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Effects of an opioid on respiratory movements and expiratory activity in humans during isoflurane anaesthesia☆

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ABSTRACT

Opioids increase abdominal muscle activity during anaesthesia. We proposed that opioid activity during anaesthesia would change chest wall size and movement, and contribute to ventilation. Using an optical system to measure chest wall volume, we studied 10 patients during isoflurane anaesthesia, first under the influence of an opioid and then after reversal with naloxone. Measurements were made during quiet breathing and with carbon dioxide stimulation. Airway occlusion pressure was measured to assess inspiratory and expiratory muscle activity. Chest wall volume decreased with the onset of spontaneous breathing, and decreased further when breathing was stimulated by carbon dioxide. Reversal of opioid activity increased chest wall volume. Breathing movements were predominantly abdominal. Opioid action affected the timing and amplitude of breathing but the pattern of abdominal movement was not affected. Since opioids augment abdominal muscle action during expiration, the unchanged pattern of movement can be attributed to both diaphragm and abdominal activity displacing the abdominal wall reciprocally, in the inspiratory and expiratory phases of the respiratory cycle, respectively.

1. Introduction

1.1. Opioid effects during clinical anaesthesia

Opioid agents are frequently administered in the course of general anaesthesia, primarily to reduce autonomic and motor responses to stimulation. Opioids have profound effects on breathing. Opioids prolong expiration and thus reduce breathing frequency (Drummond, 1983; Lalley, 2003), reduce responses to stimuli such as carbon dioxide (Rigg et al., 1981), and activate expiratory muscles (Freund et al., 1973; Howard and Sears, 1991). The primary cause of some of these effects is unclear: for example, if an opioid reduces respiratory rate, the cause of increased tidal volume and altered muscle activation may be the result of hypoventilation and the resulting hypercapnia (Ferguson and Drummond, 2006).

1.2. Muscle action with opioid administration

Abdominal muscle activation after opioid administration may reduce lung volume (Chawla and Drummond, 2008; Wyche et al., 1973) and impair gas exchange (Drummond and Lafferty, 2010) as well as augment respiratory depression. Although the effects of general anaesthetics such as halothane on muscle activity and chest wall movements have been studied (Warner et al., 1995; Warner and Warner, 1995) the effects of opioids on chest wall volume and respiratory movements have not been formally assessed. In circumstances such as exercise, abdominal contraction can augment ventilation. The activation of abdominal muscles by opioids during anaesthesia (Drummond et al., 2011) may have similar effects.

1.3. Study aims

We set out to compare breathing movements in the presence and absence of opioid activity, using an optical method to characterise chest wall size and movement. We studied anaesthetised subjects, breathing spontaneously. In addition we used occlusion of inspiration to assess possible chest wall distortion, and occlusion of expiration to quantify the force generated by the expiratory muscles. To assess these features under different conditions, we

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antagonised the activity of the opioid with naloxone, and stimulated respiration with carbon dioxide.

2. Methods

2.1. Subjects

The study was approved by the appropriate French ethical and regulatory authorities (Comité Consultatif de Protection des Personnes se Prêtant à la Recherche Biomédicale de l'Hopital Henri Mondor, dossier 95-038) We recruited patients about to undergo superficial or peripheral surgical procedures (for details, see Section 3) We did not recruit patients who were obese or gave a history or had clinical evidence on routine testing of either cardiac or respiratory disease. The patients provided written consent after being given full information about the study.

2.2. Anaesthesia

Anaesthesia was induced with propofol and maintained with nitrous oxide, isoflurane, and intravenous fentanyl, which were clinically appropriate agents at the time of the study. The trachea was intubated. Vecuronium or atracurium were used for neuromuscular block, carefully monitored by train of four stimulation of the ulnar nerve. After the surgical procedure was complete, we placed the patient on a measurement board with the body, from shoulders to hips, supported by a plastic bead mattress that was then made rigid by removing the air within it (Vac Pac, Howmedica, Newbury, UK). We made sure that the lumbar spine and flanks were fully supported. The head rested on a pillow and the lower body on a folded cotton sheet, adjusted to support the legs and protect the heels. The arms were covered in non reflective material.

