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The effect of continuous positive airway pressures on lung volumes in tetraplegic patients

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Continuous positive airway pressure (CPAP) is widely advocated for the treatment of respiratory complications. However the effects of CPAP on the respiratory function of tetraplegic patients have not yet been investigated. The purpose of this study was to examine the effects of breathing with different levels of CPAP on the relationship between closing volume (CV) and functional residual capacity (FRC) in ten recently injured, but otherwise healthy tetraplegic patients with lesions between the fourth and eighth cervical segments. Lung volumes were measured before, during and after 32 min of zero end-expiratory pressure and 5 and 10 cm H_2O of CPAP. FRC was measured by the open-circuit nitrogen washout method and CV was measured by the single breath nitrogen washout method. FRC was unaffected by zero end-expiratory pressure, but both 5 cm H_2O and 10 cm H_2O of CPAP caused significant increases in FRC. FRC returned to pre-CPAP values by the first minute after removal of 5 and 10 cm H_2O of CPAP. We were unable to measure CVs in any subjects. It was concluded that 5 and 10 cm H_2O of CPAP increase FRC in healthy tetraplegic individuals, but that these increases are rapidly lost with the subsequent removal of CPAP. These results suggest that CPAP may have a role in the treatment and prevention of respiratory complications in tetraplegics.

Keywords: tetraplegia; continuous positive airway pressure; atelectasis

Introduction

Continuous positive airways pressure (CPAP) therapy is widely used to prevent and treat atelectasis.[1,2,3,4] It is believed to increase functional residual capacity (FRC) and widen the gap between FRC and closing volume (CV), reducing the likelihood of airway closure during tidal breathing.[4,5,6] It has been hypothesised that, by preventing airway closure within tidal breathing, atelectasis can be treated and prevented with CPAP.[4]

There are a number of studies that have examined the effect of CPAP on FRC in both healthy subjects[7,8,9,10] and in various patient populations.[10,11] These studies have reported significant increases in FRC with the application of CPAP. In addition, a number of more clinically orientated studies have examined the effectiveness of CPAP for the treatment and prevention of various respiratory conditions, including atelectasis.[1,2,4,12] These studies have reported positive effects from the periodic application of CPAP.

Tetraplegics are at particular risk of atelectasis[13,14,15,16] both because of the inactivity they experience and because of respiratory muscle denervation.[15,17,18,19] To date no studies have looked at the possible uses of CPAP for the treatment and prevention of respiratory complications (other than sleep apnea) in such people, or for that matter, in subjects with similar patterns of respiratory neuromuscular weakness. This study, therefore, was designed to determine the effect of CPAP on the respiratory function of healthy people with tetraplegia. Specifically, the aim was to examine the effects of 5 and 10 cm H_2O of CPAP on the relationship between CV and FRC.

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Methods

Subjects

Ten male subjects participated in the study. All subjects were either inpatients or had recently been discharged from a specialist spinal injuries unit. All had sustained a clinically complete (motor only) cervical spinal cord injury with lesions between the fourth and eighth cervical segments, as determined by a standard clinical neurological examination. Subjects were healthy, with no history of respiratory disease.

Approval for all procedures was given by the institution's Human Ethics Committee and all subjects gave their informed written consent to participate in the study.

Testing protocol

Subjects were required to attend the respiratory laboratory on three separate occasions. With two exceptions, each visit was separated by at least 24 h and by no more than 1 week. In one subject the interval between two tests was 25 days, and in another 33 days. Subjects were asked to refrain from smoking or eating large meals for a 3 h period prior to each test. All testing was done with the subject sitting in his own wheelchair. Restraining straps were removed, and any restrictive garments were loosened.

On the first visit subjects were familiarised with all lung function testing procedures. On this and each subsequent visit the same format was followed. Initially vital capacity (VC), CV and FRC were measured, in that order. Two consecutive measurements were taken of each lung volume and averaged. At least 2 min were allowed between measuring CV and FRC, and 5 min were allowed between subsequent measurements of FRC.

On each visit, measurements of lung volumes were made, and then the subjects were required to breathe for 32 min whilst one of three airway pressures was maintained. The order of pressure application over the three visits was randomised. In this way subjects could act as their own controls. The three pressures were zero end-expiratory pressure, 5 cm H_2O of CPAP and 10 cm H_2O of CPAP. The zero end-expiratory pressure was used to control for the effects of the testing system and testing protocol on respiratory function. CPAPs of 5 and 10 cm H_2O were chosen to represent the range of pressures most commonly used in clinical settings.

