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ORIGINAL ARTICLE

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Intermittent negative pressure ventilation may increase urine flow in normal subjects

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In order to analyze the effect of intermittent negative pressure ventilation (NPV) on renal function, we studied 20 healthy male volunteers (mean age 29±4.1 years). NPV was performed with an "Emerson Chest Respirator Pump", adjusted to a breathing frequency of 10 respirations per minute, with inspiratory time/total respiratory time ratio of 0.4 and negative pressure of 25 cmH_2O. The experimental protocol was carried out in two phases of two hours each - spontaneous breathing and NPV breathing. At the end of each phase, urine volume of the whole period was collected as well as venous blood sample for biochemical determinations. During NPV there was significant increase ($P<0.05$) in urine flow rate (1.43±0.81 to 2.76±1.95 ml/min) as well as in natriuresis (258±201 to 389±175 mcEq/min), kaliuresis (61±45 to 98±49 mcEq/min), fractional sodium excretion (1.38±0.88 to 1.96±0.98%), osmolar clearance (3.13±1.82 to 4.32±1.24 ml/min) and pH (7.37± 0.04 to 7.41±0.07) with unchanged creatinine and free water clearances. We concluded that NPV increases urine flow rate, kaliuresis and natriuresis but the data we have do not allow us to explain the mechanisms underlying such a phenomenon.

UNITERMS: Antidiuretic hormone (ADH), atrial natriuretic factor (ANF),negative pressure ventilation (NPV), positive end expiratory pressure (PEEP).

Changes in pleural pressure have long been associated to changes in renal function (11,15). The ventilation of dogs with continuous positive end expiratory pressure (PEEP) leads to a reduction in urine flow with high plasma level of anti-diuretic hormone (ADH) (5,10) whereas the use of PEEP in humans in acute respiratory failure may induce a siginicant reduction of diuresis and natriuresis with a fall in plasma atrial natriuretic factor (ANF) (2).

Increased diuresis in response to continuous negative pressure ventilation has been described in anesthetized dogs (8) but its action in humans has been somewhat controversial: while Sieker et al. (14) have shown an increased diuresis Andoh et al. (3) showed no effect at all.

On the other hand, the use of negative pressure ventilation in humans has been performed more commonly with the intermittent procedure (7).

The purpose of this investigation was to evaluate the renal function of normal subjects on ventilation with poncho intermittent negative pressure ventilation, that is, using a sealed suit from neck to waist.

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MATERIAL AND METHODS

We studied 20 health males, aged 29.0±4.1 years (mean±SD) weighing 75.0±9.6 kg and 177±6.8 cm tall.

The study was approved by the Institutional Committee on Human Research and informed consent was obtained from all individuals.

The subjects were studied in supine position during two hours of intermittent negative pressure ventilation and in a similar period of spontaneous breathing. Half of the individuals started the experiment with NPV. Subjects were asked to completely empty their urine bladder before starting the study. At this time, venous blood and urine samples were collected for the following measurements: osmolarity, sodium, potassium, chloride, creatinine and blood pH, carbon dioxide partial pressure ($PvCO_2$), bicarbonate (HCO_3). After each period of study, blood samples and the total urine volume were collected in order to determine urine flow rate, creatinine, osmolar and free water clearances, and sodium and potassium excretions. Fractional sodium excretion was calculated.

Statistical analysis: the non parametric Wilcoxon Test that allows paired test analysis was used. A value of P smaller than 0.05 was considered significant.

RESULTS

The mean values of all parameters are expressed on Tables 1 and 2.

The urine flow rate increased by 96% ($P<0.05$) during the NPV period. Sixteen of the subjects showed an increase of urine volume of at least 20%, while there was no change in 3 and reduction in 1 patient.

There was a mean percent increase of 50.7% in natriuresis ($P<0.05$) and of 60.7% in kaliuresis ($P<0.05$). All but 1 of the 16 subjects who increased the urine flow rate had also an enhancement of urine sodium and potassium (Table 1). When NPV was added, an increase in osmolar clearance from 3.13 to 4.32 ml/min ($P<0.05$) and in fractional sodium excretion from 1.38% to 1.96% ($P<0.05$) was observed (Table 2).

Plasma sodium and potassium as well as plasma and urinary osmolarity were unchanged during NPV breathing. There was a slight but significant increase in venous pH during NPV breathing associated with a small but not significant decrease in $PvCO_2$ and associated with an unchanged HCO^-_3 (Table 1).

The creatinine and free water clearances did not vary throughout the study: 113.8 vs 129.2 ml/min and -1.73 vs -1.60 ml/min, respectively (Table 2).

