The Effect of Changing From Pressure Support Ventilation to Volume Control Ventilation on Renal Function

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ABSTRACT

Objective: *Mechanical ventilation increases intrathoracic pressure and decreases cardiac output, and the associated hormonal changes may affect the free water, sodium and creatinine clearance. We sought to establish if there was any difference in creatinine clearance, urine volume and fractional excretion of sodium (FE_{Na}) between pressure support ventilation (PSV) and volume controlled (VC) ventilation.*

Methods: *The study took place in a 10 bedded metropolitan intensive care unit that admitted both medical and surgical patients. The study was a within subjects, non-randomised, controlled procedures design. Patients were included if they were ventilated on volume control ventilation (VC) with a constant positive end expiratory pressure (PEEP) and suitable for pressure support ventilation (PS), a mean arterial pressure of > 65 mmHg, a normal serum creatinine, well-hydrated and catheterised. Exclusion criteria were administration of a loop diuretic or renal dopamine in the six hours preceding the onset of the study, clinical adrenal dysfunction or clinically unstable requiring a change in intravenous fluid therapy. Eight patients completed four hours of VC ventilation and had renal functions monitored and then changed to PS ventilation for a one hour washout period. Four hours of PS were maintained and renal function monitored over a second four hour period. Patients remained on PS and then after a one hour washout on VC the final four hour monitored period on VC was completed. Urine and serum samples were collected for urine volume, fractional excretion of sodium and creatinine clearance during each four hour cycle on VC and PS ventilation.*

Results: *Friedman's test statistical analysis revealed no significant difference in creatinine clearance ($p = 0.54$), fractional excretion of sodium ($p = 0.58$) or urine volume ($p = 0.42$).*

Conclusions: *VC ventilation had no adverse effects on renal indices in comparison to spontaneous PS ventilation.* (**Critical Care and Resuscitation 2005; 7: 303-309**)

Key words: Pressure support ventilation, volume control ventilation, renal function

The physiological effects of positive pressure ventilation on pulmonary and cardiac function have been well documented.[1] Despite the frequent use of mechanical ventilation in the intensive care to treat respiratory failure, little is known about the effects of positive pressure ventilation on renal function. We sought to establish if there was any difference in creatinine clearance, urine volume and fractional excretion of sodium (FE_{Na}) when comparing spontaneous ventilation as is delivered with pressure support ventilation to volume controlled ventilation.

MATERIALS and METHODS

Eight patients from our intensive care unit were recruited over a 12 month period. Informed consent was obtained. The study was a within subjects, non-randomised, controlled procedures design. Patients were considered suitable for inclusion into the study if they were ventilated patients who were considered suitable for either pressure support or volume control ventilation. They had to be adequately hydrated with either a central venous pressure (CVP) of > 8 mmHg or a pulmonary capillary wedge pressure of > 14

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mmHg. Patients had to be catheterised with a mean arterial pressure of > 65 mmHg and a normal plasma urea or creatinine. Positive end expiratory pressure (PEEP) was to remain constant throughout the duration of the study.

Patients were excluded from the study if they had been administered a loop diuretic or dopamine (< 5 μg/kg/hr) in the 24 hours preceding onset of the study. They were also excluded if they had documented adrenal dysfunction or were considered clinically unstable necessitating rapid changes in their intravenous fluid requirements. Intra aortic balloon pumping was a further exclusion criterion. If the patients fulfilled inclusion and exclusion they or their families were approached and a patient information sheet provided and consent obtained. Patients completed four hours of volume control (VC) ventilation. They then changed to pressure support (PS) ventilation for a one hour washout period followed by four hours of PS ventilation. Patients remained on PS for a further four hour period and then, after a one hour washout period on VC, the final four hour period on VC ventilation was completed. Urine and serum samples were collected for urine volumes, fractional excretion of sodium (FE_{Na}) and creatinine clearance during each four hour cycle on VC and PS ventilation. All specimens were taken two hours after the onset of a particular mode of ventilation.