Closing volume and FRC were measured 8 and 12 min after the application of CPAP, respectively. Closing volume was measured again at 20 min and FRC was measured again at 22 min. Functional residual capacity was then measured at 1 and 21 min following the removal of CPAP and CV was measured at 11 and 31 min following the removal of CPAP.

Instrumentation

Functional residual capacity was measured by the open-circuit nitrogen washout method. Closing volume was measured using the single breath nitrogen (SBN_2) washout method.[20] Measurement of FRC, CV and VC were made with a computerised pulmonary function testing system (SensorMedics 2200) which incorporated pneumatically controlled valves for switching between O_2 and room air (see Figure 1). Precise measurement of CV is dependent on subjects maintaining an expiratory flow rate of between 0.3 and 0.6 $l.min^{-1}$. Subjects were instructed to maintain, as far as possible, the required flow rates. They were given feedback about their expiratory flow rates from a computer monitor which indicated when the target flow rates had been obtained.

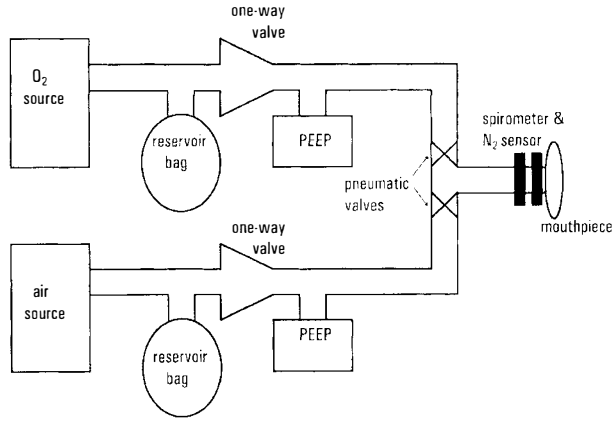

Figure 1 The Sensor Medics Circuitry incorporating the two CPAP circuits

A system was designed to enable CPAP to be administered via the mouthpiece and associated circuitry of the testing system (see Figure 1). Two identical CPAP systems were set up to maintain the CPAP both when the subjects were breathing 100% O_2 for the measurement of FRC and CV, and when the subjects were breathing room air between these tests. The pneumatic valves incorporated within the testing system were used to switch between the two CPAP circuits. Subjects wore a nose-clip throughout the testing sessions. In this way both CV and FRC could be measured whilst maintaining CPAP. The CPAP was maintained using a continuous flow system (60 $l.min^{-1}$) that incorporated a 5 litre anaesthetic bag on the inspiratory limb and a threshold resistor valve (Vital Signs PEEP valve) on the expiratory limb of each of the two circuits. One-way valves were used to prevent rebreathing.

The mass flow sensor was calibrated at the beginning of each testing session and the N_2 analyser was calibrated prior to each CV and FRC measurement. All PEEP valves were initially tested to ensure they were maintaining the desired pressures. In addition, airway pressure was monitored throughout testing by a piezoelectric pressure transducer, placed just distal to the mouthpiece.

Analysis

From the measurement of VC, CV and FRC, values were derived for residual volume (RV) and total lung capacity (TLC). A mean for each of these lung volumes was calculated from all pre-CPAP lung volume measurements. All data was expressed as a percentage of predicted values for able-bodied subjects, as established by the European Community for Coal and Steel.[21] Intra-class correlation coefficients (type 2,1[22]) were generated to test the within-testing-session

and between-testing-session reliability of pre-CPAP FRC data.

All inferential analyses of the effect of CPAP on FRC were performed on the FRC data expressed as a percentage of predicted FRC values. Pressure and time were crossed factorially in a 3×5 repeated measures ANOVA to test for the effect of pressure, time and the interaction of pressure and time. To determine the effect of each level of CPAP on FRC, three separate one-way repeated measures ANOVAs were used. A Dunnett's post hoc test was then performed to determine if any significant differenccs existed between pre-CPAP FRC values and the subsequent FRC values.[23]

Results

Ten subjects completed all testing sessions (mean age 32.9 years with SD of 10.4; height 180.5 cm ($\pm$ 7.7); weight 76.4 kg ($\pm$15). Two subjects had a C4 lesion, five subjects had a C5 lesion, one subject had a C7 lesion and two subjects had a C8 lesion. Two subjects had some intact sensation below the level of the lesion (ie, sensory incomplete injuries). All subjects had sustained their injury no more than 5 years prior to testing (median time since injury 12.5 months with an interquartile range of 10.3 – 18.5 months).

