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Enhanced Renal Function Associated with Intermittent Mandatory Ventilation in Acute Respiratory Failure*

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Abstract. In ten patients suffering from acute respiratory failure (ARF) renal function was evaluated during 2-h periods of intermittent mandatory ventilation (IMV) or controlled mechanical ventilation (CMV). Urine flow, osmolal and creatinine clearances were significantly lower during CMV in comparison to both IMV phases and the free water clearance was less negative. Potassium excretion declined with CMV but remained reduced during the second IMV phase. There was no change in sodium excretion. This study suggests that in order to maintain renal function and prevent water retention the use of IMV should be considered whenever a sufficient mechanical reserve for partial spontaneous ventilation is present.

Key words: Mechanical ventilation – Renal function – Acute respiratory failure

Introduction

In patients with acute respiratory failure, controlled mechanical ventilation (CMV) has been shown to be associated with decreased urine flow, increased plasma antidiuretic hormone (ADH) [1, 2] decreased arterial blood pressure and decreased cardiac output [3 – 6]; the addition of a positive endexpiratory pressure may further aggravate these effects of mechanical ventilation [7]. These consequences of positive airway pressure often lead to water and salt retention [8].

Intermittent mandatory ventilation (IMV) because of the patient's own inspiratory effort and the reduced rate of mechanical ventilation [6], is associated with a decrease of the intrathoracic pressure when compared with CMV. As a consequence of this the unfavorable effects of positive pressure ventilation described above should be minimized.

The purpose of this study was to compare the renal effects of intermittent mandatory ventilation with those of controlled mechanical ventilation in patients suffering from acute respiratory failure.

Methods

Ten patients receiving IMV for the treatment of ARF were studied. The biometric data, diagnoses and inspiratory O_2 requirements are summarized in Table 1. Patients with a serum creatinine above 2 mg percent were excluded from the study.

The study protocol consisted of three phases each of two hours duration. During Phases I and III IMV was used and during Phase II CMV.

Prior to the study all patients had been on IMV for a minimum of 12 h. During IMV the ventilator[1] frequencies were set at 4 – 10/min in accordance with the patients ability to breathe spontaneously. This was judged by clinical as well as by blood gas criteria. With the change from IMV to CMV the ventilatory frequencies were increased to 10 – 16/min in order to suppress the patients own respiratory efforts (Fig. 1). The delivered tidal volumes ranged from 12.0 – 13.0 cm^3/kg bodyweight and the levels of endexpiratory pressure ranged from 0 – 12 cm H_2O. The tidal volumes of the respirator, the endexpiratory pressures and the O_2 concentrations were constantly maintained throughout the study.

All patients were stable and there was no change of therapy during the study. Fluid administration was constant for at least 12 h prior to the study and no drugs with effects on renal function were given, e.g. furosemide and dopamine.

* This paper is dedicated to Martin Zindler on the occasion of his 60th birthday

1 Modified Monaghan mechanical ventilator

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Table 1. Clinical data

Case No.	Age (years) Sex	Height (cm)	Weight (kg)	Diagnosis	F_IO_2	PEEP (cmH_2O)
1	57M	175	80	Mitral stenosis, s/p mitral valve replacement	0.3	4
2	41M	172	80	Gastric neoplasm, s/p total gastric resection	0.3	10
3	75M	165	45	Perforation of gastric wall	0.4	5
4	42M	178	85	Coronary artery disease, s/p aorto-coronary bypass.	0.3	6
5	68M	172	80	Perforation of the small bowel	0.3	12
6	55F	164	75	Multiple injuries	1.0	12
7	58M	174	80	Neoplasm of the common bileduct, s/p Whippels operation	0.3	0
8	21M	175	65	Multiple injuries	0.3	12
9	7M	118	18	Transposition of the great vessels, s/p total correction	0.6	12
10	36M	175	70	Gastric neoplasm, s/p total gastric resection	0.4	8

The patients were turned from side to side each hour. At the end of each 2-h period arterial blood was taken from an indwelling arterial cannula and urine was collected from an indwelling catheter.

The following determinations were carried out for each of the three defined periods: urine flow, plasma and urinary creatinine, sodium and potassium excretion[1], plasma and urinary osmolarity[2]; respective clearances were calculated. Statistical evaluation was carried out using the Student's t-test for paired observations. Arterial and central venous pressures were recorded using appropriate transducers.