2.3. Measurements

Respiratory gas flow was measured with a pneumotachograph (Mercury FC10, Mercury Instruments, Glasgow, UK) and differential transducer (Furness FC044, Bexhill-on-Sea, UK) calibrated with flows of 70% nitrous oxide in oxygen. The flow signal was used only to measure the timing of respiration. Volume changes were measured by the optical system described in Section 2.4. Pressure at the airway opening was measured with a Validyne DP 45 transducer (Northridge, CA, USA). Patients breathed from a custom made breathing system designed to keep airway pressure close to ambient (Drummond et al., 2011). Large bore taps placed in the inspiratory and expiratory tubing, close to the valve, were used to intermittently occlude single episodes of inspiration or expiration. Gas was sampled from the centre portion of the valve for continuous analysis of carbon dioxide (Normocap 200) and isoflurane concentration (Normac, both Datex Instrumentation, Finland). Gas sampling was discontinued during occlusion manoeuvres. The inspired and expired gas tubing was connected via wide bore sidearms so that when the fresh gas supply to the inspiratory tubing was reduced, partial rebreathing of exhaled gases could occur. Thus excessive fresh gas flows were not required when ventilation was stimulated by adding carbon dioxide to the inspired gas, to facilitate induction of a stable state of hypercapnia.

2.4. Optical measurements

Chest wall movement was measured using an optical measurement system (Drummond and Duffy, 2001). Briefly, a narrow beam of red laser light is spread by a cylindrical lens into wide beam that forms a narrow line when it falls on the measured surface (Fig. 1). With a precisely controlled mirror, the beam is rapidly moved to a series of known pre-set positions on the surface. The shape of these lines of light depends upon the contour of the body surface, and is detected by a video camera placed in an accurately known position above the subject. We used subdued green ambient lighting and a filter specific for HeNe laser light on the video camera, so that the red laser light showed up brightly in the video picture. By use of the scanning process of the video picture system, the light beam position in the video image can be measured extremely rapidly. The exact vertical contour of the line of illumination, measured as the distance above the reference surface, is calculated. These vertical contours are then assembled to form sections of the object. The horizontal position of the light strips is known from the degree of movement of the mirror galvanometer. From the contour of the vertical plane and the distance between each contour, changes in chest wall volume are computed and the changes in volume during respiration are calculated. These measures of respired volume are unaffected by drift, which is a weakness of systems that use flow integration. Before each patient study the system calibration was checked by scanning a test object of known volume, placed on the reference surface.

2.5. Measurement procedure

On each subject, we set line positions between which we expected to detect movement, to define the limits of the chest wall (Fig. 1). The top line was placed at the manubrium, at the junction of the first rib, and the bottom line at a level midway between a line joining the anterior superior iliac spines and the cranial margin of the pubic bone. The interface between the rib cage and abdomen was defined by a middle line placed 2 cm below the caudal tip of the xiphisternum (in Fig. 1, this middle line is also labelled Ab1, RC5). For scans of the complete chest wall, from manubrium to pubis, lines were placed equidistant between top and middle lines, and between middle and bottom lines, and these 5 lines were used to scan the movements of the whole chest wall. For scans of the rib cage, three lines were placed equidistant between the top and middle lines, so that the section of chest wall between the top and middle lines could be scanned using 5 lines. For a scan of the abdomen, three lines were placed equidistant between middle and bottom lines so that the abdominal part of the chest wall was scanned with 5 lines. The middle line was included as the most caudal line in scans of the rib cage and as the most cranial line in scans of the abdomen. The central lines of the ribcage and abdomen scans were the same lines as those used in the scan of the complete chest wall (Fig. 1). Those lines that were common for scans of the whole chest wall, rib cage, and abdomen, were used to assess the repeatability of the measurements during mechanical ventilation. During a measurement sequence, a profile was measured at each individual line position every 20 ms, so that all five lines were measured in 0.1 s. During subsequent data analysis, the areas in the intervening periods for each line were estimated by linear interpolation between the successive values, to allow calculation of the chest volume each 20 ms, and provide synchronous data. Each successive volume was thus derived from 1 contemporary and 4 time-adjusted interpolated values.

2.6. Data management

For quantitative measures, volumes of the scanned surface were calculated using data from separate scans of the rib cage, abdomen, and the entire chest wall, using the distance between adjacent line positions and the area under each measurement line. For qualitative purposes, such as plotting the pattern of movement of the chest wall, scans of rib cage and abdomen were