Three of the ten subjects were smokers at the time of testing. The number of cigarettes smoked varied from 12 to 50 cigarettes per day. In addition, five subjects had previously been smokers, with two of these subjects ceasing smoking at the time of their accident and the remaining three subjects ceasing smoking up to 25 years prior to testing. Two subjects had never smoked.

The mean ($\pm$SD) VC, TLC, RV and FRC were 2.73 ($\pm$1.03), 5.94 ($\pm$1.26), 3.21 ($\pm$1.22) and 3.83 ($\pm$1.22), respectively, corresponding to 50.4 ($\pm$19.4), 80.3 ($\pm$12.5), 171.1 ($\pm$56.3) and 110.3 ($\pm$30.5) per cent of predicted values. It was not possible to detect a CV in any of the subjects, with or without the application of CPAP. That is, there was no distinct onset of phase 4 with which to identify a CV. This was despite the fact that all subjects could maintain satisfactory expiratory flow rates.

The procedure used for measuring FRC in this study was highly reliable. The intra-class correlation coefficient describing the agreement between repeat measurements made prior to the application of CPAP was 0.98. The intra-class correlation coefficients describing agreement between testing sessions were 0.88 for the first measurement made in each session, and 0.92 for the second measurement made in each session. This means that more than 88% of the observed between-subject variability was attributable to real differences between subjects, rather than to measurement error.

The FRC data is presented in Figure 2. Functional residual capacity increased with the application of zero end-expiratory pressure and with 5 and 10 cm H_2O of CPAP and then decreased to near pre-CPAP values with its subsequent removal. The effects of pressure ($P = 0.042$), time ($P < 0.001$) and the interaction of pressure and time ($P < 0.001$) were significant. The shape of the FRC-time relationship for the three conditions and the finding of an interactive effect of pressure and time suggests that the effect of pressure on FRC was progressively larger with the progressively higher pressures.

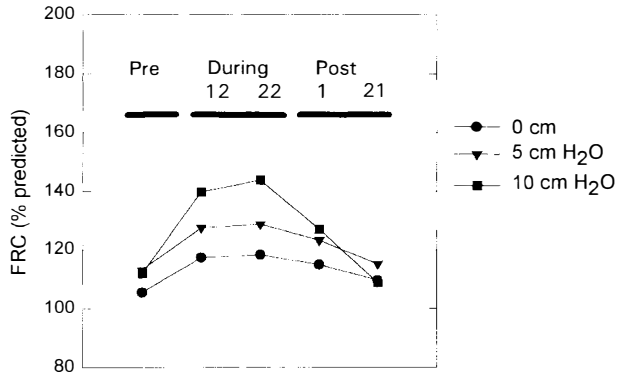

Figure 2 FRC (% predicted) pre, during and post application of zero end-expiratory pressure and 5 and 10 cm H_2O CPAP. The squares represent 10 cm H_2O of CPAP, the triangles 5 cm H_2O of CPAP and the circles zero end-expiratory pressure

The one-way repeated measures ANOVAs for the three different pressures showed that FRC was affected by time for zero end-expiratory pressure ($P = 0.003$), 5 cm H_2O CPAP ($P < 0.001$) and 10 cm H_2O CPAP ($P < 0.001$). The two-tailed Dunnett's test results showed no significant change in FCR with the application of zero end-expiratory pressure. However, with the application of 5 cm H_2O CPAP there was a significant increase at 22 min in FRC. In the 10 cm H_2O condition, FRCs measured at both 12 and 22 min after the application of CPAP were both significantly larger than the pre-CPAP FRC.

Discussion

The results of this study are of interest for three reasons. Firstly, they demonstrate that CPAP increases FRC in healthy tetraplegic subjects, although FRC returns to normal soon after the removal of CPAP. Second, and unexpectedly, subjects did not have a decreased FRC, as has been previously reported. Third, it was not possible to detect a CV in our tetraplegic subjects.

In this study, FRC increased by a mean of 9% and 34% with the application of 5 and 10 cm H_2O of CPAP, respectively. Previous studies that have looked at the effects of similar levels of CPAP on healthy able-bodied subjects have also reported increases in FRC,[7,8,9,10] although the extent to which FRC has been found to increase is highly variable. These studies

have reported mean FRC increases of between 16%[9] and 50%[10] with the application of 5 cm H_2O of CPAP, and of between 24%[7] and 56%[8] with the application of 10 cm H_2O of CPAP. Given the variability in these findings, it is not possible to determine whether the effects of CPAP on healthy tetraplegic subjects are more or less than the effects on other patient groups.