Fig. 1a, b. Tracheal pressure pattern during **a** IMV **b** CMV. In this case the level of mean PEEP was maintained at 8 cm H_2O according to the airway pressure manometer of the ventilator. These tracings show that during IMV the mean tracheal pressure is reduced. Using planimetry the mean tracheal pressure was 24.3 cm H_2O during CMV and 18.6 cm H_2O during IMV

Results

The mean values of urine flow, osmolal, free water and creatinine clearances and of sodium and potassium excretion are shown in Table 2. The individual values of urine flow and of the clearances are shown in Figs. 2 and 3.

Controlled mechanical ventilation (Phase II) was associated with significant reductions in urine flow and creatinine- and the osmolal clearances. The free water clearances were negative during all three phases and became 33% less negative during CMV.

During the reapplication of IMV (Phase III) the mean values of urine flow and of the creatinine – and osmolal clearances returned to the levels observed during the first IMV phase.

During the second application of IMV (Phase III) the urine flow of some patients exceeded the values of the first IMV phase (I), possibly indicating a compensatory excretion of urine which may have been retained during CMV (Fig. 2). The U/P ratio did not change significantly (Table 2). The potassium excretion fell with the change from IMV to CMV, but remained low during the reapplication of IMV (Table 2). No statistically significant changes of sodium excretion were observed (Table 2).

Arterial blood gases, arterial blood pressure and central venous pressure did not change significantly throughout the study.

Discussion

The principal finding of this study is that a 2-h period of controlled mechanical ventilation (CMV) in ARF

1 Eppendorf flame photometer
2 Knaur osmometer

Table 2. Renal function

	IMV/Phase I	CMV/Phase II	IMV/Phase III
V (ml/min)	1.429 ± 0.189	1.20 ± 0.1[a]	1.54 ± 0.248
C_{osm} (ml/min)	3.433 ± 0.39	2.69 ± 0.31[b]	3.702 ± 0.51
C_{H_2O} (ml/min)	−1.963 ± 0.258	−1.56 ± 0.22[a]	−2.133 ± 0.316
C_{creat} (ml/min)	82.136 ± 12.85	70.21 ± 11.63[c]	89.78 ± 12.23
$K_{excretion}$ (mval/min)	0.47 ± 0.11	0.42 ± 0.04[d]	0.41 ± 0.14
$Na_{excretion}$ (mval/min)	0.41 ± 0.11	0.48 ± 0.11 n.s.	0.53 ± 0.14
U/P ratio	2.452 ± 0.163	2.39 ± 0.13 n.s.	2.48 ± 0.17

