Possibilities and limitations in the pharmacological management of PONV today*

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Introduction and background knowledge

Incidence of postoperative nausea and vomiting

The incidence of PONV after a standard anaesthetic technique consisting of inhalational anaesthetics plus opioids and no postoperative nausea and vomiting (PONV) prophylaxis is still up to 30%. Being one of the most common complaints following surgery under general anaesthesia, it is not surprising that PONV remains a considerable cause of dissatisfaction with recovery from anaesthesia and remains one of the most commonly applied items in surveys assessing patient satisfaction with the peri-operative period as well as scoring systems for the quality of recovery following anaesthesia. It is estimated that anaesthesia is administered to approximately one in ten of the population in France each year [1]. It is reasonable to assume that these figures can be extrapolated to other European countries. This means that in a worst case scenario up to 22 million patients suffer from some degree of PONV every year in Europe (estimated population ~ 731 million [2]) if no prophylaxis is used.

Importance of the medical problem

Due to the fact that – at least for healthy patients – anaesthesia-related mortality and morbidity have fallen dramatically in the recent decades [3, 4], outcome parameters focusing on the dimensions of ‘well-being’ and ‘patient satisfaction’ are gaining importance. PONV can lead to a substantial prolongation of recovery room stay or even lead to a prolongation of hospital stay or unplanned overnight hospital admissions with the associated increased costs for patient care and may have significant financial consequences. For paediatric patients these consequences have been recently explored in detail from information in a large database. This revealed that PONV is among the most common causes of ~ 1-2% of unplanned hospital admissions following outpatient surgery [5]. Despite their rarity, serious consequences secondary to the occurrence of vomiting may occur and are described in the anaesthesia literature every year. These may include aspiration pneumonia, Boerhaave’s syndrome, severe subcutaneous emphysema, pneumothorax, rupture of the trachea and loss of vision. Such complications may be viewed as the visible part of the iceberg, but may equally be considered as a warning sign not to underestimate this problem [6-13].

Current guidelines and consensus statements

Despite the existence of recommendations to manage PONV on an international [14], European [15] and national or local level [16], surveys published on guideline-adherence or the actual application of institutional PONV-policies in routine patient care strongly suggest that the implementation is rather poor. This is surprising since associated costs or the fear of severe adverse effects with the liberal use of prophylactic antiemetics are not valid arguments to withhold them any more. Furthermore, the existing consensus recommendations not only provide vague and abstract recommendations regarding the use of preventive measures but sometimes even give examples on how these recommendations can be implemented in terms of standard operating procedures.
Guideline adherence with PONV protocols

In view of the aforementioned framework it is surprising that in a recent analysis even close and individual feedback for anaesthetists in conjunction with CME activities was unable to significantly improve compliance with PONV standard operating procedures and did not prevent insufficient therapy for medium or high risk patients only [17]. In the latter group (patients with three risk factors [18]), in which – according to the standard of care in that hospital – patients should receive three antiemetics, only one-third of patients received the scheduled treatment. In another recent survey it was concluded that, irrespective of the existence of a carefully worded institutional policy to manage PONV better that was published in multiple formats (intranet, print version, booklet), ‘... PONV in routine clinical care is likely to be underreported’ [19]. If such a scenario cannot be ruled out in a given hospital setting, this may be an argument not to rely on treatment as opposed to thorough prophylaxis [20]. Instead, such findings suggest that sufficient prophylactic antiemetics should be applied ‘to reduce the incidence of PONV as much as possible’ [21].

These considerations may be viewed as an argument to critically re-assess the existing guidelines and recommendations, which mainly rely on a risk-adapted approach, with respect to their practicability. The guidelines frequently suggest that antiemetics should not be administered in low-risk patients. Some of the consensus guidelines advocate the use of risk-models by stating that ‘the use of prophylactic antiemetics should be based on valid assessment of the patient’s risk for PONV or PONV’ [14]. Most colleagues inherently interpret such statements as advice to use anti-emetic prophylaxis only if the patient’s individual risk is sufficiently high. Although such a recommendation seems to be convincing at first sight, actual clinical implementation is far less clear. So far there is no common consensus of the ideal threshold when the risk for PONV is sufficiently high to warrant anti-emetic prevention. Furthermore, the ideal way of performing an individual risk assessment for the likelihood for PONV remains unclear. One option for a risk assessment, and thus for the implementation of a risk-adapted algorithm, consists in applying one of the numerous risk scores for PONV that have been developed in the past years. The plethora of available risk scores to predict PONV in adult patients witnesses the fact that, at least so far, none of the available tools seems to satisfy all needs. While being excellent tools to educate colleagues regarding the most important risk factors for populations, recent analyses [22] demonstrate that the predictive properties of such PONV-scores are limited and it is unlikely that future scores will improve this situation.

