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BRIEF REPORT

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Variation in natriuretic peptides and mitral flow indexes during successful ventilatory weaning: a preliminary study

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Abstract *Objective:* To assess the cardiac consequences of successful respiratory weaning using the variations of circulating B-type and atrial natriuretic peptides (BNP, ANP) and Doppler mitral flow. *Design:* A prospective preliminary observational study. *Setting:* A 14-bed medical ICU in a French university hospital. *Patients:* Thirty-one patients undergoing a spontaneous breathing trial on a T-tube. *Interventions:* Circulating BNP and ANP levels and Doppler-derived E/A ratio and deceleration time of the E wave were measured before and 1 h after disconnection. *Results:* BNP levels increased from 299 pg/ml (range 56–1079) to 412 pg/ml (147–1324) ($p = 0.02$) in patients with systolic left ventricular dysfunction, decreased from 98 pg/ml (25–337) to 45 pg/ml (38–180) ($p = 0.04$) in patients with right ventricular dilation and remained unchanged in patients with neither of these cardiac abnormalities. Overall ANP levels increased from 33 pg/ml to 67 pg/ml ($p < 0.001$) regardless of ventricular function. The E/A ratio increased from 0.91 (0.66–3.56) to 1.17 (0.5–4.76), ($p = 0.01$), after disconnection, whereas deceleration time of E wave decreased from 185 ms (120–280) to 160 ms (70–206) ($p = 0.02$). *Conclusion:* During successful weaning from mechanical ventilation ANP levels increase in all patients whereas changes in BNP levels depend on underlying cardiac function. Changes in Doppler mitral flow indexes following ventilator disconnection suggest an increase in left-ventricular filling pressure.

Keywords Weaning · Mechanical ventilation · Brain natriuretic peptide · Atrial natriuretic peptide · Echocardiography · Mitral Doppler

Introduction

Weaning from mechanical ventilation markedly modifies cardio-pulmonary interactions [1–3]. It increases venous return and left-ventricular preload and afterload [1, 3]. This left-ventricular afterload increment increases the myocardial wall stretch. Brain natriuretic peptide (BNP) and atrial natriuretic peptide (ANP) are secreted by myocytes in response to ventricular and atrial wall stretch respectively [4–7]. Changes in left-ventricular filling pressure can be assessed by mitral flow, which correlates to end-diastolic left-ventricular pressure [8]. We sought to assess the changes in natriuretic peptides and Doppler mitral flow following successful respiratory weaning in ICU patients.

Patients and methods

This preliminary observational study was conducted from July 2003 to November 2004 in a 14-bed medical ICU in a 780-bed hospital. The local institutional review board

waived the need for written informed consent. All the patients gave their oral informed consent before entering the study.

Consecutive patients recovering from respiratory failure in need of mechanical ventilation were eligible if they fulfilled weaning criteria [9]. The spontaneous breathing trials (SBTs) were performed in a semi-recumbent position with supplemental oxygen and a T-tube device. Patients were ineligible if they had no arterial catheter, if they had arrhythmia and if apical four-chamber view or mitral flow analysis were impossible.

Bedside monitoring

Arterial blood gases and plateau pressure were measured just before disconnection (T0). Heart rate, respiratory rate, blood pressure, pulsed oximetry and consciousness were closely monitored during SBTs. In the event of poor tolerance, the patient was immediately reconnected to the ventilator. Arterial blood gases were measured after 1 h of spontaneous breathing (T1).

Given published data relative to the kinetics of circulating BNP [4, 10], we studied only patients able to tolerate 1 h of spontaneous breathing.

Bedside Doppler echocardiography

Echocardiography was performed at T0 and at T1. It included two-dimensional examination, visual assessment of left-ventricular ejection fraction and right-to-left-ventricle end-diastolic area ratio in the four-chamber view, as well as pulsed-wave Doppler analysis of mitral inflow with measurement of E and A waves, maximal velocities and the E wave deceleration time (DTE) [7]. During mechanical ventilation, E and A waves were measured during the very beginning of insufflation. During SBTs, measurements were performed at the very beginning of inspiration. The mean of five consecutive measurements was calculated.

Patients were considered to have left-ventricular systolic dysfunction when the visually assessed left-ventricular ejection fraction was less than 50% and right-ventricular dilation when the right-to-left-ventricle end-diastolic area ratio in the four-chamber view was more than 0.6. Normal heart was defined by absence of both these criteria and the absence of relevant valvulopathy. Patients with biventricular dysfunction were excluded from the study.

