EFFECT OF CIGARETTE SMOKE ON FUNCTIONAL RESIDUAL CAPACITY (FRC) IN DOGS

Smoking causes an immediate increase in airway resistance and decrease in expiratory airflow, presumably through airway reflex effects. The consequences of these changes on lung ventilation, pattern of respiratory muscle activation, control of functional residual capacity (FRC) and the cough reflex are unknown. These issues are important to distinguish between potentially harmful and potentially beneficial reflex effects of cigarette smoking. Inhalation of cigarette smoke results in activation of irritant receptors and consequent more rapid, shallow breathing pattern (1,3,4). We hypothesize that: a) lung defence reflexes induced by cigarette smoke serve to prevent deep inhalation of smoke and maintain appropriate ventilation; b) smoking alters the pattern of respiratory muscle activation resulting in greater expiratory muscle activation and associated changes in FRC. Activation of expiratory muscles may increase the mechanical advantage of the diaphragm and improve electromechanical coupling of this muscle and b) smoking results in a heightened expiratory muscle response to a given stimulus, thereby enhancing the cough reflex.

Both irritant receptors and C-fiber endings are stimulated by cigarette smoking (1,3,4). At least a portion of the acute responses to cigarette smoke are evoked by stimulation of these receptors. The most common reflex responses evoked by stimulation of irritant receptors and C-fibers are a reduction in tidal volume and increase in breathing frequency. In **Objective I**, we will assess the acute changes in tidal volume, breathing frequency and blood gas exchange in response to cigarette smoking. The contribution of various respiratory muscles to breathing pattern will be assessed by monitoring thoraco-abdominal motion via inductance plethysmography. Since studies are to be performed in anesthetized animals, factors related to external monitoring, subject bias, mood and non-specific other psychological factors will be controlled.

An increase in airway resistance during smoking produces respiratory load which may be compensated by an increase in expiratory muscle activation (5). There are, however, opposite reflex mechanisms evoked by stimulation of irritant receptors and C-fiber endings. The defense reflexes from lungs increase the tonic activity of inspiratory muscles during expiration and shorten the expiratory phase. These effects, accompanied with an increase of airway resistance, are known as elements of expiratory braking. The phenomenon of expiratory braking serves an important role in adjusting functional residual capacity (FRC) and maintain appropriate ventilation. Overall effect of cigarette smoke on expiratory muscle performance and expiratory

braking has never been evaluated. The action of expiratory muscles, however, is crucial for the regulation of FRC and optimizing the work of the diaphragm (5,7). In **Objective II**, we plan to assess the effects of cigarette smoke on the pattern of respiratory muscle activation and control of FRC. The electrical activity of the major inspiratory muscles (diaphragm, external intercostal and parasternals) and major expiratory muscles (internal intercostals, triangularis sterni, transversus abdominis and external oblique) will be monitored before and after smoke inhalation. The mechanical output of these muscles will also be monitored by measuring respective length changes with sonomicrometry. The level of FRC will be measured by monitoring thoracoabdominal motion by means of inductance plethysmography.

One of the most pronounced lung defense reflexes during cigarette smoke inhalation is cough. During cigarette smoke inhalation airway mucosal sensitivity may be enhanced resulting in facilitated expiratory muscle activation. We have shown that mechanical stimulation of trachea potentiate expiratory muscle action. On the other hand, stimulation of C-fibers endings by cigarette smoke inhibits expiratory muscle activation (2) and may reduce expiratory effort during cough. In our preliminary experiments (6), however, we have documented that inhibitory phasic vagal input from pulmonary stretch receptors during cough is abolished. It is also possible that inhibitory input from vagal C-fibers is also gated during cough. In **Objective III**, we will evaluate the sensitivity of the cough reflex before and after smoke inhalation. We will also study the role of vagal afferents during cough evoked by mechanical laryngeal stimulation. Experiments will be performed before and after vagal cooling.

METHODS

Experiments will be performed on anesthetized dogs in supine position, tracheostomized and breathing spontaneously. EMGs of laryngeal, rib cage and abdominal respiratory muscles will be recorded. Airway, gastric and esophageal pressures, tidal volume, and end-expiratory pCO_2 will be recorded. Abdominal and rib cage circumference will be monitored separately by means of inductance plethysmography.

Animals will be breathing from large airbags filled with air or the mixture of air with cigarette smoke of different concentration. Cough will be evoked by mechanical stimulation of trachea with and without simultaneous inhalation of cigarette smoke. Some experiments will be performed before and after vagal cooling to abolish vagal reflexes. Cough will also be evoked by mechanical stimulation of the larynx. Expiratory muscle activation, airway pressure generation and airflow will be monitored. All above-mentioned experimental procedures are routinely performed in our laboratory. Results will be elaborated statistically using ANOVA, t-test and post-hoc Neuman-Keuls test.

OBJECTIVE I

Experiment 1. We will measure parameters of lung ventilation, rib cage and abdominal circumference as well as end-tidal PCO_2 and arterial blood gas exchange. The experiments will be repeated after cooling the vagi to block nerve conductance. In this study, we will evaluate the role of vagal reflexes in shaping the respiratory rhythm to maintain ventilation and protect the lungs against irritating agents.

OBJECTIVE II

Experiment 1. We will record activation of expiratory rib cage and abdominal muscles during cigarette smoke inhalation.

Experiment 2. Recording of upper airway laryngeal muscles (sternohyoid, genioglossus) and hypoglossal nerve activation in response to cigarette smoke inhalation.

Experiment 3. Recording of upper airway resistance by means of continuous airflow passing by isolated upper airway. We will compare the changes of upper airway resistance produced by cigarette smoke inhalation with effects induced by applying mechanical expiratory load. In Experiments 1-3, we will study the braking mechanism and reflex control of FRC.

Experiment 4. Measurements of diaphragm, parasternal and external intercostal EMGs and operating muscle length before and during cigarette smoke inhalation. In this experiment, we will study the effect of changes in FRC on the work of respiratory pump muscles.

OBJECTIVE III

Experiment 1. We will compare action of expiratory muscles during cough evoked by mechanical stimulation of trachea with and without inhalation of cigarette smoke. In this experiment, we will study the role of cigarette smoke in sensitization of expiratory muscles during cough.

Experiment 2. We will study vagal facilitatory influences during cough by means of vagal cooling. Cough will be evoked by mechanical laryngeal stimulation.

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