Without doubt systematic research to elucidate risk factors for PONV have condensed the long list of supposed risk factors into a memorable number of important factors, which seems important for both research questions (e.g. calculating an average expected risk in a group of patients), as well as individual risk assessment in selected cases and facilitates evidence-based teaching. However, taking into account the results of recent research regarding the implementation of PONV scoring systems into clinical practice and the reluctance to act according to institutional standard operating procedures and to provide effective antiemetic prophylaxis especially in high risk patients [23-26], it may be concluded that the statement to save anti-emetic interventions for those patients who need them most, i.e. high risk patients, and thus withhold antiemetics for a considerable proportion of patients, is among the most important hurdles to eliminating this complication.

Barriers to the implementation of PONV guidelines

It may be speculated that the most dominant hurdle to overcome is not the risk-adaptation per se (which could theoretically mean the administration of two antiemetics to every patient and then to increase the number of antiemetics to three or more if the risk seems to be above average) but the fact that restricting antiemetics to patients at risk implicitly suggests that current available antiemetics put patients at risk of suffering side-effects. To fully account for such a laudable risk-benefit analysis using each individual patient’s preferences would require an extensive pre-operative assessment. All that we know so far, for example by using conjoint analyses, willingness-to-pay investigations and other techniques frequently used for marketing management, is that patients simply do not want to suffer from PONV and appreciate the avoidance of this annoying symptom [27, 28]. This, in the author’s opinion, may be viewed as a sufficient justification for a more liberal use of pharmacological management of PONV. Such reasoning may even be applied if the hurdles of insufficient guideline adherence and assessment of symptoms when using a traditional risk-adapted PONV-algorithm [14, 29] are overcome in an institution.
Looking at the previously cited arguments to withhold effective anti-emetic prevention such as acquisition costs, unknown efficacy and supposed adverse effects, we should take for granted that a huge body of evidence suggests that these are not valid any more, provided relevant contra-indications are taken into account.

Steps to better prevent PONV in routine practice

The evolving question that is important today must be therefore: how can we ensure that patients really benefit from the huge amount of studies performed in the area of PONV and thus translate evidence into patient benefit? A provocative and prominent statement by Phil Scuderi recently concluded that: “….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 three or more antiemetics during the course of surgery to reduce the incidence of PONV as much as possible” [21]. These changes in attitude, from questioning the value of prophylactic antiemetics in terms of improved patient satisfaction [20] to the suggestions of a surprisingly liberal use of anti-emetic agents without individual risk-calulation, is based on shifting environmental conditions (perception of PONV as a relevant outcome, decreasing costs of antiemetics, increasing demand for a smooth and predictable recovery, well-investigated drugs in terms of their efficacy and effectiveness as well as their side-effect profile) and may be viewed as a shift in the paradigm of PONV prevention.

Irrespective of the ‘ideal implementation strategy’, which depends on the population and institution being studied, it is reasonable to conclude that all patients undergoing a general anaesthetic consisting of inhalational anaesthetics plus opioids should be deemed eligible to receive at least two antiemetics. This liberal assumption should then be modified in the light of previous experience (no previous nausea or vomiting), patient specific contra-indications (such as Parkinson’s disease) and patient preferences (for example, always has PONV following anaesthesia and wishes not to experience this annoying symptom any more).

Strategies to reduce the incidence of PONV

Reducing the baseline risk

Apart from pharmacological management involving administration of molecules acting as an anti-emetic, an important part of PONV prevention is the avoidance of significant and clinically relevant pro-emetic factors. Therefore, in patients reporting previously bad experiences in conjunction with the occurrence of PONV, techniques of regional anaesthesia should be considered. These should be applied either alone or in conjunction with general anaesthesia as an opioid- and anaesthetic-sparing strategy. Regional anaesthesia, including both central neuraxial regional anaesthesia and peripheral nerve blocks or local anaesthesia techniques [30], is associated with a significantly lower risk of PONV in adults than general anaesthesia. Such an effect is likely to be due to the avoidance of two potent triggers in the peri-operative phase, namely opioid and inhalational anaesthetics [31]. However, providing regional techniques as sole components of the anaesthesia is not a viable option for many surgical procedures. In this case, using propofol rather than volatile anaesthetics to maintain anaesthesia is a better choice in reducing the incidence of PONV. As a rule of thumb, the relative risk reduction of this intervention together with the avoidance of nitrous oxide comes close to that of antiemetics with well-documented efficacy that is described later [32-35]. Since opioids are among the most relevant intra- and postoperative triggers for PONV, strategies that allow a dose-reduction or even avoidance decrease the incidence of PONV [36].

