Turk J Anaesthesiol Reanim 2017; 45: 59-62 DOI: 10.5152/TJAR.2017.84770

Some Considerations Regarding the Pro and Con articles between Drs. Hedenstierna and Pelosi on Intraoperative Ventilation and Pulmonary Outcomes

Dr. Hedenstierna ile Pelosi'nin İntraoperatif Ventilasyon ve Pulmoner Sonuçları Konusundaki Lehte ve Aleyhte Makaleleri Hakkında Bazı Düşünceler

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Dear Editor,

I have carefully read the instructive pro and con articles by Drs. Hedenstierna and Pelosi et al. in this journal regarding protective pulmonary ventilation and positive end expiratory pressure (PEEP) use (1-4). I wish to make some comments. Throughout the years, 'protective lung ventilation' during anaesthesia -low tidal volume (VT), low to moderate PEEP and recruitment manoeuvres- a concept evolved from intensive care unit (ICU) ventilation therapy, was developed and clinically applied, as stated by the authors. Moreover, this was not without controversies. In addition, the role of respiratory rate, driving pressure and FiO_2 has been underlined in the articles. However, from my point of view, the application of these physiology-based concepts has some flaws.

First, we need to distinguish lung ventilation in a critically ill patient from that in the intraoperative procedures with general anaesthesia. The authors have adequately addressed this topic, so it does not require more comments (4). However, only some patients under general anaesthesia perhaps need individualized treatment (approaching these of the ICU patients), such as the obese, the elderly, patients suffering from an obstructive/restrictive pulmonary disease and trauma patients. Moreover, measurements were performed in a standby/resting/without surgical manipulation status, and this is far from real-life situations.

Second, we need to distinguish between the intraoperative and immediate postoperative period. Classically, it was realized that after anaesthesia induction, functional residual capacity decreased, and this was due, in part, to the loss of inspiratory muscle tone (5) (see ref 5 for related articles from the 70s to 90s of the past century). Please take into account here that muscle tone has been cited for the first time. This includes muscles acting on the rib cage and the diaphragm (2). Again muscle strength is involved.

In the postoperative period, mainly following abdominal and cardiothoracic surgery, these considerations persisted (5). In fact, experts stated that the mechanism is the combined effect of incisional pain and reflex dysfunction of the diaphragm (5). However, this has been inferred from studies in animals and physiology models, and several types of pre- and post-operative respiratory rehabilitation procedures (3, 5) and epidural analgesia (5-7) did not perform as expected.

It is evident that partial neuromuscular blockade in awake, supine subjects results in a markedly reduced functional residual capacity (5). The muscles involved one more time.

Here I cite Pelosi et al. (3): …*it is mentioned that recent large number of multicentre studies on "protective ventilation" and post-operative lung complications have not sufficiently taken the emergence from anaesthesia into account and have not had any control over lung aeration postoperatively*…, and *The emergence from anaesthesia may be the most important part of the peri-operative period and focus should be switched from the anaesthesia per se to the emergence*… In my opinion this is the key question.

However, this has largely been addressed to date. There are several large observational studies and controlled trials demonstrating the residual effects of neuromuscular blocking agents (8, 9) (see ref. 8 for detailed explanation) that interact with

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Received / Geliş Tarihi : 12.12.2016
Accepted / Kabul Tarihi : 23.12.2016

other patient, procedure-related and drug factors. Dealing with these residual effects is easy and affordable, in order to provide strength to the (respiratory) muscles.

The most deleterious complications after surgery are of respiratory origin. The most important factor in the immediate postoperative recovery of muscle tone is the muscle itself. Thus, we need to make the (respiratory) muscles stronger.

Intraoperative ventilation management is, of course, important, but are the actions taken during this period long lasting? Sophisticated studies have been devoted to this topic, showing promising results and improvement in the intraoperative oxygenation, improvement sometimes, but not always, in postoperative outcomes (10), furthermore not all factors of the protective ventilation play a definite role (3).

If you read carefully the material and methods part of all these articles, you can realize that no data on neuromuscular management have been provided (11-15). At the very best, neuromuscular blocking agent use is left at the discretion of the anaesthesiologist-in-charge. In addition, scores developed to predict postoperative pulmonary complications did not consider muscle relaxants (6, 7), and neuromuscular blockade management is included in a whole item as 'intraoperative management' or 'intraoperative drugs'. This way, one of the main determinants of postoperative pulmonary complications remains uncontrolled..

Linking this paragraph with the previous ones, we can deduce that one possibility (perhaps not the only one, but important) is to completely reverse the effects of neuromuscular blocking agents using antagonists, i.e., correctly titrated neostigmine or SPACE-better-SPACE sugammadex and to not allow a spontaneous reversal (8). If the anaesthesiologist can control pain, core temperature, residual blockade and, of course, ventilation, the patients' immediate recovery would be significantly improved. But consciousness recovery and postoperative cognitive dysfunction is another story altogether (16). The management and reversal of neuromuscular blocking agents should be registered in the methods and showed in the results section of studies focussing on postoperative pulmonary complications.

