A randomized crossover study of pressure and volume non-invasive ventilation in chest wall deformity

Online Appendix – Detailed Methodology

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Methods

The study protocol was approved by the Local Research Ethics Committee of Leeds Teaching Hospitals. Patients gave written consent to participate in the study.

Patients

An a priori power calculation suggested that a sample size of 10 would have 90% power to detect a difference in mean arterial oxygenation of 1kPa using a paired t-test at 95% significance level. 13 patients with chronic respiratory failure due to chest wall deformity were invited to participate in the study. All were established on and compliant with nocturnal NIV (Mean duration (standard error) of NIV 32 (8) months) and had been stable for at least six weeks. All patients had been using the NIPPY 1 ventilator (B & D Medical, Stratford upon Avon, UK). These ventilators provide pressure controlled ventilation. None were using oxygen at home.

Ventilator Settings

The Breas PV403 (Mölnlycke, Sweden) was chosen for this study since this ventilator offers both pressure support and volume ventilation as an option within the same machine, and was therefore useful in reducing patient bias. Like the NIPPY 1, it uses an exhalation valve and does not provide positive end expiratory pressure. In either mode inspiration is triggering either by patient effort or when the backup setting of the ventilator takes over. During volume ventilation it delivers a constant flow achieving the desired tidal volume (Vt) by the end of a set inspiratory time (Ti). During pressure ventilation, the PV403 delivers a maximal (set) pressure which is maintained until inspiratory flow has dropped to the level of the expiratory trigger or a maximum of 3 seconds has passed. During both modes the inspiratory trigger was set at the most sensitive (-0.1cmH_2O) without autotriggering, and that of the expiratory trigger to 50% of maximal flow (pressure ventilation only). The plateau function (i.e. rise time) was set at the shortest available on the ventilator (arbitrary scale).

During a daytime titration period the patient was initially ventilated using their usual nasal mask (adjusted to minimise leak) and ventilator. Baseline measures of tidal volume, minute ventilation and ventilator set pressure were obtained using a pneumotachometer (Model 3700, Hans Rudolph, Kansas City, MO, USA) placed proximal to the exhalation valve in the ventilator circuit.

The patients were then setup using the Breas ventilator initially in volume mode. The ventilator settings (set tidal volume and inspiratory time) were altered during volume ventilation to obtain the highest comfortable tidal volume with a set ventilator back up rate of 15 breaths per minute. The resultant expired minute ventilation (MVe) was recorded. The ventilator was then changed to pressure mode. Backup rate was kept at 15 min^{-1}. The level of pressure support chosen was that which delivered the same expired minute ventilation as obtained during volume ventilation. Adequacy of ventilation was confirmed by comparison with the daytime minute ventilation obtained with the patients 'usual' ventilator and pulse oximetry. Minute ventilation was at least equivalent to that achieved with the patient's usual ventilator.

Crossover Study

The study design was a 4 week crossover with 2 week washout during which time the patients used their usual, established ventilator. Patients were randomized (concealed computer generated randomization allocation) to receive either four weeks pressure targeted ventilation or four weeks volume targeted ventilation. Settings were defined as obtained above. Patients spent the first (acclimatization) night in the sleep laboratory using their usual ventilator. Full polysomnography and daytime measurements as described below were performed. Patients were then instructed on how to use the 'new' ventilator and went home. The chosen settings were concealed from the patient by a tamperproof cover. A check telephone call was made after 48 hours, and a check overnight oximetry (Pulsox-3, Minolta Corporation, Ramsey, NJ, USA) was performed in the home. Ventilator settings were changed if necessary during the first week to improve patient comfort or to improve oxygenation. When this was performed, the settings for the other period of ventilation (pressure or volume) were altered to maintain equivalence of minute ventilation. At the end of the four week period, patients returned for a full sleep study using the Breas ventilator using the same mode, and subsequent measures as described. A washout period of two weeks then followed when the patient used their usual ventilator before a further sleep study and a further four weeks using the alternate ventilator mode.

Overnight Measurements

At each of the 4 hospital attendances, patients slept in a quiet familiar room. The following measurements were made. Full polysomnography was performed using the Alice 4 sleep system (Respironics, Murrysville, PA, USA). Electro-encephalogram, submental-electromyogram and electro-oculogram were measured with silver cup electrodes and standard lead placements (C3A1, C4A2, O1A1, O2A2)[1]. Oximetry was recorded continuously using a finger probe connected to the Alice 4 system. Transcutaneous carbon dioxide tensions ($tcCO_2$) were measured using a heated skin electrode (TINA, Radiometer, Copenhagen, Denmark). Flow and pressure waveforms were recorded using a calibrated pneumotachometer (model 3700, Hans Rudolph) connected to the Alice 4. Polysomnographs were scored according to standard criteria.[1] The following morning (8am), arterial blood gas tensions were measured using a radial artery puncture (Model 1604, Instrumentation Laboratories, Warrington, England). Patients were awake, and off ventilation for at least 30 minutes prior to arterial puncture.

Daytime Measurements

Following a light breakfast without any caffeinated drinks, patients underwent a series of psychometric and physiological measurements. Spirometry was measured using a Microlab portable spirometer (Micromedical, Gillingham, UK). Maximal (peak) inspiratory and expiratory mouth pressures (PI_{max} and PE_{max}, from residual volume and total lung capacity respectively) and sniff nasal inspiratory pressures (SNIP)[2] were recorded using Pmax Mouth Pressure Monitor (P. K. Morgan, Rainham-Gillingham, Kent, UK). Spontaneous minute ventilation was measured using a heated pneumotachograph connected to a flanged mouthpiece. 3 minutes of recording was made using proprietary software (Research Pneumotach System version 3.07, Hans Rudolph, Kansas City, MO, USA). Hypercapnic ventilatory responses (minute ventilation and mouth pressure 100ms after an occluded inspiratory effort, p0.1) were

recorded using standard techniques.[3][4] The signals from the pneumotach and pressure transducer (MPX 5100, Motorola, Denver, CO, USA) were processed by PC and in-house written software. Further analysis was performed using Origin version 6.1 (Originlab Corporation, MA, USA). A nose clip was worn during these tests.

Chronic hypoxia and sleep deprivation affect frontal lobe function. A series of psychometric measures sensitive to changes in frontal lobe function were used.[5][6][7][8] Health status was assessed by disease specific (MRF-28[9]) and non-specific (SF-36[10]) questionnaires together with the Hospital Anxiety and Depression Scale.[11] The SF-36 has recently been validated for use in patients receiving non-invasive ventilation.[12] Patient activity was estimated using an actimeter (Fitty 3, Kasper & Richter Company, Uttenreuth, Germany). which was used at home in the final week of each pressure or volume 4 week period.[13] Patient comfort in each mode was assessed by 10 centimetre visual analogue scales (VAS).

Reference List for Online Appendix

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