PONV prevention using anti-emetic pharmacotherapy

A huge variety of antiemetic molecules, grouped into different drug classes, are used for drug-based PONV prevention. Such a selection of different drugs is needed to manage PONV. Most of these agents antagonise the action of emetogenic substances at specific receptors, for example, in the area postrema or on the free nerve endings of the vagus nerve (Table 1).
Table 1

Summary of the key features of pharmacological anti-emetic agents with well-established efficacy in the prevention of post-operative nausea and vomiting (PONV) for adult and paediatric patients

<table>
<thead>
<tr>
<th>Name</th>
<th>Type of agent</th>
<th>Fixed dose for adult patients</th>
<th>Adjusted dose (per kg of body weight) for paediatric patients</th>
<th>Recommended time of administration</th>
<th>Adverse effects (AE) and absolute or relative contraindications (CI)</th>
<th>Additional information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone</td>
<td>Corticosteroid</td>
<td>4-8 mg</td>
<td>0.1-0.15 mg</td>
<td>Early (e.g. at induction)</td>
<td>AE: increased blood glucose, hypo-/hypertension CI (relative); diabetes mellitus, paediatric oncology / lymphoproliferative diseases</td>
<td>Mechanism of action still unclear</td>
</tr>
<tr>
<td>Granisetron</td>
<td>Serotonin antagonists (5-HT3 receptor antagonists)</td>
<td>1 mg</td>
<td>0.02 mg/kg</td>
<td>Late (e.g. towards the end of anaesthesia)</td>
<td>AE: headache, constipation, raised liver enzymes CI: prolonged QT-interval (ECG)</td>
<td></td>
</tr>
<tr>
<td>Ondansetron</td>
<td>Serotonin antagonists (5-HT3 receptor antagonists)</td>
<td>4 mg</td>
<td>0.1 mg/kg</td>
<td></td>
<td>CI: prolonged QT-interval (ECG)</td>
<td>Second choice in paediatric patients</td>
</tr>
<tr>
<td>Palonosetron</td>
<td>Serotonin antagonists (5-HT3 receptor antagonists)</td>
<td>0.075 mg</td>
<td>No data available</td>
<td></td>
<td>CI: prolonged QT-interval (ECG)</td>
<td></td>
</tr>
<tr>
<td>Tropisetron</td>
<td>Serotonin antagonists (5-HT3 receptor antagonists)</td>
<td>2 mg</td>
<td>0.1 mg/kg</td>
<td></td>
<td>CI: prolonged QT-interval (ECG)</td>
<td></td>
</tr>
<tr>
<td>Droperidol</td>
<td>Dopamine antagonists (D2 receptor antagonists), butyrophenones</td>
<td>0.625-1.25 mg</td>
<td>0.01 – 0.015 mg/kg</td>
<td>Late (e.g. towards the end of anaesthesia)</td>
<td>AE: psychomimetic side effects, extrapyramidal disturbances, sedation CI: Parkinson’s disease, prolonged QT-interval (ECG)</td>
<td></td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Dopamine antagonists (D2 receptor antagonists), butyrophenones</td>
<td>1.0-2.0 mg</td>
<td>No data available</td>
<td>Unknown</td>
<td>CI: Parkinson’s disease, prolonged QT-interval (ECG)</td>
<td></td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Dopamine antagonists (D2 receptor antagonists), benzamides</td>
<td>20-50 mg</td>
<td>0.15 mg</td>
<td>Late (e.g. towards the end of anaesthesia)</td>
<td>AE: extrapyramidal disturbances, hypotension (rapid injection) CI: Parkinson’s disease</td>
<td>Second choice in paediatric patients</td>
</tr>
<tr>
<td>Dimenhydrinate</td>
<td>Histamine antagonists (H1 receptor antagonists)</td>
<td>62 mg</td>
<td>0.5-1.0</td>
<td>Late (e.g. towards the end of anaesthesia)</td>
<td>AE: sedation</td>
<td></td>
</tr>
<tr>
<td>Scopolamine</td>
<td>Anticholinergic agents (antagonist at muscarinic acetylcholine receptors)</td>
<td>Transdermal therapeutic system (TTS)</td>
<td>No data available</td>
<td>Early (e.g. at premedication the day before surgery or prior to induction of anaesthesia)</td>
<td>AE: dizziness, dry mouth, visual disturbances</td>
<td></td>
</tr>
<tr>
<td>Aprepitant</td>
<td>Neurokinin antagonists (NK1 receptor antagonists)</td>
<td>40 mg (in some countries only available as capsule containing 80 or 125 mg)</td>
<td>No data available</td>
<td>Early (e.g. at premedication on the day of surgery)</td>
<td>AE: headache, constipation</td>
<td>Only available in an oral formulation. However, IV application (off-label) of NK1-antagonists via fosaprepitant feasible.</td>
</tr>
</tbody>
</table>

