



**Karolinska
Institutet**

Institutionen för Fysiologi och Farmakologi
Sektionen för Anestesiologi och Intensivvård

Airway Protection and Coordination of Breathing and Swallowing in Health and Anesthesia

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Karolinska Institutet
offentligen försvaras på engelska i Nanna Svartz Auditorium,
Karolinska Universitetssjukhuset Solna,
Fredagen den 8 November 2013, kl 09.00

av

Anna Hårdemark Cedborg

Huvudhandledare:

Professor Lars I Eriksson
Karolinska Institutet
Institutionen för Fysiologi och Farmakologi
Sektionen för Anestesiologi och Intensivvård

Bihandledare:

Med. Dr. Eva Sundman
Karolinska Institutet
Institutionen för Fysiologi och Farmakologi
Sektionen för Anestesiologi och Intensivvård

Fakultetsopponent:

Professor Shiroh Isono
Chiba University, Chiba, Japan
Graduate School of Medicine
Department of Anesthesiology

Betygsnämnd:

Docent Silvana Naredi
Umeå Universitet
Institutionen för Kirurgisk och
Perioperativ Vetenskap

Professor Mikael Norman
Karolinska Institutet
Institutionen för Kvinnors och Barns Hälsa

Adj. Professor Magnus Ruth
Göteborgs Universitet
Sahlgrenska Akademien
Avd. för Öron-, näs-, halssjukdomar

Stockholm 2013

ABSTRACT

Swallowing and breathing is coordinated to ensure that the airway is protected from aspiration. During the pharyngeal phase of swallowing, breathing is interrupted to allow safe passage of bolus. However, details on the complex coordination of breathing and swallowing and their precise temporal relationship are not fully understood. Respiratory complications are common in the postoperative period and drugs used in anesthesia impair pharyngeal function and airway protection in young adults. The aims of this thesis were first to characterize key mechanisms for airway protection, *i.e.* pharyngeal function and coordination of breathing and swallowing and secondly to describe the impact of age and drugs used in anesthesia.

A newly developed airflow discriminator was validated by comparisons with spirometry, diaphragmal and abdominal EMG and integrated with pharyngeal manometry and videoradiography into a multimodal platform recording swallowing and breathing simultaneously with high temporal resolution. Normal coordination of breathing and swallowing was studied in young volunteers, while swallowing different bolus types, changing body position and during hypercapnia. Moreover, effects of morphine and midazolam were studied at two occasions during spontaneous decay of drug concentration. Effects of partial neuromuscular block were examined during rocuronium infusion in elderly volunteers (>65 years) at steady state adductor pollicis train-of-four ratios of 0.70, 0.80 and >0.90.

The airflow discriminator proved highly reliable and provided detailed information on timing of respiratory airflow unambiguously in relation to pharyngeal and diaphragmatic activity. The diaphragm was activated in the apneic period during swallowing, presumably a mechanism for preserving respiratory volume and to promote expiratory airflow after swallowing. This finding has to our knowledge not been described in humans before. Coordination between breathing and swallowing remained mostly unchanged regardless of age, body position, bolus characteristics, respiratory drive or partial neuromuscular block. In contrast, morphine and midazolam dys-coordinated breathing and swallowing, increasing the incidence of inspiration immediately after swallowing. Moreover, clinically relevant doses of morphine and midazolam caused pharyngeal dysfunction and impaired airway protection in young adults. Partial neuromuscular block profoundly aggravated age-dependent pharyngeal dysfunction by predominantly impairing mechanical properties of the pharynx.

In conclusion, swallowing occurs during expiration in young and elderly individuals and drugs used in anesthesia cause pharyngeal dysfunction and dys-coordination of breathing and swallowing, ultimately compromising the protection of the airway against aspiration.

Keywords: pharynx, control of respiration, breathing, swallowing, deglutition, anesthesia, morphine, opioids, midazolam, benzodiazepines, partial neuromuscular block, partial paralysis, rocuronium, airway protection, aspiration, sedation, postoperative pulmonary complications