General multimodal or scheduled risk-adopted postoperative nausea and vomiting prevention: just splitting hairs?

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Worldwide, more than 230 million major surgical procedures are performed each year. For these patients, postoperative nausea and vomiting (PONV) are among the most frequently observed adverse events associated with the provision of general anaesthesia. It is distressing to patients and impairs the quality of recovery as judged by the patients and anaesthesiologists alike. Our patients obviously dislike PONV and are willing to spend a considerable amount of money to eliminate the problem.

Decades ago, this clinical nuisance was named the ‘big little problem’ of anaesthesia, indicating that it may not be a big issue for anaesthesiologists, but it matters to our patients. When Patricia Kapur used the term ‘big little problem’, it was not entirely possible to eliminate PONV and the knowledge about the additive effects of antiemetics was still in its infancy. In the subsequent years, various drugs were investigated in-depth by adequately powered randomized clinical trials and meaningful meta-analyses; these drugs now constitute the core armamentarium of any anti-PONV algorithm. Finally, PONV has been among the most investigated adverse effects of the perioperative period. After Phil Scuderi’s statement with the title ‘Multimodal antiemetic management prevents early postoperative vomiting after outpatient laparoscopy’, the PONV community has been working on how to get rid of the ‘big little problem’.

To achieve this goal, there is more than one option to consider. First, owing to the fact that the existing armamentarium consisting of low-dose corticosteroids (dexamethasone), ondansetron, a potent D2-antagonist (e.g. droperidol), anthihistamines (e.g. dimenhydrinate), and NK-1 antagonists, and the omission of trigger factors by means of using a total i.v. anaesthesia, are considered relatively safe; so far, there is little indication to withhold these strategies for fear of side-effects. Indeed, there is rationale to give more than one or two antiemetics to everybody as Scuderi recently pointed out in an editorial: ‘given the extremely low cost of all the currently available generic antiemetics and the extremely low incidence of adverse side-effects, I would suggest that all patients might benefit from 3 or more antiemetics during the course of surgery to reduce the incidence of PONV as much as possible’.

The second principal option would be to tailor the therapeutic decisions to specific groups of patients based on their relative risk and thus embracing a kind of ‘stratified medicine’. The baseline risk of PONV in an individual having a specific surgery and anaesthetic may be assessed using a validated risk score that is based on the (weighted) sum of independent predictors. Such prognostic models have been used to guide preventive therapy. Yet, there are conflicting results on the use of PONV risk scores to significantly reduce the institutional rates of PONV. After an enthusiastic update—based on established guideline recommendations—of totally risk-adopted approaches to prevent PONV with zero prevention in supposed low-risk patients, there has been an intense debate and discussion whether these approaches actually work in a busy clinical environment. Up to now, for all of us who are not convinced about the overall positive net benefit of the antiemetic interventions mentioned earlier, such an approach would be the best way to achieve as much benefit as possible with the least potential for adverse effects; providing that the scores do work.

A third approach would be to treat PONV if symptoms actually arise. Clearly, this would lead to an increased PONV incidence, but if symptoms are detected early enough and then an aggressive treatment by means of multimodal drug-administration can be instituted without delay, at least the best net benefit (in terms of numbers-needed-to-treat) would be generated. However, the findings of a recent clinical trial showing that emetic symptoms, and particularly nausea, are frequently missed in a busy clinical scenario render such an approach invalid. This observational study shows that only 42% and 29% of PONV episodes were actually detected by the regular staff in the post-anaesthesia care unit (PACU) and on the ward, respectively. Therefore, such a concept would clearly demand a very alert environment in which patients are adequately informed and encouraged to report any signs of nausea, and moreover, a rapid and aggressive treatment would need to be ensured. These two prerequisites prohibit such an approach based on aggressive treatment, in particular in children, where a valid assessment of emetic symptoms, especially with respect to the feeling of nausea, is limited. Further, such an approach is incompatible with busy environments where nursing staff and physicians are short of time and a close monitoring of PONV symptoms and an appropriate response (instant and effective treatment) cannot be ensured for at least 24 h after anaesthesia.