Adjuvants and non-drug-based PONV prevention

Increasing the inhaled oxygen concentration may have some effect on the incidence of PONV, but, according to the results of a recent meta-analysis, this effect is neither clinically relevant nor statistically significant for many PONV-outcomes [37]. The same holds true for ginger and ginger extracts [38]. The effects of aromatherapy, for example with isopropyl alcohol, are not convincing so far and the study designs used are inferior to those used for established pharmacological agents. Fluid replacement strategies are thought to play a significant role in the occurrence of PONV. However, at this stage studies that have investigated the effect of fluid replacement on the incidence of PONV are heterogeneous to an extent (for example, with respect to the definition of a ‘liberal’ versus a ‘restrictive’ fluid replacement strategy and the type of surgery) rendering these studies unsuitable to serve as a reliable basis for valid general recommendations. Acupuncture or acupressure at point Pericardium 6 (Neiguan) on the wrist has been associated with better PONV prevention than placebo (sham acupuncture or acupressure) [39].
Irrespective of any positive results, there is an ongoing debate about what importance should be attributed to such non-pharmacological techniques in view of well-proven pharmacological interventions [40]. The most controversial discussion is that many different techniques and application modes have been investigated so far and have been grouped together in meta-analyses. This means that irrespective of the significant reduction in nausea (RR 0.71; 95% CI 0.61–0.83) and vomiting (RR 0.7; 95% CI 0.59–0.83) when compared with placebo in adults and children in a recent update of the Cochrane Review, these conclusions must be interpreted with caution [41]. On the other hand, these techniques may be the first choice if pharmacological management is objectionable or the number of available interventions is decreased, for example in pregnant patients.

**Combination prophylaxis and multi-modal anti-emetic treatment**

When the benefit of single interventions had been established, research shifted towards combining antiemetics for improved efficacy. Many interventions, each characterised as effective single interventions have thus been analysed and the take-home message was that the combination was better than a single intervention. If the finding that most of the different classes of anti-emetic exert their effects independently of each other [34] can be confirmed, then it is reasonable to conclude that the overall effect of such a bundle of interventions can be computed by simply adding up the relative effect of each single component [42, 43]. For many commonly used pharmacological interventions the additive effect has been formally established [44-46]. Good clinical evidence exists for the combination of a 5-HT3 receptor antagonist with dexamethasone or droperidol [47] and for the combination of droperidol with dexamethasone.

The next step is to combine several interventions into a bundle of a ‘multi-modal approach’. Another technical term used for such an approach (among others) was ‘balanced anti-emesis’ [48]. While this term highlights the fact that different targets of emetic pathways are attacked, the term ‘multi-modal anti-emetic management’ [49] emphasised the fact that multiple components were used in a single patient. One of the early investigations using multi-modal prevention was able to show that even in a high risk setting it is feasible to almost eliminate PONV [49]. The majority of the trials using a multi-modal approach combined different interventions and strategies with various targets [50] such as reducing the emetic potency of the anaesthesia itself (for example by using propofol), the combination of several pharmacological and non-pharmacological techniques to prevent PONV, or the use of other measures to further decrease the incidence of PONV, such as using regional analgesia techniques or the provision of sufficient peripherally acting analgesics or non-opioid analgesics in order to minimise the need for opioid analgesics in the peri-operative phase.

The extent to which each of the components contributed to the overall benefit in terms of the observed risk reduction remains speculative, since a factorial design [32] that would have allowed elucidating relative benefits was rarely used.

