture and that the effects diminish after prolonged posture. One could expect that HDT induces larger changes in effective central blood volume as compared with supine position, especially in patients with ascites in whom total blood volume is higher than in non-ascitic patients. However, we could not observe this after prolonged tilting. Urinary collections and blood samples were performed for 12 h in our study. It is possible that FENa, haemodynamic changes and the effects on hormones were more pronounced during the first hours after HDT, but became less important later on because of the attenuating effects of acute posture change after several hours. This has been shown in the study of Maillet *et al.* (24) in normal subjects during 37.5 h in – 6° HDT. Plasma volume increased maximal after 6.5 h and returned to pre-study levels after 13.5 h (24). From 1.5 h to 4 h of HDT, ANP concentration increased with 50% and thereafter declined to pre-HDT levels (24). Furthermore, PR decreased maximally after 4 h (24). Noradrenaline decreased immediately and remained low during 37.5 h in these normal subjects (24). Initial hormone changes (ANP and PR) during HDT did not last more than 13 h and after 24 h a new steady state seemed to have been established to adopt the body to hypovolemia in normal subjects (24). Further studies with fractional urine analysis and frequent blood analysis shortly after posture change are needed to clarify this problem.

In addition, in ascitic patients, especially those with tense ascites, compression of the inferior caval vein by ascites may be present, thereby preventing the expected increase in central blood volume and thus counteracting the beneficial effect of HDT. Another explanation could

be that –10° HDT is not enough to induce significant changes compared with the supine position. However, -10° HDT was shown to induce haemodynamic changes comparable with head-out water immersion in normal persons (9,11).

In accordance with the study of Hartleb *et al.* (25), CO and heart rate decreased significantly after 12 h in supine and HDT position in both ascitic and non-ascitic groups as compared with the upright position. No significant changes in MAP were observed in our study.

Previous reports of haemodynamic measurements during 2 h after supine position have been controversial. Bernardi *et al.* (16), found an increase in CI whereas Lollgen *et al.* (9) did not find any difference in CO when measured every 15 min during 2 h after supine position. Iowa *et al.*, found an increase in CI and ANP 30 and 60 minutes after adopting supine position (26). PR, PA and noradrenaline are markers for arterial volemia whereas ANP is a marker for atrial filling. In our patients, a decrease in PR, PA and urinary noradrenaline were observed after supine position and HDT, suggesting that the central blood volume was increased in these positions, probably early after changing in posture. As the sympathetic nervous systems and renin-angiotensin-aldosterone systems (RAAS) are downregulated when central blood volume is normal or increased, this has a negative inotropic and chronotropic effect after several hours, resulting in a decreased CI and heart rate after 12 h in supine or HDT position. Most probably, an increase in central blood volume early after recumbency and HDT deactivates the sympathetic nervous system and vasoconstrictory systems.

There was no significant difference between patients with and without ascites for haemodynamic measurements. Despite a significant difference in Child-Pugh score however, CI and HR tended to be higher and MAP tended to be lower in the ascitic group. Because excessive body water and an inaccurate assesment of the inner distance between the electrodes may play a role, the use of the non-invasive cardiac output monitor is not so accurate as thermodilution monitoring, especially for comparing 2 patients groups. However, the non-invasive cardiac output monitor is a reliable tool for repetitive measurements in the same patient.

There was a significantly lower increase in urinary volume (supine and HDT) and FENa (supine) and a lower decrease in urinary noradrenaline (supine, HDT), PRA (3 positions) and PA (HDT) in the ascitic group compared with the non-ascitic group. It is well known from the literature (27), that patients with ascites have a more important activation of the RAAS and catecholamine systems than patients in the preascitic phase. This results in a more important renal vasoconstriction and an increase in sodium and water retention. In those patients with ascites, head-out-water-immersion and supine position, which induce an increase in central blood volume, not always result in an increase in sodium excretion (7,8,18).

It is important to underline that these differences in urinary parameters and vasoconstrictory hormones between ascitic and non-ascitic patients were more pronounced in HDT and supine position than in upright posture. Thus, patients without ascites are capable to normalise more or less their vasoconstrictory hormones and urinary parameters in supine and HDT position, while patients with ascites can not.

In conclusion, this study showed that prolonged HDT had no superior effect on natriuresis, diuresis and vasoconstrictory hormonal systems compared with prolonged supine position in both ascitic and non-ascitic patients. The short term beneficial effects of HDT may only be present the first few hours after posture change. Diuresis and natriuresis in pre-ascitic patients were significantly higher in supine position, compared with ascitic patients and this was associated with lower urinary noradrenaline levels and plasma renin activity. Cardiac index and heart rate decreased after 12 h supine and HDT, suggesting a downregulation of RAAS and catecholamine system, probably secondary to an increase in central blood volume early after change in posture.

