

Current developments in anaesthesia and neuromuscular transmission

This supplement is based on two interesting meetings where experts and opinion leaders were invited to present the state of art in their particular fields of interest. The first meeting, a symposium on the Current Developments in Anaesthesia, took place in Barcelona earlier this year, whereas the second meeting, the 7th International Neuromuscular Meeting was held last June in Belfast. The latest developments in the field of pharmacology and physiology of the neuromuscular transmission were presented in the meeting in Belfast and investigators were invited to illustrate their recent work not only in oral presentations but also in poster-discussion sessions. Only the abstracts of the posters of this meeting could be included in this supplement. The majority of scientific information presented in this supplement is from the meeting held in Barcelona. The central theme of this meeting, 'Current Developments', covered various aspects of concern to anaesthesiologists such as developments in health care, science, surgery, and of course, developments in anaesthetic care.

The first two contributions in this supplement are dedicated to quality management and pharmacoeconomics. Two important developments can be established in the process of quality improvement, i.e. the patient becoming more and more a customer requiring optimal service and the anaesthetist evolving in the role of the perioperative physician, who manages the patient from the preoperative visit, during the operative procedure and in the postoperative period assuming responsibility for optimal management of pain and any other discomfort [1].

Pharmacoeconomics is more than simply bringing down the cost of acquisition of anaesthetic drugs [2]. Although cost-minimization is essential, a more holistic approach to anaesthetic practice appears indicated to improve quality of care. Efforts should be made to measure other potential benefits of a particular anaesthetic procedure such as the satisfaction of

the surgeon and well-being of the patient. The outcome of these cost–benefit studies should be employed to optimize daily clinical practice.

Anaesthetic care has been improved to a large extent due to long-term close co-operation between clinicians and the university and industrial scientists [3]. The technology of pharmaceutical research has evolved from small scale chemical synthesis and testing in animal models to selection of possible drug candidates out of huge molecular libraries followed by a high throughput large scale screening of these molecules and their structural relatives in target-assays [4]. University investigators have been working in parallel to unravel the factors governing the effect and the time-course of action of drugs [5]. Industrial funding has facilitated much of the work in the universities. Still, more and more basic research is carried out within the pharmaceutical industry itself. Although this collaboration in drug research appears essential for both the pharmaceutical companies and the universities, funding from the industry for fundamental research is under pressure. This is due on one hand to an exponentially increasing drug development cost and shortage of new leads and, on the other hand to declining profits due to increased competition and governmental price controls.

Reduction in health care costs is an important argument for the transition from inpatient to day care surgery, although the growth of minimally invasive surgery has contributed much to this development [6]. The success of day care surgery has been paralleled by increase in outpatient departments for anaesthetic pre-assessment, availability of better anaesthetic drugs, and developments in surgical procedures [7]. The growth in the number of surgical interventions that can be carried out under day care conditions suggests that the boundaries of outpatient surgery in the future will be almost solely dictated by the preoperative condition of the patient. It is still an open

question as to how far further progress in quality of anaesthetic care can stretch these boundaries.

The use of muscle relaxants in day care surgery seems limited and restricted to surgery requiring tracheal intubation and for interventions that require profound paralysis [8,9]. The interventions in day care surgery are usually short lasting requiring a muscle relaxant and/or a dose with a short duration and a fast recovery. The variation in response even to the short acting non-depolarizing muscle relaxants is large, necessitating pharmacological reversal at the end of the procedure. When this reversal is carried out appropriately, an increase in postoperative nausea and vomiting is unlikely [10]. Both the provision of optimal muscle relaxation and optimal reversal of effects of the relaxant require the use of monitoring of neuromuscular block.

Developments in some important areas in anaesthesia, such as in management of the airway, the use of the rapid sequence induction, anaesthetic strategies in day care and introduction of new relaxants such as rapacuronium, that could play an important role within the areas mentioned above were presented at the meeting in Barcelona. Management of the airway is crucial for the anaesthetist. A broad range of tools helpful in securing the airway are now available [11]. Every anaesthetist should make a selection for his/her own armamentarium, that will enable them to solve difficult airway problems from supraglottic abnormalities like restricted mouth opening to infraglottic abnormalities like a traumatic tracheal rupture. Fibre optic intubation is currently regarded as a gold standard in the treatment of the difficult airway and anaesthetists should therefore have the skills to perform this technique.

Rapid-sequence induction (RSI) is a collective term for a variety of techniques used for securing the airway rapidly in those at risk of regurgitation and aspiration of gastric contents. It may or may not include the use of opioids and/or relaxants [12,13]. The use of opioids in this technique is still open to debate. The use of succinylcholine as the sole neuromuscular relaxant for RSI has been challenged by some investigators, who showed that high dose rocuronium could be an alternative, at least in some situations. Anaesthesia needs to be deep to enable smooth and rapid intubation with non-depolarizing agents; this can be obtained by using hypnotics in high doses (with

increased risk of hypotension) or by adding an opioid to the induction regimen (with theoretical likelihood of vomiting and aspiration). While choosing between the two, it is important to remember that nausea and vomiting are rarely observed when opioids such as fentanyl are administered during induction of anaesthesia in elective cases, whereas opioids can prevent nausea and vomiting due to hypotension and attenuate the stress response of intubation.

Rapacuronium, a new non-depolarizing relaxant with a short to intermediate duration has been developed for short-lasting interventions and was therefore regarded as a potential agent for inducing paralysis for day care procedures [14]. Its time course of action with a rapid onset and a fast recovery may be due to its fast equilibration with the effect compartment due to on one hand, a high equilibration rate constant and on the other hand, a high initial clearance from the plasma [15]. While the onset of action of rapacuronium may be close to that of succinylcholine, intubating conditions and the offset characteristics do not seem to match those of succinylcholine. In the United States the first experiences were quite promising one year after its introduction in daily clinical practice [16]. However, bronchospasm and/or increased airway pressure, the aetiology of which remains undetermined at this time, have been reported after its use. Although most of these events have been mild and self limiting, some have been severe enough to result in oxygen desaturation and requiring treatment with bronchodilators. Based on these reports, Organon decided to voluntarily withdraw rapacuronium temporarily from the market and undertook efforts to identify the mechanism by which the drug causes bronchospasm. However, it was announced recently that these efforts have not given any hope for finding the mechanism. Organon has therefore decided not to reintroduce rapacuronium. It was already known from earlier experiences with low potency compounds that a compromise between the desirable characteristics of rapid onset and short duration of action and the occurrence of side-effects would have to be accepted. Rapacuronium was the result of the search for such a suitable compromise that did not fulfil the initial high expectations.

It appears to be difficult, if not impossible, to design and produce a rapid and short acting non-depolarizing relaxant (equivalent of succinylcholine) from the

current series of competitive neuromuscular blocking agents. An alternative may be to facilitate early reversal of block from a rapid acting agent such as rocuronium. Recently successful experiments have been carried out in this direction using the principle of chelation. A specially designed encapsulating cyclodextrine has been shown to fully reverse a rocuronium-induced block within 2 min in monkeys as well as in other animal species without causing cardiovascular and/or pulmonary side-effects [17,18]. Further developments in this direction will be keenly awaited. There is still hope that the industry and anaesthetists together will attain the ultimate goal of having a non-depolarizing block of rapid onset and very short and/or flexible duration!

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