A survey of antiemetic dexamethasone administration—frequency of use and perceptions of benefits and risks

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Summary
Postoperative nausea and vomiting (PONV) is a significant concern for anaesthetists. There are many agents from different classes that are effective in both preventing and treating PONV. Dexamethasone is a very effective antiemetic, but there are concerns regarding its safety. We performed an anonymous survey of a random selection of the fellows of the Australian and New Zealand College of Anaesthetists to ascertain patterns of practice in relation to PONV prophylaxis and treatment and also to determine awareness of the risks and benefits of perioperative dexamethasone administration. The response rate was 33%. From the responses, 71.2% of all patients undergoing general anaesthesia in the respondents’ institutions receive PONV prophylaxis in total and 46.6% receive dexamethasone. No respondent gives more than a single dose of dexamethasone and there was an almost equal split between those who administer 4 and 8 mg, with a smaller number dosing on a weight basis. 5HT-3 receptor antagonists and dexamethasone are the preferred first-line PONV prophylactic agents and 5HT-3 receptor antagonists and droperidol are the preferred first-line PONV therapeutic agents. Concerns relating to the safety of dexamethasone were expressed by 80% of respondents. From this survey, we concluded that the PONV practice of the respondents is largely compliant with recent consensus guidelines, although PONV prophylaxis appears to be given more routinely. It also appears that more education is required on issues regarding dexamethasone safety.

Key Words: antiemetics, dexamethasone, postoperative nausea and vomiting, risk
.current guidelines and to ascertain the level of awareness amongst anaesthetists in Australia and New Zealand of the current debate surrounding its use.

Methods
This survey was approved as a Clinical Audit/Quality Assurance activity by the West Australia South Metropolitan Health Service Human Research Ethics Committee (Approval No.: A-13.05). An electronic survey was created using a commercially available internet-based service, SurveyMonkey® (Portland, OR, USA)22. The survey complied with the ANZCA policy and was administered by this organisation. A summary of the question set is provided in Table 1. This question set was refined following discussion with colleagues and trialling of its interpretability and ease of use. The final survey was reviewed and approved by the Trials Group of ANZCA prior to delivery. A cover letter and invitation to participate in the survey was sent by electronic mail to a randomly selected sample of 1000 fellows of ANZCA. The respondents’ identity was concealed from the investigators, who likewise had no involvement in the randomisation process. The sample size represented approximately one quarter of the fellowship of the College and the recipients were determined by ANZCA in order to minimise survey fatigue. Due to blinding, non-responder data could not be collected. The responses were anonymous and no internet protocol addresses were collected. A follow-up reminder was sent to non-responders at four weeks after the initial invitation. A total of 14 questions were asked. Two of the questions were free-text only, five had additional free-text options and four had multiple answer options.

Statistical analysis
All data were examined using descriptive methods to ascertain the percentages of responses to specific questions and are presented as n (%).

Results
Of 1000 invitations to participate, 333 responses were received, indicating a response rate of 33%. When the proportions of patients in specific surgical treatment groups who received PONV prophylaxis were examined, two patterns emerged—the majority of cardiac surgical patients (65%) do not and the majority of neurosurgical patients do receive PONV prophylaxis (over 54%)—with other surgical subspecialties in between these figures. The breakdown of the percentage of respondents administering PONV prophylaxis and the proportion who administer dexamethasone is shown in Figures 1 and 2 (n=326). To determine an estimate of the total percentage of patients receiving PONV prophylaxis, the frequency in each category was multiplied by the midpoint for that category (0.55 for the 50% to 60% category, 0.65 for the 60% to 70% category etc.), summated and then divided by the maximum possible value if all patients received prophylaxis (n×0.95) to produce an estimate of the total percentage of patients who receive PONV prophylaxis. Hence, 71.2% of all patients undergoing general anaesthesia received PONV prophylaxis. Of those who responded (n=326), the percentage of patients receiving PONV prophylaxis who received dexamethasone as a prophylactic agent are shown in Figure 2. When an estimate was achieved, as above, this amounted to 65.5% of those patients who received PONV prophylaxis.
Survey of PONV practice

Figure 2: PONV=postoperative nausea and vomiting.

Figure 3: PONV=postoperative nausea and vomiting.