What remains the best choice at the end of the day is highly dependent on the environment and the clinical scenario, and especially the guideline compliance of the suggested
algorithm to prevent PONV. Modelling various scenarios, however, has clearly shown that under the assumption of additive effects, the eventually observed PONV incidence is highly dependent on the amount and number of antiemetics used. This means that it is unlikely that significant effects can be generated with little investment in antiemetic use.

In principle, the overall performance and validity of stratified approaches mainly rests upon

- the ability to correctly classify the PONV risk,
- the potential of antiemetics to cause adverse effects,
- the cost of antiemetics, and
- the clinical applicability and compliance with strictly stratified algorithms.

While the first question is subject to ongoing analyses of prognostic tools to assess the risk for PONV, the second issue is already extensively addressed with no convincing evidence to withhold antiemetics in an appropriate (low) dose. The costs may be an argument for some of the newer molecules, but these have decreased dramatically, and should not be a significant hurdle to effective PONV management.

The clinical applicability and compliance with stratified algorithms is a decisive question and a tricky one since a proper answer may only be valid for a specific scenario.

Kappen and colleagues\(^ {24}\) have picked up the weaknesses of simple automated PONV score generators with a more sophisticated approach of adding therapeutic recommendations based on the calculated risk. This paper is in line with a set of investigations taking into consideration one major weakness of current risk-adapted approaches: apart from the accuracy of the prediction rules—the actual implementation in a clinical scenario.

The latter, unfortunately, indicates poor compliance with most of the investigated algorithms. This phenomenon was described for adults\(^ {25} \) and paediatric patients.\(^ {26}\) Therefore, some studies suggested the introduction of electronic reminders to improve compliance with standard operating procedures.\(^ {27,28}\) The bottom line of these papers was that it is feasible to increase guideline compliance as long as the automated reminder is active. However, the compliance seemed to be relatively short-lived and it quickly wore off if an automated reminder was switched off.

The argument that poor education is the root cause for the reluctance to administer appropriate antiemetic prophylaxis seems to be invalid, since the problem persists even after intense educational activities.\(^ {29}\) In this study, after training and continuous provider feedback, only 47% of the patients at moderate (two risk factors present) and 37% of the patients at high risk (three risk factors present) actually received the scheduled prophylactic treatment using a very simple algorithm that suggested administering one antiemetic per risk factor. In contrast, almost all patients received single antiemetic prophylaxis, which was the de facto standard at the site where the study was conducted before the interventions took place. The message in this analysis clearly was that ‘keep it simple’ does not seem enough to succeed with an antiemetic algorithm. An effective PONV prevention needs to be self-evident and accepted in the clinical routine, and it needs to be coupled with specific advice on how to deal with an increased risk; this has been the basis of the current paper published in this issue of the British Journal of Anaesthesia.\(^ {24}\)

In this prospective before–after study including more than 1400 elective surgical inpatients, the before-period included care-as-usual and the after-period incorporated a directive risk-based (intervention) strategy.

Some of us may feel it reassuring that during the intervention period, anaesthetists administered 0.5 [95% confidence interval (CI) 0.4–0.6] antiemetics more per antiemetic advised. Further, the sophisticated analysis confirms recent findings\(^ {30}\) that an increased administration rate of PONV prophylaxis actually resulted in a reduction in the observed PONV incidence [odds ratio (OR) 0.60, 95% CI 0.43–0.83], with an even greater reduction in PONV incidence in high-risk patients (OR 0.45, 95% CI 0.28–0.72).