**Tackling the practical aspects of the management of PONV**

Single agent use with dexamethasone, droperidol or ondansetron has been shown to have comparable anti-emetic efficacy, with a relative risk reduction (RRR) for PONV of ~ one-third in large clinical trials. The same reduction holds true for changing the anaesthetic technique and for using total intravenous anaesthesia (TIVA) with propofol instead of volatile anaesthetics together with using air instead of nitrous oxide. A combination of these measures (dexamethasone, droperidol, ondansetron and TIVA) is associated with a cumulative effect, and it is reasonable to conclude that this effect is also valid for other drug-based measures described in Table 1, providing these interventions act on different receptors.

So far there is no evidence that specific antiemetics work particularly well in conjunction with a specific patient profile (for example, female versus male patients) or a particular surgical procedure (for example, laparoscopy or middle ear surgery). Thus, patient or procedure-related (relative) contra-indications or previous drug-related side-effects in a specific patient should be taken into account when choosing anti-emetic interventions from a predefined anti-emetic armamentarium.

Using a multimodal approach by choosing various components out of the range of anti-emetic drugs it is feasible to achieve a significant reduction in the incidence of PONV even in high-risk patients. In patients having a negative experience with PONV after previous anaesthetics, such success is usually associated with a substantial increase in patient satisfaction [49, 50].


**PONV treatment**

An early trial comparing (single) prevention with treatment after PONV occurred concluded ‘although PONV is unpleasant, the data indicate little difference in outcomes when routine prophylactic medications are administered versus simply treating PONV should symptoms occur’ [20]. Considering the currently available anti-emetic substances in conjunction with the knowledge that the assessment of PONV symptoms in the PACU and on the ward is usually less than optimal [19], which results in a significant delay and denial of effective treatment, better efforts should be made to prevent PONV. If PONV occurs despite prevention or in patients having not received any prophylactic antiemetics, prompt treatment is indicated as the likelihood of PONV persisting or recurring (following a brief relief of symptoms) is ~65% [51]. The use of 5HT3 receptor antagonists, particularly ondansetron, for this indication has been extensively investigated and confirmed as being effective [52, 53]. Providing that no previous prophylactic antiemetics have been used these agents may be considered first-line drugs for treatment of PONV. The data available on other pharmacological and non-pharmacological methods are less extensive. However, other interventions, such as dexamethasone, haloperidol, dimenhydrinate and promethazine, have been shown to be effective agents in the treatment of PONV [54-56].

So far, there is no evidence that molecules that are effective for prevention fail to work when administered as treatment. Therefore, taking into account some basic pharmacokinetic considerations, it is reasonable to extrapolate data and results from trials investigating the prevention of PONV.

Interventions associated with a slow onset of action (such as dexamethasone, or transdermal scopolamine) should not be used in isolation, but should be used in combination with a fast-acting agent. For some drugs such as ondansetron, the minimum effective dose for treatment is less than that used for prevention [52, 53]. For the sake of practicality, the same doses as those used for prevention are usually recommended for treatment [16]. When PONV occurs despite preventive pharmacological measures it is recommended that drugs from another class should be administered. This is particularly true in the immediate postoperative phase [55-57]. So far, anaesthetists have had to rely on basic pharmacokinetic considerations when re-administering a specific drug in order to prolong its anti-emetic effect since reliable data do not exist. Even in the treatment of PONV, combination therapy should be considered. Promising data already exist for the combination of dexamethasone with dolasetron or haloperidol [54]. Such treatments are supported by a recurrence rate of PONV over the subsequent 24 hours in the range of 35% to 50%, despite active intervention using a single agent.

**PONV in children**

The incidence of PONV is strongly age-dependent. While children below 3 years of age are rarely affected, the incidence of PONV increases from this age onwards and reaches a peak between 5 and 9 years of age [58]. Nausea is much more difficult to assess in infants. Therefore, studies of PONV in this patient population are usually restricted to the incidence of postoperative vomiting (POV). As in adults, a simplified prognosis system that is based on the most dominant risk factors (the Postoperative Vomiting in Children, or POVOC-score) can be used to predict vomiting in children [59, 60]. However, the same restrictions and limitations apply to individual risk prediction in children as described above for an adult population. Therefore, the aim should be clearly to prevent PONV in that patient population. Because symptom assessment is difficult in children, many patients may be described erroneously as free from nausea.

