Göteborg, 2018

Isocapnic hyperventilation in anaesthesia practice
Clinical and experimental studies

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Hjärtats Aula, Sahlgrenska Universitetssjukhuset, Göteborg, fredagen den 23 februari 2018, kl. 9:00

av Katarina Hallén
Leg. Läkare

Fakultetsopponent:

Professor Claes Frostell

Institutionen för kliniska vetenskaper, Danderyds sjukhus, Karolinska Institutet, Stockholm

Avhandlingen baseras på följande delarbeten

I. **A simple method for isocapnic hyperventilation evaluated in a lungmodel**.
Hallén K, Stenqvist O, Ricksten S-E, Lindgren S
Acta Anaesthesiologica Scandinavica 60 (2016) 597–606

II. **Isocapnic hyperventilation shortens washout time for sevoflurane – an experimental in vivo study**.
Hallén K, Stenqvist O, Ricksten S-E, Lindgren S
Acta Anaesthesiologica Scandinavica 60 (2016) 1261–1269

III. **Evaluation of a method for isocapnic hyperventilation: a clinical pilot trial**.
Hallén K, Jildenstål P, Stenqvist O, Ricksten S-E, Lindgren S
Acta Anaesthesiologica Scandinavica 62 (2018) 186-195

IV. **Isocapnic hyperventilation provides early extubation after major ear-nose-throat surgery: a prospective randomized clinical trial**.
Hallén K, Jildenstål P,Oras J, Stenqvist O, Ricksten S-E, Lindgren S
Manuscript

SAHLGRENSKA AKADEMIN
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Abstract

Background: Isocapnic hyperventilation (IHV) has been shown to shorten recovery time after volatile anaesthesia by accelerating elimination of inhalational agents by increasing minute ventilation while maintaining normal carbon dioxide (CO_2) levels. It has also been shown that IHV reduces time spent in postoperative care units (PACUs). There are several principally different ways to maintain the CO_2 level during hyperventilation but IHV methods currently in clinical use has unfortunately not reached wider clinical implementation. The original method of directly adding CO_2 to the breathing circuit of the anaesthesia apparatus during hyperventilation was abandoned in the 1980ies, partly due to development of short acting anaesthetic agents and partly due to the risk of hypercapnia associated with this procedure. Thus, this particular IHV-method has not been studied to a great extent since then, although a considerable technical development of anaesthesia delivery systems and methods for monitoring airway gas concentrations have taken place in the last 30 years.

Aims: The aims of the present thesis were: 1) to investigate if a method of adding CO_2 directly into the breathing circuit using standard monitoring equipment and mechanical hyperventilation, provides effective and safe isocapnic hyperventilation, 2) to quantify the amount of delivered CO_2 and to construct a nomogram for CO_2 delivery during isocapnic hyperventilation at various physiological conditions, 3) to assess whether elimination of volatile anaesthetics can be accelerated using this IHV method, 4) to evaluate the clinical feasibility of this IHV method, 5) to compare the perioperative outcome for this IHV method to a routine wake-up method in a two-armed randomized study

Methods: Studies were performed in a mechanical lung model with simulated metabolism, in an experimental porcine model and in patients undergoing major head and neck surgery. A standard breathing circuit with a 450-ml CO_2-mixing box connected to the inspiratory limb was used. A CO_2 bottle was connected to the mixing box. CO_2 flow was manually regulated by a high precision mechanical flow meter, dosed according to a nomogram during a standardized hyperventilation procedure using mechanical ventilation. The expired ($FETCO_2$) and inspired ($FICO_2$) fraction of CO_2 values provided by the standard monitoring equipment, were used to monitor CO_2-levels, also confirmed by arterial blood samples. Electric impedance tomography (EIT) was used in the porcine study for monitoring lung volume changes during hyperventilation. In the clinical studies, the end-points were time to extubation, eye-opening and time to discharge from the operation room (OR) as well as postoperative measurements of pain, nausea and cognition according to the Postoperative Quality of Recovery Scale (PQRS).

Results: In a bench study, we established a nomogram for CO_2 delivery when base-line minute ventilation was doubled, to achieve IHV. In an animal experiment, the method proved to increase the elimination rate of anaesthetic gas without any relevant respiratory or circulatory side-effects. In a clinical pilot study, the nomogram was validated. In all studies a $FICO_2$ level of about 3 % produced stable isocapnia, provided that the study protocol was followed. In the randomized prospective study, a shortening of time to extubation by 50 %, time to eye-opening by 34 % and time to discharge from OR by 30 %, was noted. We could not find any statistical difference in cognitive ability in the PACU after waking with IHV compared with a "standard" wake up procedure.

Conclusions: The described method for isocapnic hyperventilation is a safe technique when used in the clinical setting with the intention to decrease emergence time from inhalation anaesthesia. It has been shown to present no increased risk to patients.

Keywords: Hypercapnia, Hyperventilation, Hypocapnia, Electric Impedance Tomography, Weaning, Ventilator Weaning, Anesthesia Recovery Period

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