Conflict of Interests: CLE has received payment for consulting MSD for the past 3 years. There are no conflicts of interest regarding the present article.

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Author's Reply

Injurious Ventilation and Post-Operative Residual Curarization: A Dangerous Combination

We have read with interest the commentary from Dr. Errando (1) regarding our debate concerning the use of positive end-expiratory pressure (PEEP) (2-5), which appeared on the *Turkish Journal of Anaesthesiology and Reanimation.* We agree with most of the observations raised by our colleague, but some issues deserve further comments.

We believe that, as pointed out by Dr. Errando, knowledge on the intraoperative management of the surgical patient has increased strikingly in the last decade: it is now commonly accepted, following pathophysiologic studies and large randomized trials, that a low tidal volume (6-8 mL kg^{-1} predicted body weight) can reduce the incidence of postoperative pulmonary complications (PPCs), while additional controversies have arisen concerning the role of PEEP (2-5). It has also been suggested that the observed reduction of postoperative lung complications need not only be attributed to "protective ventilation" but also to postoperative lung care (6).

Nonetheless, we recognize the need to identify specific categories of patients that might benefit from tailored protective ventilation during surgery (7). The PROBESE trial (8) will clarify whether obese patients benefit from a fixed higher PEEP level, while the iPROVE study (9) is investigating the efficacy of a complex bundle of interventions, including individualized PEEP titration based on the best compliance of the respiratory system measured during a decremental PEEP trial. In the latter case, the investigators employ a method similar to that in use in critically ill patients, as claimed by Dr. Errando, while in the former, a more pragmatic approach with a standard PEEP level was preferred. Recent studies have identified that driving pressure (i.e. plateau pressure minus PEEP), is independently associated with outcome in critically ill patients with acute respiratory distress syndrome (ARDS) (10) and in surgical patients (11). At a given tidal volume, the driving pressure is inversely proportional to the compliance of the respiratory system. Despite disagreements on optimal setting of initial PEEP value, these recent findings on driving pressure translate into a clear clinical message: in case the clinician decides to change PEEP, it should be titrated on the best compliance rather than rely only on improvement in gas exchange, which might be influenced by changes in regional perfusion. In addition to the parameters mentioned in this discussion, such as respiratory rate, energy load, and fraction of inspired oxygen, another field of research we expect will grow in the next years is the role of spontaneous breathing during anaesthesia (12). The increasing availability of sophisticated anaesthesia machines, allowing easy detection of respiratory mechanics parameters as well as combination of controlled/assisted/spontaneous modes of ventilation, might increase the possibility of translating the results of such studies to clinical practice.

Postoperative respiratory dysfunction is a complex entity, comprising pathophysiologic elements due to baseline patient conditions, intraoperative surgical and anaesthesiological management, as well as factors peculiar to the postoperative period (13). Among the latter, a major role is played by postoperative atelectasis, pain, analgesic drugs, and muscular dysfunction, including postoperative residual curarization. The diaphragm, the major inspiratory muscle, is an important regulator of expiration, and its activations prevent decreases in lung volume and formation of atelectasis. The loss of diaphragmatic expiratory contraction during mechanical ventilation and muscle paralysis may be an important factor contributing to the development of atelectasis during the extubation phase and immediate postoperative period, leading to pulmonary complications and respiratory failure (14). Dr. Errando focused most of his discussion on the latter aspect. While we recognize a role of neuromuscular blocking agents (NMBAs) in contributing to PPCs, we point out that is very difficult to include a systematic analysis of the role of NMBAs in prospective cohort studies (such as those aimed at developing risk assessment scores), due to the extreme variability in the choice of drugs, reversal agents, and intraoperative monitoring. Sugammadex, mentioned by our colleague, is an almost perfect model for rapid and complete reversal of neuromuscular blockade (15). However, a recent meta-analysis comparing it to neostigmine (16) could only include small-sampled randomised trials, few of which reported postoperative clinical outcomes. Therefore, we must be cautious when advocating the use of NMBA reversal for preventing PPCs, since those drugs have side-effects. Nevertheless, we do not believe that the lack of information concerning NMBA management should compromise interpretation of results arising from large multicentre randomised trials; like any other confounding factor, its effect is mitigated by the randomisation process, provided that the sample size is adequate. Several other factors, e.g., fluid administration, transfusion policies, analgesic regimens, and temperature management, have also been poorly investigated in studies focusing on intraoperative mechanical ventilation and PPCs.

Another important issue that must be clarified in future research is the role of noninvasive continuous airway pressure or noninvasive ventilation as a preventive measure to restore respiratory function in the immediate postoperative period. While its value for a treatment of hypoxemia in the surgical patient is well established (17), there is little evidence to support its routine use as a preventive strategy in moderate- to high-risk patients (18). Ongoing trials are expected to build stronger evidence (19).

In conclusion, it is likely that in the next few years a considerable body of evidence concerning intraoperative mechanical ventilation will be obtained. Therefore, we agree fully with Dr. Errando: it is time to focus also on the postoperative period!

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