The authors tested the hypothesis that, in the paediatric population, the Hering-Breuer reflex would be provoked by the positive pressure inflation of mechanical ventilation (IPPV), and that the strength of the reflex would relate to the child's age and compliance of the respiratory system (CRS). During IPPV, changes in air flow, volume and airway pressure were recorded simultaneously. From the traces, expiratory times and CRS were calculated. The mean expiratory time (Te₁) prior to each inflation and the mean expiratory time (Te₂) immediately following an inflation were determined. The presence of the reflex was indicated by Te₂ being longer than Te₁, and the strength of the reflex was calculated as the difference between Te₂ and Te₁ expressed as a percentage of Te₁. Twenty children were studied who had a mean age of 0.7 years (range 0.1-9.8 years). The reflex was provoked in 19 of the 20 patients and was not seen in the oldest patient. The strength of the reflex varied from 22 to 144% and was inversely related to postnatal age significantly (r = -0.73) but not CRS or inflation volume. It is concluded that the Hering-Breuer reflex is provoked during IPPV in young children; whether, as in neonates, this influences the efficacy of ventilation deserves investigation.

Introduction

The Hering-Breuer reflex has been studied extensively in neonates and demonstrated to be easily elicited in both pre-term (1,2) and term infants (3). There is, however, little information available in older children regarding the occurrence of the reflex or its relationship to postnatal age. Witte and Carlo (4) have suggested that the reflex may also be present outside the neonatal period, as they demonstrated prolongation of inspiration following airway occlusion in children less than 3 years of age. In addition, Greenough and Pool (5) demonstrated the reflex in 13 of 30 asthmatic and six of 18 healthy children aged between 2 and 10 years. The authors postulated that, in children, the Hering-Breuer reflex might be provoked by the positive pressure inflation of mechanical ventilation, as the reflex is usually provoked in adults by a stimulus outside the tidal volume range (6). The aims of this study were, therefore, to assess whether the Hering-Breuer reflex did occur during mechanical ventilation of a paediatric population and, if it did, did the strength of the reflex relate to the patient’s age or compliance of the respiratory system (CRS).

Methods

Children admitted to the Paediatric Intensive Care Unit at King’s College Hospital, London, U.K., who were intubated and ventilated, were eligible for entry into the study. While ventilated, children have measurements of CRS to facilitate choice of optimum ventilator settings. Recordings from children who were making spontaneous respiratory efforts during such studies were analysed to determine the presence of the Hering-Breuer reflex. During ventilation, changes in air flow, volume and airway pressure were recorded simultaneously (Fig. 1). A pneumotachograph (Mercury F100L) attached to a Validyne pressure transducer (range ± 2 cmH₂O) was inserted between the endotracheal tube and ventilator circuit. The pneumotachograph measured flow changes which were integrated electronically to give volume (Gould 13-4615-70). Airway pressure was measured from the child’s side of the pneumotachograph using a Validyne pressure transducer (range ± 88 cmH₂O). The pressure transducers were calibrated against a water manometer. The frequencies of response of the transducers and attached tubing were checked by a balloon burst technique and were less than 6 ms.
Compliance of the respiratory system was calculated from the volume change resulting from a positive pressure inflation maintained until there was no further change in volume divided by the difference between the peak inspiratory pressure (PIP) and positive and expiratory pressure (PEEP). Only ventilator breaths in which there was no interference from spontaneous respiratory effort were included in the analysis of CRS.

**Analysis**

The relationship of the strength of the Hering-Breuer reflex to age, CRS or inflation volume was calculated using Pearson's product moment correlation coefficient. The relationship of the coefficient of variation of the reflex to age, and the length of expiratory time to the inflation or inspired volume, were assessed similarly. Stepwise regression was undertaken to further explore possible relationships.

**Patients**

Twenty children with a median age of 0.7 years (range 0.1–9.8 years) were studied. Ten patients had liver disease, eight had infection and two had intracranial pathology. At the time of study, their median PIP was 23 cmH$_2$O (range 10–36 cmH$_2$O), positive end expiratory pressure (PEEP) was 3 cmH$_2$O (range 2–6 cmH$_2$O), ventilator rate was 25 bpm (range 8–40 bpm) and inspired oxygen concentration was 0.33 (range 0.21–0.85). All of the patients received conventional ventilation in triggered mode. Their median PaO$_2$ was 96 mmHg (range 53–114 mmHg) and PaCO$_2$ was 37 mmHg (range 27–59 mmHg).

The study was approved by the King's College Hospital Ethics Committee and parents gave informed consent prior to entry to the study.