The SPSS statistical package was used to analyse the data. Descriptive data are given as mean (SD) or a median. Differences in the median scores of renal indices were assessed by Friedman's repeated measures ANOVA.

RESULTS

Eight patients were studied across the four time periods. Table 1 shows the data relating to patient baseline demographic details.

Tables 2 - 5 show the ventilation parameters during the respective first four hour periods on VC and PS ventilation. Mid-way during each four hour time period a value was obtained for creatinine clearance, FE_{Na} and urine volume (Tables 3, 4 and 5). Table 6 shows the raw data obtained for each subject across ventilation modes.

There were no significant differences in renal indices across ventilation modes (creatinine clearance: $\chi^2 = 2.14$, $p = .54$, FE sodium: $\chi^2 = 1.95$, $p = 0.58$, urine volume: $\chi^2 = 2.85$, $p = 0.42$). Figures 1 - 3 show the mean values for creatinine, sodium and urine volume across ventilation modes. Tables 7 - 9 show summary data for the three indices across ventilation modes. A repeated-measures ANOVA was performed to investigate average peak airway pressures across four ventilation modes/periods.

There was a statistically significant difference between the ventilation modes ($F = 8.24$, $p = 0.001$). *Post hoc* comparisons show that mean peak airway pressures during VC were significantly greater ($p < 0.05$) than PS.

Table 1. Baseline patient demographic details

Patient	Sex	Age	Diagnosis on Admission	Sepsis during study	Inotropes required during study
1	Female	59	Lateral medullary infarct	No	No
2	Male	75	COPD	No	No
3	Female	81	Septic shock	No	No
4	Female	55	Guillian Barré Syndrome	No	No
5	Male	79	Aspiration pneumonia	No	No
6	Female	56	Pneumonia	No	No
7	Male	69	Lobectomy	No	No
8	Male	70	Emergency AA repair	No	No

Table 2. Ventilator parameters during first four hour period on volume control ventilation (during time period T1)

Patient	PEEP (cmH20)	Tidal volume (mL)	Mean Peak Airway Pressure (cmH20)	Set Respiratory rate
1	5	500	20.2	12
2	5	720	20.5	12
3	5	600	22.5	8
4	5	750	22.0	12
5	5	650	33.0	12
6	5	750	24.7	12
7	5	670	28.7	10
8	5	700	19.0	8

Table 3. Ventilator parameters during first four hour period on pressure support ventilation (during time period T2)

Patient	PEEP (cmH20)	Tidal volume (mL)	Mean Peak Airway Pressure (cmH20)	Respiratory rate
1	5	350-500	15	10-30
2	5	500-600	18	20-24
3	5	500-600	21	23-24
4	5	550-600	15	14-18
5	5	600-650	17	20-22
6	5	550-650	22	20-22
7	5	450-550	23	24-28
8	5	750-1000	17	9-11

Table 4. Ventilatory parameters during second four hour period on pressure support ventilation (during time period T3)

Patient	PEEP (cmH20)	Tidal volume (mL)	Mean Peak Airway Pressure (cmH20)	Respiratory rate
1	5	400-600	15	10-30
2	5	430-480	15	19-24
3	5	550-600	21	23-24
4	5	550-600	15	14-18
5	5	600-650	17	20-22
6	5	550-650	23	22-24
7	5	550-650	23	26-30
8	5	720-880	17	18-28

Table 5. Ventilatory parameters during second four hour period on volume control ventilation (during time period T4)

Patient	PEEP (cmH20)	Tidal volume (mL)	Mean Peak Airway Pressure (cmH20)	Set Respiratory rate
1	5	500	19.5	12
2	5	620	23.8	10
3	5	600	30.5	8
4	5	700	22.5	10
5	5	600	42.5	10
6	5	750	25.0	12
7	5	680	27.5	10
8	5	700	18.2	10