Table 1

Urine and plasma data (means± s.d.) obtained in 20 normal subjects during negative pressure ventilation (NPV) and spontaneous breathing (SB)

	SB	NPV
Urine flow (ml/min)	1.42 ± 0.81	2.76 ± 1.95*
Plasma Na(mEq/l)	142 ± 5	144 ± 5
Plasma K (mEq/l)	4.0 ± 0.6	4.3 ± 0.7
Plasma Osm (mOsm/kg H_2O)	278 ± 9	278 ± 9
Urine Na (mcEq/min)	258 ± 201	389 ± 175*
Urine K (mcEq/min)	61 ± 45	98 ± 49*
Urine Osm (mOsm/kg H_2O)	655 ± 226	592 ± 259
Venous pH	7.37 ± 0.04	7.41 ± 0.07*
Venous PCO_2 (mmHg)	46.2 ± 6.1	43.4 ± 6.6
Venous HCO^-_3 (mEq/l)	27.3 ± 2.6	27.5 ± 3.0

*= P<0.05

Table 2

Clearance data (mean± s.d.) calculated in 20 normal subjects during negative ventilation (NPV) and spontaneous breathing (SB)

	SB	NPV
Creatinine clearance	113.8 ± 25.5	129.2 ± 39.7
Free water clearance (ml/min)	−1.73 ± 1.17	−1.60 ± 1.75
Osmolar clearance (ml/min)	3.13 ± 1.82	4.32 ± 1.24*
Na excretion fraction (%)	1.38 ± 0.88	1.96 ± 0.98*

*= P<0.05

DISCUSSION

The present study demonstrates that intermittent NPV in males may bring about an increase in urine flow rate but this enhancement was not uniform for all individuals. Analysis of Tables 1 and 2 indicates that the increased diuresis was probably not associated with changes in glomerular filtration rate as there was no significant change in creatinine and free water clearances. Concomitant with the increased diuresis, other noticeable changes were: increased natriuresis, kaliuresis, fractional sodium excretion and osmolar clearance.

Various mechanisms could have accounted for all these changes. Diuresis may follow a diminished plasma level of ADH but the observed loss of urine solutes in our subjects is not a feature of a decreased ADH level. Lower ADH concentration has been seen in dogs ventilated with negative pressure ventilation (4,10) but not in humans (3).

The recent description of atrial natriuretic factor (ANF) and the understanding of its multiple effects on extracellular volume regulation, may explain some of our results. It has been shown that ANF may increase when the pleural pressure becomes more negative such as in asthmatic patients during an asthma attack (1) and in normal subjects breathing during 30 minutes through an inspiratory resistance in such a way that maximal inspiratory pleural pressures were between -30 to -40 cmH_2O. It has also been demonstrated that the intravenous infusion of a synthetic ANF equivalent leads to an increase of diuresis, natriuresis and glomerular filtration rate, with no change in free water clearance and renin plasma levels (9,13).

The noticeable increase in diuresis, natriuresis and kaliuresis and a tendency to an increased creatinine clearance observed in our subjects with no change in free water clearance are in keeping with the above description of ANF actions (16).

The lack of some of the known ANF actions could be due to the fact that during our experiments, the intermittent NPV did not generate intrapleural negative pressure as high as that of the mentioned studies (1) which could have brought about a lower plasma ANF concentration. In fact, the pleural pressure, measured in two subjects by means of an esophageal balloon, was 12 cm H_2O. A very recent investigation in man has shown that the use of PEEP reduces plasma ANF levels, and is associated with a decrease of diuresis and natriuresis, suggesting that those changes are induced by variations of intrathoracic pressure (2).

Despite the fact that there was no significant change in the creatinine clearance, over half of the individuals showed an increase in this parameter during NPV breathing that could partially account for the diuresis. Two subjects had their free water clearance increased, suggesting that there may have occurred a decrease of ADH plasma level in these individuals.

On the other hand, we also observed changes in the venous pH and carbon dioxide. It has been shown that hypocapnia may lead to increased diuresis and kaliuresis while the opposite occurs when hypercapnia is present (6,12). In fact, in 16 of 20 subjects we observed, an association between changes in pH and urine flow rate, which raises another possibility to explain our findings even though the correlation was very slight.

The present results demonstrate that intermittent NPV may stimulate diuresis but we were not able to elucidate the mechanism(s) underlying this phenomenon. It is possible that a combination of the aforementioned events leads to the observed diuresis.

Atrial natriuretic factor and antidiuretic hormone determinations should be performed in the future in order to obtain a clearer understanding of the association of NPV and enhanced urine flow rate.

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Resumo

Com o objetivo de avaliar o efeito da ventilação por pressão negativa intermitente (NPV) na função renal, estudamos vinte indivíduos voluntários normais (idade média de 29 ± 41 anos). A NPV foi obtida utilizando-se um respirador "Emerson Chest Respirator Pump" o qual foi ajustado para assegurar freqüência de 10 respirações por minuto com relação de tempo inspiratório e tempo respiratório total de 0,4 e pressão negativa de 25 cm de água. O protocolo experimental foi desenvolvido em 2 fases com duração de duas horas cada – fase de respiração espontânea e fase de respiração com NPV. No final de cada fase, foi medido o volume urinário e coletado sangue para as determinações bioquímicas. Durante a NPV houve um aumento significante do fluxo urinário ($p<0,05$) (1,42 ± 0,81 para 2,76 ± 1,95 ml/min), da natriurese (258 ± 201 para 389 ± 175 mcEq/min), da caliurese (61 ± 45 para 98 ± 49mcEq/min), da fração de excreção de sódio (1,38 ± 1,82 para 4,32 ± 1,24 ml/min) e do pH (7,37 ± 0,04 para 7,41 ± 0,07). Os clearances de creatinina e de água livre não se alteraram significativamente. Concluímos que a respiração com NPV aumenta o fluxo urinário, a caliurese e a natriurese, porém nossos dados não nos permite explicar a origem deste achados.