When FRC was measured at 1 and 22 min after the removal of CPAP it did not significantly differ from pre-CPAP values. It would appear, therefore, that any elevating effect of CPAP on FRC is largely lost once CPAP is ceased. Interestingly, Heitz *et al*[10] and Stock *et al*[24] also found that FRC was not significantly different from pre-CPAP values shortly (10 min) after the removal of CPAP.

In this study the mean FRC of the tetraplegic subjects prior to the application of CPAP was 110% of predicted values. In contrast, previous investigators have reported FRC values of between 49%[19] and 88%[15] of predicted values in tetraplegic subjects.[13,15,18,19,25,26] These investigators hypothesize that the decreases in FRC are due to the direct effects of respiratory muscle weakness.[13,27] The present study is the first to report near normal FRCs in tetraplegic subjects.

It is not immediately obvious why our subjects had near normal FRCs. One explanation relates to our use of relatively recently injured tetraplegic patients. The mean time since injury of our subjects was less than 16 months, with a median time of 12.5 months. In contrast all studies to date have examined tetraplegic patients with a mean time since injury of at least 21 months.[13,15,18,19,25,26] It is possible that FRC progressively decreases with time after injury, as a consequence of ongoing changes in pulmonary and rib cage compliance.[17,28] It may be that our subjects had not yet experienced sufficient changes in pulmonary and rib cage compliance to adversely affect FRC. It is difficult to test this hypothesis with the currently available data. However, our data showed a trend towards subjects with more acute lesions having larger FRCs ($P = 0.25$). Similar results were found when the data from all the published studies were pooled. Ultimately longitudinal studies, rather than cross-sectional studies, will be required to test the hypothesis that FRC decreases with time since injury.

It was not possible to detect CVs either with or without the application of CPAP, because there was no clear onset of phase 4 with the SBN_2 test. This could be interpreted to mean either that the airways of those who are tetraplegic do not close at a discreet volume, or that the SBN_2 test is inappropriate for the measurement of CV in tetraplegics. The SBN_2 test may have failed to detect CVs because of the violation of some or all of the assumptions underlying the test. In particular, the test assumes that there are regional differences in the RV : VC ratios.[29,30] It is possible that such regional differences do not occur in the lungs of those tetraplegics which would have made it impossible to establish the necessary nitrogen gradient down the lung after the full inspiration of 100% O_2. The consequence would be that there was no distinct onset of phase 4. Future studies aimed at ascertaining the presence of CVs in tetraplegic people would benefit from further examination of the regional differences in RV and VC.

Without measurements of CV it is difficult to interpret the effect of CPAP on the relationship between FRC and CV. The potential advantage of increasing FRC is that it increases the gap between FRC and CV.[4,5,6] It has been proposed that widening of the gap between FRC and CV helps to prevent premature airway closure[4,5,6] and that by this mechanism CPAP can be used to treat and prevent atelectasis.[1,2,3,4] While our study has demonstrated increases in FRC with CPAP, it has not been possible to ascertain the affect of CPAP on CV. It would seem unlikely that CPAP would increase CV, but this is yet to be experimentally verified. Until the effects of CPAP on CV are known, it cannot be certain that CPAP prevents or reverses airway closure in tidal breathing.

There are several additional questions that need to be clarified before the therapeutic value of CPAP in tetraplegics is established. Firstly, the effect of CPAP on FRC in tetraplegic patients with respiratory complications needs to be determined. Second, it will be necessary to ascertain the effect of CPAP on the work of breathing in these patients. Large increases in the work of breathing would be detrimental to the overall aims of CPAP. Third, the effect of CPAP on cardiac output in tetraplegics needs to be examined. This is particularly important given the impaired cardiovascular control of such persons.[16] Without answers to these questions, it cannot necessarily be assumed that any respiratory benefits derived from CPAP would result in an increase in the delivery of oxygen to the peripheral tissues.

In conclusion, this study has demonstrated that 5 and 10 cm H_2O of CPAP significantly increases FRC in healthy tetraplegic people, but that this increase is largely reversed within 1 min of the removal of CPAP. These results suggest that CPAP may be an effective way of inducing transient increases in FRC. Even transient increases in FRC may widen the gap between FRC and CV and thereby help in both the treatment and prevention of atelectasis. However, to ascertain the precise therapeutic role of CPAP in people who are tetraplegic it will be necessary to examine the respiratory and cardiac effects of CPAP in tetraplegic patients with respiratory complications.

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