## References


1. LEVY M. Pathogenesis of sodium retention in early cirrhosis of the liver : evidence for vascular overfilling. *Sem. Liver Dis.*, 1994, **14** : 4-13.
2. SCHRIER R.W., NIEDERBERGER M., WEIGERT A., GINES P. Peripheral arterial vasodilation : determinant of functional spectrum of cirrhosis. *Sem. Liver Dis.*, 1994, **14** : 14-22.
3. ALBILLOS A., COLOMBATO L.A., GROSZMANN R.J. Vasodilatation and sodium retention in prehepatic portal hypertension. *Gastroenterology*, 1992, **102** : 931-935.
4. LEVY M. Sodium retention and ascites formation in dogs with experimental portal cirrhosis. *Am. J. Physiol.*, 1977, **233** : F572-585.
5. JIMENEZ W., ARROYO V. Pathogenesis of sodium retention in cirrhosis. *J. Hepatol.*, 1993, **18** : 147-150.
6. CAMPBELL P.J., LEUNG W.M., LOGAN A.G., DEBOWSKI T.E., BLENDIS L.M., SKORECKI K.L. Hyperresponsiveness to water immersion in sodium retaining cirrhotics : the role of atrial natriuretic factor. *Clin. Invest. Med*., 1988, **11** : 392-395.
7. SKORECKI K.L., LEUNG W.M., CAMPBELL P., WARNER L.C., WONG P.Y., BULL S. *et al.* Role of atrial natriuretic peptide in the natriuretic response to central volume expansion induced by head-out water immersion in sodium-retaining cirrhotic subjects. *Am. J. Med.*, 1988, **85** : 375-382.
8. EPSTEIN M., LOUTZENHISER R., NORSK P., ATLAS S. Relationship between plasma ANF responsiveness and renal sodium handling in cirrhotic humans. *Am. J. Nephrol.*, 1989, **9** : 133-143.
9. LÖLLGEN H., GEBHARDT V., BEIER J. *et al.* Central hemodynamics during zero gravity simulated by head-down bedrest. *Aviat. Space Environ. Med.*, 1984, **55** : 887-892.
10. FRANCO-SAENZ R., HARPER D., MULROW P. Effect of posture on the plasma level of atrial natriuretic factor. *Clin. and Exper. Hyper. Theory and Practice*, 1989, **A11** : 337-347.
11. KARNAD D.R., ABRAHAM P., TEMBULKAR P., DESAI N.K. Head-down tilt as a physiological diuretic in normal controls and in patients with fluid-retaining states. *Lancet*, 1987, **ii** : 525-528.
12. LONDON G.M., LEVENSON J.A., SAFAR M.E., SIMON A.C., GUERIN A.P., PAYEN D. Hemodynamic effects of head-down tilt in normal subjects and sustained hypertensive patients. *Am. J. Physiol.*, 1983, **245** : H194-H202.
13. HENDRIKSEN J.H., BENDTSEN F., SORENSEN T.I., STADEAGER C., RING-LARSEN H. Reduced central blood volume in cirrhosis. *Gastroenterology*, 1989, **97** : 1506-1513.

14. TREVISANI F., BERNARDI M., GARBARRINI G. *et al.* Bed-rest-induced hypernatriuresis in cirrhotic patients without ascites : does it contribute to maintain "compensation". *J. Hepatol.*, 1992, **16** : 190-196.
15. BERNARDI M., DI MARCO C., TREVISANI F. *et al.* Renal sodium retention during upright posture in preascitic cirrhosis. *Gastroenterology*, 1993, **105** : 188-193.
16. BERNARDI M., DI MARCO C., TREVISANI F. *et al.* The hemodynamic status of preascitic cirrhosis : an evaluation under steady-state conditions and after postural change. *Hepatology*, 1992, **16** : 341-346.
17. BERNARDI M., SANTINI C., TREVISANI F., BARALDINI M., LIGABUE A., GARBARRINI G. Renal function impairment induced by change in posture in patients with cirrhosis and ascites. *Gut*, 1985, **26** : 629-635.
18. BERNARDI M., FORNALE L., DI MARCO C. *et al.* Impaired supine-induced natriuresis in cirrhosis with ascites : role of hemodynamic and hormonal factors. *J. Hepatol.*, 1992, **16** (suppl 1) : S17-S18.
19. DEBEUCKELAERE S., REYNAERT H., DEVIS G., SCHOORS D. Head-down tilt induced hypernatriuresis in cirrhotic patients with ascites (Abstract). *J. Hepatol.*, 1992, **16** (suppl 1) : S30.
20. PUGH R.N.H., MURRAY-LYON I.M., DOWSON J.L., PIETRONI M.C., WILLIAM J.L. Transsection of the oesophagus for bleeding oesophageal varices. *Br. J. Surg.*, 1973, **60** : 646-649.
21. SRAMEK B.B. Comparison of thermodilution and transthoracic electrical bioimpedance cardiac outputs. *Heart Lung*, 1992, **21** : 98-99.
22. BARIN E., HARYADI D., SCHOOKIN S. *et al.* Evaluation of a thoracic bioimpedance cardiac output monitor during cardiac catheterization. *Crit. Care Med.*, 2000, **28** : 698-702.
23. GERLO E., MALFAIT R. High performance liquid chromatographic assay of free norepinephrine, epinephrine, dopamine, vanillyl mandelic acid and homovallinic acid. *J. Chromat.*, 1985, **343** : 9-20.
24. MAILLET A., PAVY-LE TRAON A., ALLEVARD A.M. *et al.* Hormone changes induced by 37.5-h head-down tilt (-6 degrees) in humans. *Eur. J. Appl. Physiol*., 1994, **68** : 497-503.
25. HARTLEB M., RUDZKI K., KARPEL E. *et al.* Cardiovascular status after postural change in compensated cirrhosis : an argument for vasodilatory concept. *Liver*, 1997, **17** : 1-6.
26. IWAO T., TOYONAGA A., SATO M. *et al.* Effect of posture-induced blood volume expansion on systemic and regional hemodynamics in patients with cirrhosis. *J. Hepatol.*, 1997, **27** : 484-491.
27. ARROYO V., JIMENEZ W. Complications of cirrhosis. II. Renal and circulatory dysfunction. Lights and shadows in an important clinical problem. *J. Hepatol.*, 2000, **32** (suppl 1) : 157-170.