BNP and ANP measurement

At T0 and T1, 5 ml of arterial blood was collected in tubes containing potassium ethylenediamine tetraacetic acid and was immediately centrifuged (190 g for 10 min at 4 °C). The plasma was immediately cooled to –20 °C and stored at –80 °C as soon as possible. Plasma ANP and BNP were determined in duplicate by means of radio immunoassays (S-1131 and S-2017, respectively; Peninsula Laboratories–Bachem, UK), as recommended by the manufacturer.

Statistical analysis

Results are expressed as medians and ranges. The effect of weaning was assessed using the Wilcoxon paired test, the Mann–Whitney test and the Kruskal–Wallis test, as appropriate. Correlations were identified using Spearman's test. Statistical significance was set at $p < 0.05$.

Results

Sixty-eight patients were considered for the study. Doppler mitral evaluation was impossible in 27 patients at T1. Seven other patients were excluded for biventricular dysfunction and three for paroxysmal supraventricular tachycardia during the spontaneous breathing trial, impeding Doppler analysis. The remaining 31 patients [24 men; mean age 54 years (18–87); SAPS II 46 (22–102); duration of mechanical ventilation 3 days (1–30)] were investigated during a total of 33 successful SBTs. Echocardiography showed left-ventricular dysfunction in 8 patients, right-ventricular dilation in 9 patients, and neither of these two abnormalities in 14 patients.

Bedside findings

Median plateau pressure was 20 cmH_2O. Systolic blood pressure increased from 130 mmHg (91–184) to 140 mmHg (99–199) ($p < 0.01$). Heart rate was not modified by disconnection: 90/min (66–117) at T0 and 92/min (54–127) at T1 ($p = 0.5$). Respiratory rate (cycles/min) increased slightly from 18 (12–27) to 20 (11–31) ($p = 0.05$). No significant change in PaO_2, $PaCO_2$ and pH were noticed. All but two patients were extubated at the end of the trial. These two patients were kept ventilated because they were considered at high risk of post-extubation stridor, received intravenous steroids and were easily extubated 24 h later.

BNP and ANP kinetics

BNP and ANP values at T0 and T1 and according to underlying cardiac function are described in Table 1. At T1, the overall median BNP value was not different from the baseline value. However, whereas the median BNP value

Table 1 BNP and ANP levels (pg/ml) before (T0) and 1 h after (T1) disconnection from the ventilator

	All patients	Neither LVD nor RVD	LVD	RVD
BNP T0	73 (1–1079)	13 (1–74)	299 (56–1079)#	98 (25–337)#¶
BNP T1	47 (6–1324)	22 (6–127)	412 (147–1324)*#	45 (38–180)*#¶
ANP T0	33 (5–737)	10 (5–324)	174 (122–737)#	18 (13–250)#¶
ANP T1	67 (13–965)*	29 (13–800)*	225 (35–965)*#	37 (13–780)*#¶

LVD, left-ventricular dysfunction; *RVD*, right-ventricular dilation
* $p < 0.05$ compared with T0 (Wilcoxon paired test)
# $p < 0.05$ compared with neither LVD nor RVD (Mann–Whitney test)
¶ $p < 0.05$ compared with LVD and neither LVD nor RVD (Mann–Whitney test)

Table 2 E/A ratio and DTE levels before (T0) and 1 h after (T1) disconnection from the ventilator

	All patients	Neither LVD nor RVD	LVD	RVD
E/A ratio T0	0.91 (0.66–3.56)	1.06 (0.73–1.5)	1.9 (0.6–3.5)	0.98 (0.69–1.6)
E/A ratio T1	1.17 (0.50–4.76)*	1.22 (0.91–1.7)*	2.4 (0.83–4.7)*#¶	1.45 (0.72–1.82)*
DTE T0	185 (120–280)	170 (140–280)	190 (140–260)	160 (120–230)
DTE T1	160 (70–206)*	150 (115–190)	155 (70–170)*#	145 (110–206)

LVD, left-ventricular dysfunction; *RVD*, right-ventricular dilation
* $p < 0.05$ compared with T0 (Wilcoxon paired test)
# $p < 0.05$ compared with neither LVD nor RVD (Mann–Whitney test)
¶ $p < 0.05$ compared with LVD and neither LVD nor RVD (Mann–Whitney test)

did not change in patients with a normal ventricular function, it decreased in patients with right-ventricular dilation ($p < 0.04$) and increased in patients with left-ventricular dysfunction ($p < 0.02$) (Table 1). ANP increased significantly in all patients whatever the cardiac function. ANP and BNP levels correlated at T0 (rho = 0.72, $p = 0.006$) but not at T1 (rho = 0.325, $p = 0.08$).

