Editorial III

Neurokinin-1 antagonists: a step change in prevention of postoperative nausea and vomiting?

The ability to reliably treat and prevent postoperative nausea and vomiting (PONV) still remains elusive, despite significant advances in our understanding of the physiology of emesis and availability of several new antiemetics. This is unfortunate as patients are really concerned about, and often fear, nausea and vomiting in the perioperative period. However, although of concern, it is not considered by many anaesthetists as one of the most important things to avoid during anaesthesia. For example, a group from San Diego asked a panel of expert anaesthetists what clinical anaesthesia outcomes are both common and important to avoid. The list in order of importance was: death, recall with pain, nerve injury, recall without pain, damage to teeth, corneal abrasion, vomiting, post-dural puncture headache, pain, and nausea. Patients’ perception of problems to avoid during anaesthesia is very different. They expect to survive, most regard being asleep and unaware as par for the course, and most would not expect to awake with damaged nerves, eyes, or teeth. Indeed, the same team in San Diego asked patients what outcomes they thought were important to avoid during anaesthesia. Their response in order of importance was: vomiting, gagging on the endotracheal tube, nausea, recall without pain, residual weakness, shivering, sore throat, and somnolence. Another measure of how much PONV is an issue for patients is to ask them how much they would pay to be free from emesis after surgery. In 2001, a survey of patients in the USA revealed that they were willing to pay $55–100.3 Quite a sum when you allow for 8 years of inflation.

The incidence of PONV is still generally regarded as ~30%, but clearly depends on patient and surgical factors. Four of the most important risk factors are: female gender, non-smoking, previous history or motion sickness, and the use of perioperative opioids.6 It has been estimated that the risks of PONV after inhalation anaesthesia is 10%, 20%, 40%, 60%, or 80% in the presence of none, one, two, three, or four of these factors, respectively.5 The incidence may be less with total i.v. anaesthesia, but there is no doubt that PONV is still a common and troublesome complication.

A recent Cochrane review gave an enlightening summary of the relative efficacy of antiemetics used for PONV (Table 1). These data show relatively disappointing efficacy compared with placebo (especially with respect to nausea) and the need for better therapy. The 1990s saw the introduction of the 5-HT3 antagonists with claims by some that they heralded the end of PONV. Sadly, this was not the case; data in Table 1 show how they compare with others. These disappointing results gave impetus to the developing concept at that time of multiple therapy for PONV which was proving to be more effective than monotherapy.8 This approach has now become standard practice in many clinical situations and has been adopted in national and local guidelines for the prevention of PONV, especially in high-risk cases.9

Mortality from anaesthesia in developed health-care services, although devastating, is very rare; service improvements are focused on quality and PONV is a major issue in this regard. In addition, the complications associated with PONV are well known, for example, aspiration of stomach contents, disruption of surgical sutures, dehydration, and electrolyte disturbance. Clearly, this problem...
is worthy of continuing research and investment, hopefully leading to the introduction of new antiemetics. In this issue of the British Journal of Anaesthesia, Diemunsch and colleagues 10 review the physiology of emesis and the present status of NK-1 antagonists in the prevention of chemotherapy-induced emesis and PONV. They describe how the work of Andrews in the early 1990s identified that NK-1 receptors were involved in the final stages of the emetic reflex (and possibly peripheral sites) and how this led to the investigation of NK-1 antagonists as antiemetics.11 Presently, there are more than a dozen compounds in various stages of development. Chemotherapy seems to be of more interest to the pharmaceutical companies than PONV and new antiemetics are often first tested for this indication; this applies also to NK-1 antagonists. The review demonstrates that the NK-1 antagonists so far studied do not represent a step change in efficacy when used alone and compared with other antiemetics. The data on PONV are slightly more promising as some studies have shown NK-1 antagonists to be more effective than 5-HT3 antagonists. Indeed, Apfel and colleagues 12 in their recent review of the current data described the antiemetic properties of aprepitant as ‘unique’ but claimed that this is hidden by the fact that it is no more effective against nausea than other agents. However, PONV data are comparatively sparse and more work is required to elucidate the full picture with confidence.

There is no doubt that NK-1 antagonists have significant efficacy for the prevention of PONV. However, the data so far do not indicate that they will become the long-awaited panacea for this indication. They will not replace the need for combination therapy in high-risk cases and not replace the need for preoperative risk evaluation and protocol-driven management of this feared and sometimes dangerous postoperative complication.

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<thead>
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<th>Nausea</th>
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