Table 6. Renal indices during different modes of ventilation

patient	Creat Clearance (ml/min)				FE Na (%)				Urine Volume (ml/min)			
	T1	T2	T3	T4	T1	T2	T3	T4	T1	T2	T3	T4
1	0.94	0.86	1.05	0.86	0.94	1.29	1.73	2.49	226	297	434	435
2	1.05	0.87	1.34	1.19	2.08	2.25	1.57	1.53	307	584	464	312
3	0.57	0.63	0.62	0.57	1.17	0.69	1.38	1.85	112	130	185	188
4	3.90	3.80	2.90	3.60	1.80	0.70	0.80	0.90	980	318	565	683
5	1.50	1.20	1.00	1.50	0.23	0.42	0.44	0.32	125	113	111	143
6	2.60	2.50	3.50	3.00	0.55	0.78	0.46	0.62	310	490	580	495
7	1.00	0.80	0.90	0.70	0.96	1.46	1.82	0.70	466	565	785	360
8	1.70	2.10	1.60	1.50	0.84	0.97	1.20	0.87	334	424	358	270

T1 - Four hour time period on Volume Control Ventilation, T2 - Four hour time period on Pressure Support Ventilation, T3 - Four hour time period on Pressure Support Ventilation, T4 - Four hour time period on Volume Control Ventilation

Table 7. Friedman's test results for creatinine clearance (mL/sec)

					Friedman's	
	N	*mean*	*SD*	*median*	χ^2	*p*
Time 1	8	1.66	1.10	1.27		
Time 2	8	1.60	1.11	1.03		
Time 3	8	1.61	1.03	1.19		
Time 4	8	1.62	1.10	1.34	2.14	0.54

Table 8. Friedman's test results for fractional excretion of sodium (%)

					Friedman's	
	N	*mean*	*SD*	*median*	χ^2	*p*
Time 1	8	1.07	0.61	0.95		
Time 2	8	1.07	0.58	0.87		
Time 3	8	1.17	0.55	1.29		
Time 4	8	1.16	0.73	0.88	1.95	0.58

Table 9. Friedman's test results for urine volume (mL)

					Friedman's	
	N	*mean*	*SD*	*median*	χ^2	*p*
Time 1	8	357.5	276.8	308.5		
Time 2	8	365.1	182.3	371.0		
Time 3	8	435.2	218.6	449.0		
Time 4	8	360.7	175.3	336.0	2.85	0.42

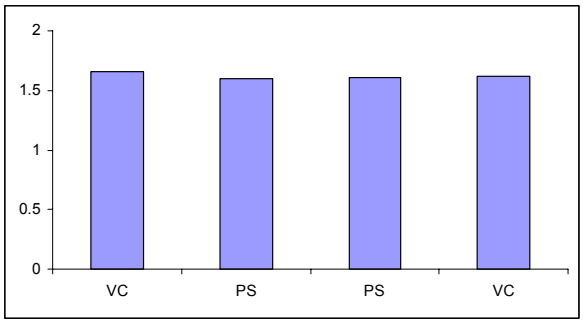

Figure 1. Mean creatinine clearance (mL/sec)

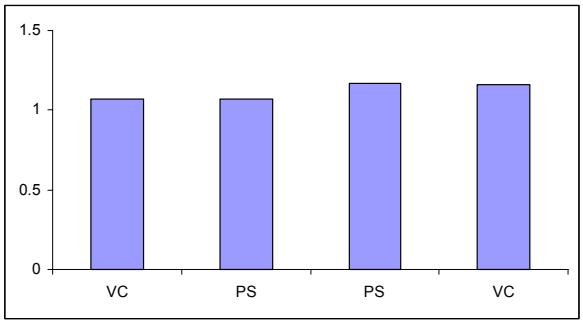

Figure 2. Mean fractional excretion of sodium (%)