**Results**

The Hering-Breuer reflex was provoked in 19 of the 20 patients and was not seen in the oldest patient. The median strength of the reflex was 72% (range 22–144%) with an intra-subject coefficient of variation of 27% (range 0–72%). The median CRS of the children was 1.85 ml cmH$_2$O$^{-1}$ (range 0.52–241 ml cmH$_2$O$^{-1}$). The strength of the reflex was related significantly to postnatal age ($r = -0.73$, $P<0.01$ (Fig. 2), but not to CRS ($r = -0.36$) or inflation volume ($r = -0.34$). The significant relationship of the strength of the reflex to age remained ($r = -0.51$, $P<0.03$) when the results of the oldest child were excluded from the analysis. The intra-
subject coefficient of variation of the reflex was also inversely related to the age of patient \( (r = -0.38) \), but this was not statistically significant. The lengths of the expiratory times were related to the respective inflation \( (r = 0.58, P < 0.02) \) or inspired volumes \( (r = -0.47, P < 0.05) \). Nevertheless, stepwise regression analysis confirmed a significant relationship between the strength of the reflex and postnatal age \( (P < 0.01) \), but not CRS or tidal volume.

**Discussion**

The present results show that the Hering-Breuer reflex can be provoked by the positive pressure inflation of mechanical ventilation in young children. An inverse relationship between the strength of the reflex and age has been demonstrated, which supports the authors' previous findings that the reflex tended to be seen in younger children with asthma (5). Witte and Carlo (4) were not able to show a correlation between the Hering-Breuer reflex and postnatal age. They, however, used a different technique to provoke the reflex, that is end expiratory occlusion, and only included nine patients aged between 2 and 29 months. Rabette et al., also using a different technique, demonstrated a statistically significant reduction in the strength of the reflex of 32% over the first year of life (7); those data would support the present findings. Although the reflex could not be elicited in the oldest child (9.8 years), it cannot be concluded that there is a critical age beyond which this reflex does not occur, as the authors demonstrated the reflex in a healthy child aged 10.2 years previously (5).

As in previous studies (8), there was a variability in the results obtained. This has been seen previously in pre-term infants (9), full-term infants (10,11) and young children (4). It thus does not seem to be related to age. That hypothesis is supported by the finding of a lack of significant relationship between the coefficient of variation of the reflex and postnatal age. Despite the variability, the authors were able to show a significant association between postnatal age and the strength of the reflex.

Previously, the authors have found (12) that in premature infants, studied in the neonatal period, the strength of the reflex increased with decreasing lung compliance. This may be explained by the discharge from pulmonary stretch receptors (via which the reflex is mediated) being increased if lung compliance is low (13). In this study, there was an inverse relationship between the strength of the reflex and lung compliance, but this did not reach statistical significance. The present patients, however, all had stiff lungs when compared with reported values for ventilated children (14,15), and this may have obscured any relationship.

In this study, the Hering-Breuer reflex was deemed present if the expiratory time immediately post-extubation was longer than that associated with the previous spontaneous inspiration. Although the expiratory times were related to the respective inspiratory/inflation volume, no significant relationship between the strength of the Hering-Breuer reflex and delivered volume were demonstrated. In addition, stepwise regression analysis confirmed that the relationship between postnatal age and the strength of the reflex was independent of delivered volume. A possible problem with the lung inflation technique is that the duration of the apnoea may be related to the chemoreceptor input during prolonged periods of stretch receptor stimulation (16). To demonstrate the reflex, however, none of the study population were subjected to maintained positive pressure inflations, but were studied during 'routine' ventilation. An alternative method of assessing the presence of the Hering-Breuer reflex is to occlude at end expiration (4) or end inspiration (8). That, however, would mean disconnecting the child from the ventilator and, thus, the authors felt that this would mean that the results were less relevant clinically. The clinical importance of demonstrating this reflex in ventilated patients was that it was provoked by positive pressure inflation and, thus, extrapolating from information from neonates, might mean that reflex activity could influence the effectiveness of ventilation.

In neonates, the nature of the infant's respiratory activity has an important influence on the outcome of mechanical ventilation (17). In particular, those...
infants in whom the active component of the Hering-Breuer reflex was demonstrated developed a pneumothorax (18). To date, no study has been undertaken to assess whether such an association occurs in children, although it is appreciated, in that population as in infants, that respiratory efforts which are thought to be ‘asynchronous’ clinically interfere with the effectiveness of ventilatory support. The authors have now demonstrated that one component of the Hering-Breuer reflex is provoked by positive pressure inflations. Therefore, it does not seem unreasonable to hypothesize that, as in neonates (17), the nature of the reflex respiratory activity may influence clinical outcome.

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References