However, we should bear in mind, that even in this study, as stated in the Results section ‘The incidence of PONV was 42% during the intervention period, compared to 50% during the care-as-usual period’. In simple words, this means that nearly every second patient experienced some degree of PONV even after the decision-support with direct advice on how to prevent PONV was set up during the observation period. Clearly, one could argue that PONV, when measured in a dichotomous way, is by no means a clinically significant impairment of the recovery. However, taking into account recent analyses on the severity of PONV episodes, as a rule of thumb, roughly one-third of the PONV patients experience severe PONV.\(^ {31}\)

The results could be interpreted two-fold. One explanation could be a too restrictive recommendation regarding the use of antiemetics leading to a relatively poor (under-treatment) protection of patients. The other explanation is simply that even with rather directive approaches and specific advice to use antiemetics, the compliance is not as good as it could be. The latter seems to be true in the current analysis if we can read that ‘during the intervention period anaesthetists complied with the recommendation of the clinical decision support tool and administered the recommended number of prophylactic antiemetics in 66% of patients’. This means that even with such a tool and in the environment of a clinical study, only two-thirds of patients were actually treated according to the suggested guideline.

The fact that during the intervention period, for each additional antiemetic advised, the anaesthetists actually administered 0.49 (95% CI 0.41 – 0.58) additional antiemetics, reflecting a statistically significant increase, is in the author’s view a weak consolation taking into account the overall poor protection against PONV.

This paper nicely reflects that personalized medicine is associated with considerable hurdles and barriers that need to be overcome, irrespective of the fact that the tools for a proper risk assessment to predict PONV may not be optimal.\(^ {32}\) With an average rate of PONV of about 20–30% and often even higher,\(^ {33}\) there is still a long and winding road to making a real change happen for our patients undergoing surgical procedures each day.
However, this important paper is not an exception with its rather pessimistic achievements. In an analysis of an educational strategy based on systematic preoperative assessment with the simplified Apfel’s score, ‘before’ and ‘after’ patient populations were actually not very different as far as the rate of administration of antiemetic prophylaxis (31.4% vs 36.8%) is concerned. The only difference was in the rate of administration of antiemetic prophylaxis in the high-risk group (with an Apfel simplified score >2), which reached statistical significance (36.4–52.8%). Such observational data again and again underscore the observed extremely low compliance with institutional PONV policies. In another report, it was stated that only 37% of medium- and high-risk patients received the specified prophylaxis, leading to suboptimal PONV prevention in moderate- and high-risk patients. In order to streamline the postoperative recovery without having postoperative sequelae, fast-track protocols have often incorporated multimodal preventive PONV strategies. These bundles of care may be viewed as being a little too simplistic, but they may prove more effective than strictly risk-based approaches in a clinical scenario where overall compliance with too much complexity and stratified action is poor.

It is reassuring and encouraging to note that the current SAMBA guideline explicitly states the goal for antiemetic multimodal prevention to become an integral part of anaesthesia. Whether you practice a liberal multimodal preventive protocol or a risk-adapted (but nonetheless liberal) anti-PONV algorithm may be indeed splitting hairs as long as anaesthetists view PONV prevention as self-evident as preventing and treating pain. With pain, we have already accepted that single interventions are not capable of eliminating the problem and we apply multimodal analgesia without totally eliminating pain in the PACU and on the ward. In contrast, the added value of additional analgesics is rather weak. Therefore, we should accept that some of the oldest problems associated with anaesthesia, that is, the ‘big little problem’ PONV, may be tackled quite effectively. This chance should be enthusiastically picked up. Providing we apply the attitude of ‘zero tolerance’ and do not accept that PONV does not really affect the outcome of our patients, the PONV-free hospital is a realistic goal. One rule of thumb for creating and implementing most efficient PONV protocols could be ‘the simpler, the better’, and a liberal use of preventive measures rather than a too restrictive one.

**Declaration of interest**

P.K. is editor of the European Journal of Anaesthesiology. As principal investigator, he has participated in numerous clinical trials investigating new substances to prevent or treat postoperative nausea and vomiting.

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