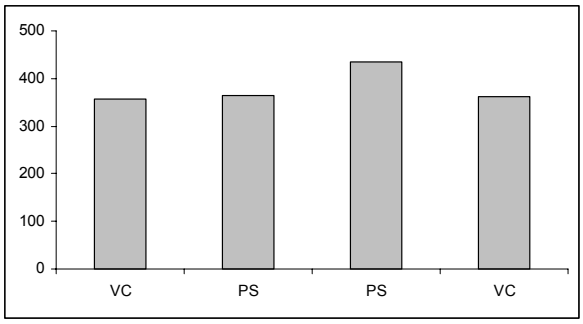

Figure 3. Mean urine volume (mL)

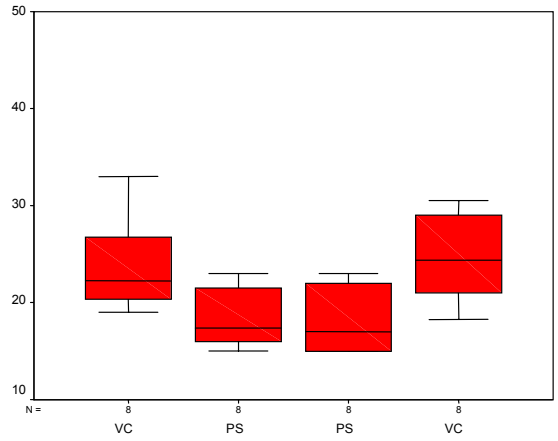

Figure 4. Mean peak airway pressures (cmH_2O) across ventilation modes

DISCUSSION

We found in patients undergoing mechanical ventilation in the intensive care unit, the creatinine clearance, fractional excretion of sodium and urine volume remained constant when patients were changed from VC to a PS mode of ventilation.

This study has limitations in that the patients were not randomised and the patient numbers were small. However, there were stringent inclusion and exclusion criteria, which lead to limited patient recruitment. Furthermore, there were no predetermined levels of pressure support throughout the study period. It is possible that to see differing effects on renal indices during different modes of mechanical ventilation, a longer washout period and a greater time on a particular mode of ventilation would be required during a crossover trial. It is also possible that varying pulmonary compliance in the different patients studied could attenuate the circulatory effects of positive pressure ventilation.

It is interesting to note that in our study, both periods of VC ventilation were associated with higher peak pressures than both periods of PS ventilation. Despite this, these differences did not translate into changes in the measured renal indices across the different modes of ventilation.

During mechanical ventilation, inspiration is generated by an artificial positive pressure input into a closed airway system. Continuous mechanical ventilation (CMV) is a mode of ventilation where all breaths are machine-delivered at a mandatory volume and rate. Spontaneous breathing does not occur during this mode of ventilation. Intermittent mandatory ventilation is a mode of ventilation in which spontaneous breathing is possible between mandatory positive pressure ventilation. In PS ventilation, patients initiate a breath and a predetermined pressure will be delivered by the ventilator until the patient's inspiratory flow decreases. In all the above modes of ventilation positive end expiratory pressure (PEEP) can be administered.

Drury *et al*,[2] reported that after administering continuous positive airway pressure (CPAP) to spontaneously breathing healthy human volunteers, changes in renal function occurred. Renal blood flow (RBF) glomerular filtration rate (GFR) and urine output decreased after application of CPAP. Murdaugh *et al*,[3] and Sladen *et al*,[4] conducted subsequent observational studies in anesthetised patients with normal lungs. They noted a decrease in GFR, RBF and free water clearance when CPAP and intermittent mandatory ventilation (IMV) were administered. These studies in healthy human study subjects implied that the consequences of positive pressure ventilation on the circulation may manifest with a decrease in urine output. A number of physiological changes secondary to mechanical ventilation have been proposed to explain the effects of positive pressure ventilation on the circulation and renal function. These include a reduction in venous return and cardiac output, a redistribution of intrarenal blood flow and hormonal changes. Positive pressure ventilation during mechanical ventilation may inhibit venous return and increase inferior vena caval pressure, resulting in a decrease in effective circulating volume. The effect of positive pressure ventilation on the pulmonary vasculature may increase right ventricular afterload. It has been postulated that these effects on cardiac output may decrease renal perfusion. Early studies have shown that mechanical ventilation restricts renal water excretion and sodium reabsorption is increased.[5-11] Hemmer *et al*,[6] demonstrated that in ventilated patients, a reduction in airway pressure, facilitated sodium and water excretion. The decrease in cardiac output associated with mechanical ventilation causes an increase in plasma anti diuretic hormone (ADH).[6,12]