Figure 4: PONV=postoperative nausea and vomiting.
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<td>1.</td>
<td>What proportion of patients from the following groups would you administer antiemetics to?</td>
<td>Paediatric Cardiac Obstetrics and gynaecology General Neurosurgical Other (free text)</td>
</tr>
<tr>
<td>2.</td>
<td>In relation to PONV prophylaxis for general anaesthesia, which of the following BEST describes your practice?</td>
<td>Universal Selective Neither of the above (please specify with free text in the space below):</td>
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<td>3.</td>
<td>What percentage of your patients receive PONV prophylaxis?</td>
<td>0% to 100%</td>
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<tr>
<td>4.</td>
<td>In relation to PONV prophylaxis for general anaesthesia, what percentage of your patients that receive PONV prophylaxis receive dexamethasone?</td>
<td>0% to 100%</td>
</tr>
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<td>5.</td>
<td>Which of the below drugs are your preferred FIRST line prophylactic antiemetic agents for general anaesthesia? (tick whichever apply – multiple answers allowed)</td>
<td>5HT_3 receptor antagonist Metoclopramide Droperidol Dexamethasone Cyclizine Promethazine Prochlorperazine Other (please specify)</td>
</tr>
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<td>6.</td>
<td>Which of the below drugs are your preferred FIRST line antiemetic agents for TREATMENT of PONV following general anaesthesia? (tick whichever apply – multiple answers allowed)</td>
<td>5HT_3 receptor antagonist Metoclopramide Droperidol Dexamethasone Cyclizine Promethazine Prochlorperazine Other (please specify)</td>
</tr>
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<td>7.</td>
<td>If you use dexamethasone as an antiemetic for general anaesthesia, which dose do you MOST COMMONLY use?</td>
<td>2 mg 4 mg 8 mg 12 mg 16 mg Dosing on a per kilogram basis 0 mg Other (please specify)</td>
</tr>
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<td>8.</td>
<td>If you use dexamethasone as an antiemetic for general anaesthesia, do you administer...?</td>
<td>Single dose Multiple doses</td>
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<td>9.</td>
<td>If you administer a SINGLE dose only, do you most frequently administer the dose...?</td>
<td>Pre-induction only Post-induction only Postoperatively only</td>
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<td>10.</td>
<td>If you administer multiple doses, do you most frequently administer the doses...?</td>
<td>Pre-induction/post-induction Pre-induction/postoperatively Post-induction/postoperatively All of the above</td>
</tr>
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<td>11.</td>
<td>Which of the following do you consider to be additional benefits of the perioperative use of dexamethasone as an antiemetic? (tick whichever apply – multiple answers allowed)</td>
<td>Improved early postoperative pain control Improved late pain control Opiate sparing effects Decreased incidence of chronic post-surgical pain Enhanced quality of recovery Decreased incidence of sore throat post-tracheal intubation Decreased swelling None of the above</td>
</tr>
<tr>
<td>12.</td>
<td>Which of the following do you consider to be real risks of the perioperative use of dexamethasone as an antiemetic? (tick whichever apply – multiple answers allowed)</td>
<td>Hyperglycaemia in diabetics Hyperglycaemia in non-diabetics Peptic ulceration Increased risk of postoperative infection Impaired wound healing Impaired bony union of fractures Neuropsychiatric complications (delirium, mania etc.) Insomnia None of the above</td>
</tr>
<tr>
<td>13.</td>
<td>Do you use dexamethasone for indications other than as an antiemetic? Y/N</td>
<td>If yes, please specify which indications in the free text below:</td>
</tr>
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PONV=postoperative nausea and vomiting.
prophylaxis received dexamethasone. Hence, given that 71.2% of all patients received PONV prophylaxis and 65.5% of those received dexamethasone, a total figure of 46.6% (0.655x0.712) of all patients received dexamethasone as an antiemetic during their general anaesthetic.

In terms of dosing strategy, of 327 valid responses, three (0.9%) do not use dexamethasone, 41 (12.5%) employ a weight based dosing strategy, 105 (32.1%) administer a dose of 8 mg and the remaining 178 (54.4%) administer a dose of 4 mg. All respondents who use dexamethasone administer a single dose—20 (6.1%) administer the dose prior to induction, 301 (92%) administer it post-induction/intraoperatively and 6 (1.8%) administer it postoperatively.

The popularity of individual antiemetic agents as either prophylaxis or treatment is shown in Figures 3 and 4. It is clear from this data that 5HT-3 receptor antagonists (239 [71.3%]) and dexamethasone (210 [63.1%]) are the preferred first-line PONV prophylactic agents and 5HT-3 receptor antagonists (256 [76.9%]) and droperidol (111 [33.3%]) are the preferred first-line PONV therapeutic agents. Dexamethasone was selected as a front-line agent for the treatment of PONV in 26 (7.8%) of responses.