In children the same interventions for PONV prophylaxis and treatment can be used as for adults. Table 1 provides an overview of recommended body weight adjusted dosing regimens for PONV prevention and treatment in children. Total intravenous anaesthesia using propofol and the avoidance of nitrous oxide should be used at an early stage in the anti-emetic protocol in children, since the overall armamentarium is more restricted compared with that for adults due to limitations regarding the use of D2-antagonists (such as metoclopramide, droperidol or haloperidol) in children [61] and the fact that transdermal scopolamine and NK1-antagonists are not available in paediatric doses. Irrespective of recent disputes regarding the administration of dexamethasone in children undergoing tonsillotomies, the current recommendations of the Task Force for Pediatric Anesthesia of the German Society of Anesthesia state that it is too early to draw meaningful conclusions regarding potentially harmful effects and the administration of 0.15 mg/kg dexamethasone is considered a useful agent to prevent PONV in children [62, 63].
Prevention and treatment algorithms

As previously described, the effectiveness of specific algorithms depends on the risk distribution in a given population. Thus, no generally valid recommendations can be given about a single ‘ultimate’ prevention algorithm being universally effective and efficient [42]. The underlying rational for using a risk-adapted approach is to save resources in certain patients (those who do not need anti-emetic prevention) and use these resources for patients who are in need of multi-modal prevention. Inherent limitations regarding risk prediction and oft reported problems in the enduring implementation of a risk-adapted individual approach clearly support easy to use and simple algorithms. Being easy to use is a vital prerequisite to facilitate their use becoming as routine as providing analgesia during and after the surgical procedure. The acquisition costs and the side-effect profile of many of the available antiemetics should not represent a major obstacle with respect to widespread use any more. In simulation studies, the efficacy of general prevention regimens are usually comparable to risk-adapted approaches [42], without being hampered by a dependency on the accuracy of strategies used to determine those patients that would not benefit from preventive measures [22].

It appears that it is more important to monitor local factors and ensure sufficient prophylactic administration of antiemetics than to deciding upon the most sophisticated anti-emetic prophylactic strategy [64, 65]. At this stage no sufficient data exist to justify specific recommendations based on pharmaco-genetic considerations (‘tailored anti-emesis’). All the pharmacological interventions listed in Table 1 have been investigated in many clinical trials and, according to current knowledge, have demonstrated a convincing risk (of adverse events) to benefit ratio. Thus, a liberal and multi-modal prophylaxis regime is justified in high-risk patients. However, since the potential of anti-emetic interventions to cause specific adverse events is variable, patient-specific considerations must be included in an overall risk-benefit analysis in the light of the patient’s individual profile and his or her preferences.

The costs of the different antiemetics are varied. This may allow some opportunities for cost-savings. However, the purchase prices of antiemetics for different institutions varies to such an extent that any general pharmaco-economic analyses based on available price levels are unreliable. Simulation analyses using institutional data on the local population may help overcome these limitations and facilitate an a priori assessment of the most suitable algorithm [42]. However, the decision for or against specific antiemetics should be based primarily on medical reasoning.

Conclusion

In summary, all practising anaesthetists should be invited to join the anti-emetic crusade to make actual change happen. It is clearly up to every individual anaesthetist to decide that PONV will eventually stop or if PONV will remain a never-ending story. The weakest link in the chain from research to patient benefit is clearly the implementation of well-proven strategies. In this aim, we should appreciate new pharmacological agents to cope with PONV, such as the NK1 antagonists or newer 5-HT3 antagonists (and there is room for further, new molecules), but we should also not forget about the traditional and well-established antiemetics that represent valuable components in our current portfolio and may contribute to the fact that a (nearly) PONV-free hospital may eventually become a reality [66].

Key learning points

• Postoperative nausea and vomiting (PONV) impairs satisfaction with recovery of anaesthesia and patients are willing to pay between US$56 and US$100 for a completely effective anti-emetic.
• Serious consequences, such as aspiration pneumonia, subcutaneous emphysema, pneumothorax or rupture of the trachea, are unlikely, but may occur.
• PONV is treatable and can be prevented using the current armamentarium, providing sufficient measures, such as combining pharmacological treatments and/or adapting the anaesthesia regimen, are used.
• Efforts should be intensified to prevent PONV in the majority of our patients by applying existing evidence-based interventions for preventing and treating PONV.
• Considering the huge amount of knowledge in this area of research, implementation of that knowledge offers considerable room for further improvement.
Conflict of interest

Professor Kranke has received speaker’s fees from Fresenius Kabi (Germany) and ProStrakan (Germany).

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