values are the mean ± standard error

[a] $p < 0.025$
[b] $p < 0.010$ } as compared to Phase I and III
[c] $p < 0.001$

[d] $p < 0.025$ as compared to Phase I

n.s. = not significant

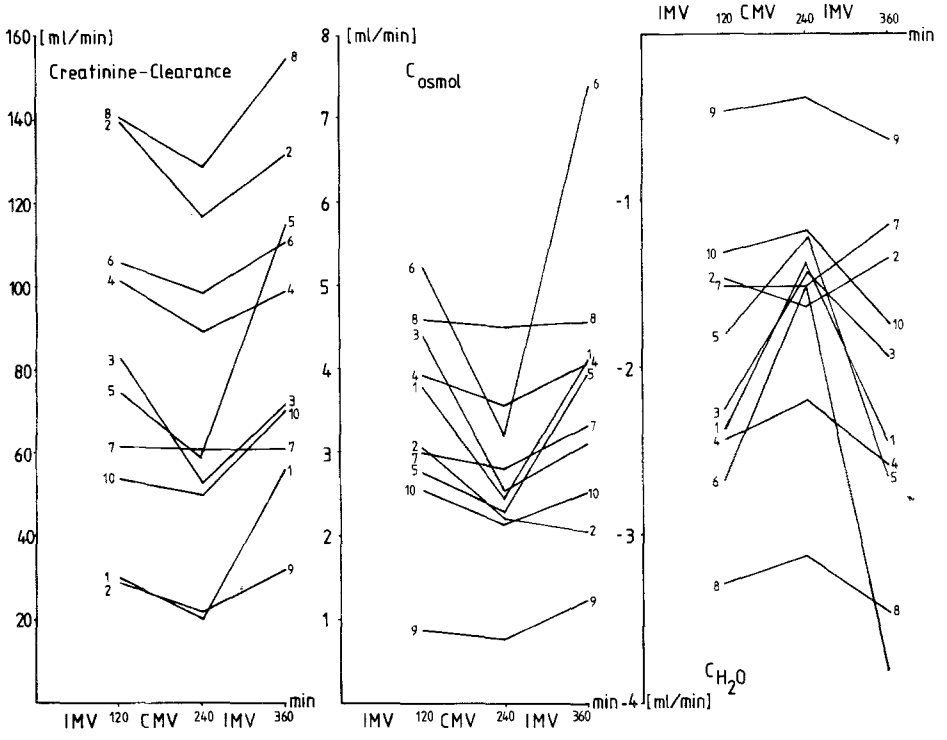

Fig. 2a – c. Individual results for **a** creatinine clearance **b** osmolal and **c** free water clearances

patients managed by intermittent mandatory ventilation (IMV) is associated with a clinically important reduction of the urine flow, the osmolal and creatinine clearance, and an increase of the negative free water clearance.

The change from IMV to CMV was associated with an increase of the mean airway pressure and vice versa (Fig. 1). It has previously been shown that changes of intrathoracic pressure, due to different mean airway pressures, influence renal excretory function. This relationship is probably mediated by alterations of the intrathoracic blood volume [9]. A reduction of mean airway pressure causes a rise in the transmural filling pressures of the heart [10, 11]. This

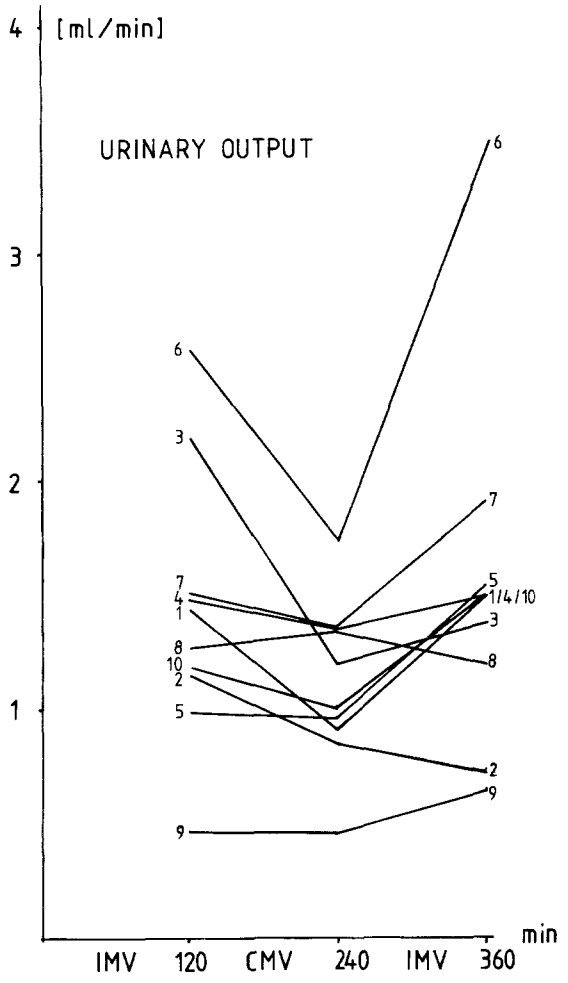

Fig. 3. Individual results of urinary output

is due to translocation of blood from the extra- to the intra-thoracic vascular bed. The concomitant hemodynamic alterations and their repercussions on renal function are similar to those observed during, head out, under water immersion of the body [12]. Under both circumstances a brisk rise in renal excretory function occurs.

This phenomena has been attributed to two differing physiological mechanisms:

(1) The change in ventricular filling causing either increase or reduction of cardiac output which has a direct influence on renal plasma flow [3, 4].

(2) The stimulation of intrathoracic stretch receptors in the vascular and atrial walls activating hormonal reflexes such as the suppression or release of antidiuretic hormone, aldosterone and others [2, 13].

Kumar et al. [7] investigated an increase of positive airway pressure due to the addition of PEEP to controlled mechanical ventilation in patients with acute respiratory failure. They concluded that the antidiuretic effect of CMV with PEEP was principally due to reduced cardiac output and not to the observed increased plasma levels of ADH. The influence of PEEP during CMV on effective renal plasma flow was first studied in patients by Järnberg et al. [14] using a similar protocol to that of Kumar et al. [7]. They found a 12% decrease, without a change in glomerular filtration rate. Studies in healthy anesthesized dogs [3] and in normal volunteers [15] also revealed a reduction in renal plasma flow when airway pressures were elevated. However in contrast to patients with respiratory failure [14] glomerular filtration rate was also reduced.