Mitral flow

The three investigators performed five measurements in 12 ventilated patients. With regard to E waves, intra-observer and inter-observer variability was $7 \pm 4\%$ and $8 \pm 5\%$ respectively. For A waves, the intra-observer and inter-observer variability was $8 \pm 7\%$ and $8 \pm 6\%$ respectively. The intra-observer and inter-observer variability for DTE was $9 \pm 5\%$ and $7 \pm 4\%$ respectively.

The E/A ratio and DTE changes are shown in Table 2. The E/A ratio increased from 0.91 (0.66–3.56) to 1.17 (0.50–4.76) ($p = 0.01$). The DTE was 185 ms (120–280 ms) at T0, and decreased to 160 ms (70–206 ms) at T1 ($p = 0.02$). No relevant mitral insufficiency occurred at T1.

Discussion

The aim of this preliminary study was to assess non-invasively the cardiac consequences of successful weaning from mechanical ventilation.

At T0, patients with ventricular abnormalities had higher BNP levels than patients without left-ventricular dysfunction or right-ventricular dilation. Interestingly, we found that BNP levels were higher in the case of left-ventricular than in right-ventricular abnormalities. This is in agreement with previous studies documenting increased BNP levels in right-ventricular failure but to a lesser extent than in left-ventricular disease [11, 12]. Among patients with left-ventricular dysfunction, disconnection increased BNP levels suggesting a raise in ventricular wall stretch. The left-ventricular afterload and preload increase following weaning and could account for this BNP increase. Conversely, the decrease in BNP levels observed in patients with right-ventricular dilation suggests a decrease in right-ventricular constraint. This could be explained by the documented deleterious effect of mechanical ventilation on the right ventricle [13, 14].

We observed that ANP level at T0 was higher in patients with ventricular abnormalities than in patients with neither left-ventricular dysfunction nor right-ventricular dilation. Interestingly, ANP levels increased after disconnection in every patient, suggesting an increase in the atrial wall stretch reflecting the augmentation of venous return.

We observed a correlation between ANP and BNP before but not after weaning. This discrepancy could be due to a slower kinetics of BNP. However, recent studies revealed BNP secretion to occur less than 8 min after stimulation [15, 16]. Moreover, the fact that we observed BNP increase 1 h after disconnection suggests that BNP secretion can be detected at least 1 h after stimulation.

We observed subtle changes in Doppler mitral indexes during weaning. The E/A ratio and DTE have been demonstrated to correlate with left-ventricular filling pressure [8]. The E/A ratio increase and the DTE decrease observed after disconnection suggests, therefore, an increase in left filling pressure.

The present study has several limitations. First, the population studied is small and our results have to be confirmed in a larger population. Second, the design of the study focused on patients able to tolerate 1 h of SBT. Similar investigations among patients failing SBT remain to be performed. Third, E/A ratio depends on several parameters such as heart rate and compliance, not only on left-ventricular filling pressure. Recent indexes have emerged as accurate indicators of left-ventricular filling pressure (i.e. E/Ea ratio and color-M mode). However, these indexes have been validated mostly in non-ventilated patients; their contribution to the assessment of cardiac consequences of weaning has still to be confirmed. Fourth, whereas mitral flow measurement has to be done at the end of expiration, we measured mitral indexes at the very beginning of insufflation, when the effect of positive pressure is the most important. We focused more on the variation of mitral flow induced by the shift from positive pressure to spontaneous ventilation than on the absolute values of mitral flow indexes. Fifth, our data could be strengthened by the measurement of other distension indexes such as atrial and ventricular areas.

Conclusions

Successful weaning from mechanical ventilation is associated with an ANP level increase, whereas BNP level variation depends on underlying cardiac abnormalities. Doppler mitral flow analysis using E/A ratio and DTE suggest an increase in the left-ventricular filling pressure.

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