During mechanical ventilation, the unloading of baroreceptors as well as the decrease in mean arterial blood pressure leads to an increase in renal renin release. This increase has been shown in studies in patients.[13,14] Renin catalyses the conversion of angiotensin into the biologically active angiotensin II by the angiotensin converting enzyme. Angiotensin II causes an increase in tubular sodium and water reabsorption independently of aldosterone.[15]

Increases in intrathoracic pressure are often associated with an increase in plasma vasopressin concentration.[16] Vasopressin has various effects on renal function. It decreases medullary blood flow, and it increases water reabsorption in the distal tubule. Furthermore, renal sympathetic nerve activity initiates renal vasoconstriction and increases tubular sodium and water reabsorption.[17,18] The unloading of intra-thoracic baroreceptors and the loss of vagal tone during ventilation with PEEP increases sympathetic activity and plasma catecholamine levels.[19]

During mechanical positive pressure, right and left atrial pressure increases. Due to the increase in surrounding intrathoracic pressures, the resulting atrial transmural pressure decreases. It could thus be expected that atrial naturetic peptide (ANP) release decreases during mechanical ventilation.

Given the widespread physiological changes that occur during mechanical ventilation, changes in ventilatory patterns may vary these effects considerably. Ventilatory modes that partially allow spontaneous breathing such as intermittent mandatory ventilation, facilitate renal excretion of sodium and water.[8,9] The inhibiting influences of positive pressure ventilation on the kidney results in sodium and water retention, but more recent modes of ventilation which allow for spontaneous ventilation may not lead to such a significant decrease in sodium and water excretion.

The fractional excretion of sodium has been offered as a more precise index of renal tubular sodium reabsorption. It is unclear from previous studies if these data can be extrapolated to the critically ill population where the adverse effect of positive pressure ventilation on the kidney may be more profound.

Marquez *et al*,[20] examined the effects of PEEP in a small number of ICU patients. They found that the administration of PEEP lead to a decrease in glomerular filtration rate and Fe_{Na} in seven ICU patients. Other studies by Andrivet *et al*,[21] and Farge *et al*,[22] independently reported decreased urine flow rates and sodium excretion with the institution of PEEP in critically ill patients, but no effect on GFR. Vivino *et al*,[23] prospectively studied risk factors for acute renal failure in 153 trauma patients in whom renal failure was

defined as a creatinine level greater than 2 mg/dL. Mechanical ventilation increased the odds ratio of developing renal failure in both univariate and multivariate analysis. This study raises the question as to whether mechanical ventilation *per se* predisposes to acute renal failure or whether other factors play as important a role. Previous studies on the effects of positive pressure ventilation and PEEP on renal function have been small in number, often in healthy animals or small numbers of ventilated patients. The role of volume depletion, haemodynamic instability diuretics and dopamine may also bedevil any measurements of renal function in renal patients. Previous studies have usually used creatinine clearance to estimate glomerular filtration rate, which may not be accurate in catabolic critically ill patients with abnormal renal function.[24] Modes of ventilation have also changed over the last two decades and pressure support ventilation is now commonly used as a mode of ventilation in the intensive care setting.

We tried to eliminate the above variables by selecting stable patients who were volume replete with stable renal function and not receiving diuretics or dopamine. As most of our patients are ventilated with VC or PS we considered a comparison between these two modes as clinically relevant. Our data suggest that in our subgroup of patients the measured renal indices were not compromised by increased peak airway pressures as noted during VC ventilation. These data also suggest that many factors other than peak airway pressures could compromise renal function in ventilated patients.

Further research is needed before there is convincing data to indicate which ventilatory strategy optimises renal function in the critically ill.

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