Hall et al. [16] who also studied the addition of PEEP to CMV in anesthesized dogs found the decrease in cardiac output to be associated with a preferential decrease in renal cortical blood flow. Thus, a direct influence of the fall in cardiac output due to increased ventilatory pressures on renal function most likely plays a role in normal individuals and in patients with acute respiratory failure. This is supported by our finding of a reduced creatinine clearance during CMV (Fig. 3).

Studies by Baratz et al. [3, 4] and others [17] provide evidence that the elevation of positive airway and intrathoracic pressure is associated with increased levels of plasma ADH in normal subjects. According to the studies of Gauer et al. [9] and others [18], the retention of water and salt during the elevation of ventilatory pressures may be seen as an attempt by the body to re-establish previous levels of intrathoracic blood volume and cardiac output. This is caused by the stimulation of stretch receptors in the left atrial wall and typically results in a reduction of the urine flow, the osmolal and the free water clearances [15].

The studies in patients reveal abnormally high plasma levels of ADH [2, 7, 19]. Khambatta's and our own finding show that in contrast to anesthesized animals or healthy men the decreases in urine flow and osmolal clearance were concomitant with an increase in free water clearance.

These findings indicate that the patients were kept relatively dehydrated and that under clinical conditions a generally high ADH activity may probably be due to a variety of other stimuli [2, 20]. The increases in free water clearance observed by Khambatta et al. [2] with the institution of IPPB and by us following the change from IMV to CMV suggest that the drop in urine flow cannot be the sole response to an ADH release.

The few available studies in patients, including our own, do not allow any further conclusions with regard to the role of humoral reflex mechanisms when ventilatory pressures are altered under clinical conditions.

Clinical Considerations

The abrupt rise in left ventricular filling pressure following the reduction of airway pressure [23] e.g. from mechanical to spontaneous ventilation may be dangerous to patients suffering from impaired ventricular function [21, 22]. IMV does allow a gradual transition from high to normal ventilatory pressures, preventing an abrupt volume overload. Thus, sufficient time may be provided for volume adaptation by the observed facilitation of excretory renal function. The described use of IMV under these circumstances represents a further refinement of the weaning technique utilizing a stepwise reduction of continuous positive airway pressure [22]. In the managment of our patients IMV was not considered only as a useful weaning technique. It was rather used as a principle setting of the ventilator. The frequencies of mechanical ventilation were chosen according to clinical and blood gas criteria and in some cases remained relatively high during IMV. Under these circumstances arterial blood gases were maintained during IMV as well as during CMV (Table 3).

Based on the available data of the effects of IMV on renal function, the earliest possible institution of IMV may counteract the tendency to water- and salt retention, a problem of mechanical ventilation which was first described by Sladen et al. [8]. Beneficial long term effects of IMV on renal function could not be established in the limited study period.

In conclusion, we have found evidence that the early institution of intermittent mandatory ventilation facilitates urine flow in patients with ARF whose respiratory problems are often associated with an abnormal retention of water and salt. This may indicate that IMV deserves increased application in the clinical management of patients requiring mechanical ventilatory assistance.

Abbreviations

CMV	controlled mechanical ventilation
IMV	intermittent mechanical ventilation or intermittent mandatory ventilation
IPPB	intermittent positive pressure breathing
PEEP	positive endexpiratory pressure
F_IO_2	fraction of inspired oxygen
ADH	antidiuretic hormone
ARF	acute respiratory failure

Measurements

V = *urinary output*	(ml/min)
P = *osmolarity in the plasma*	(mosm)
U = *osmolarity in the urine*	(mosm)
C = *creatinine*	

Calculations

$$C_{osmol} = \text{osmolal clearance} = \frac{U \times V}{P} \quad \text{(ml/min)}$$

$$C_{H_2O} = \text{free water clearance} = V - C_{osmol} \quad \text{(ml/min)}$$

$$C_{creat} = \text{creatinine clearance} = \frac{\text{creatinine in urine}}{\text{creatinine in plasma}} \times V \quad \text{(ml/min)}$$

$$\text{U/P ratio} = \frac{U}{P}$$

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