Additional indications for use were identified from free-text responses (including treatment of cerebral oedema, airway oedema and postextubation stridor, use as replacement in patients with concurrent chronic glucocorticoid consumption, to prevent pruritus in intrathecal opioid administration, bronchospasm and severe asthma and to prolong the duration of regional anaesthesia blocks). The responses as to the perceived benefits and risks of dexamethasone administration are shown in Table 2. A reduction in swelling (190 [57.1%]) and improved early analgesia (123 [36.9%]) were the most commonly reported perceived additional benefits of dexamethasone administration. Two hundred and thirty-eight (71.5%) of all respondents admitted to being concerned about the occurrence of hyperglycaemia in diabetic patients with dexamethasone administration, whilst only 22 (6.6%) believed this risk to extend to non-diabetics. In total, 79.3% of all respondents admitted to concerns in relation to at least one adverse effect of the administration of perioperative dexamethasone.

**Discussion**

This is the first published survey to capture contemporary PONV practice and the use of dexamethasone amongst anaesthesia specialists in Australia and New Zealand. There are a number of key messages. Firstly, the majority (71.1%) of the patients undergoing general anaesthesia in the respondents’ institutions receive a prophylactic antiemetic. Secondly, dexamethasone and 5-HT<sub>3</sub> receptor antagonists are the preferred prophylactic agents, whilst 5-HT<sub>3</sub> receptor antagonists and droperidol are the preferred therapeutic agents once PONV develops. Thirdly, almost half of all patients undergoing general anaesthesia administered by the respondents receive dexamethasone as an antiemetic. Finally, 20% of respondents perceived there were no additional benefits or no possible side-effects.

From this survey, it is clear that PONV practice amongst fellows of ANZCA is largely consistent with the best evidence currently available to guide such practice. The most apparent deviation from the Society of Ambulatory Anesthesiology guidelines is that, based upon the patterns reported by respondents, most patients receive at least one antiemetic. The guidelines recommend a “wait and see” approach for patients at low risk of PONV, recommending that the economic costs and risks of side-effects of antiemetics may not be justified. The 71.1% of patients undergoing general anaesthesia who receive PONV prophylaxis, as estimated in this survey, are not all likely to be at a higher than ‘low risk’ of PONV and therefore, should not receive prophylactic antiemetics. Surveys in both the Netherlands and the United Kingdom have indicated a prevalence of less than 41% use of prophylactic antiemetics<sup>24,25</sup>. Although these surveys are older and relate primarily to ambulatory anaesthesia, it would still seem that fellows of ANZCA are much more likely to administer PONV prophylaxis than their overseas counterparts.

The pattern of agent selection is also noteworthy. Whilst our colleagues overseas use metoclopramide quite liberally, in this cohort it was the fourth least commonly used prophylactic agent and third least commonly used therapeutic agent.
There is good evidence to support alternative agents to metoclopramide, as it is a weak antiemetic and there are more effective alternatives. A recent survey of fellows of the Australian College of Emergency Medicine has identified that metoclopramide is overwhelmingly used as their first-line therapeutic agent for nausea and vomiting in the emergency department. We did not ascertain from our survey as to whether multi-agent prophylaxis was used routinely, nor did we interrogate the frequency patterns or doses of agents other than dexamethasone. We also did not make a distinction between ambulatory and other anaesthesia.

The use of dexamethasone was also consistent with the best available evidence. The respondents were evenly split between doses of 4 mg and 8 mg. The small number dosing on a per kg basis may have represented those with a largely paediatric practice. No respondents administered more than a single dose and only a small number administered it postoperatively, presumably as rescue therapy. It may be however, that the recent increase in awareness of the frequency (up to a third) of post-discharge nausea and vomiting in ambulatory surgery and its late presentation, has influenced the practice of ANZCA fellows. The administration of a long-acting agent such as dexamethasone would certainly seem to be a sensible prophylactic strategy in this respect. It may also have been that the fellows who responded to this survey were those involved in surgical procedures that are associated with a higher risk of PONV. Hence, these fellows are more likely not only to be current with the literature in their antiemetic practice but are also more likely to administer antiemetics given the higher incidence of PONV in their individual practices. Given the low response rate, this may have caused some bias in terms of the representative nature of our results.

The level of awareness amongst respondents of the additional benefits of dexamethasone administration that are reported in the literature (analgesia, decreased sore throat, improved quality of recovery and decreased swelling) is reassuring. This is consistent with practice in other specialties where potential side-effects appear to guide the choice of agents. Similarly, there appears to be reasonable awareness amongst respondents as to the concerns expressed widely in the literature with respect to the safety of perioperative dexamethasone. The use of dexamethasone as an antiemetic is an off-label use. Despite meta-analyses asserting that the use of perioperative dexamethasone and other glucocorticoids in the perioperative period is safe, there is growing concern in relation to hyperglycaemia, infection risk, malignancy recurrence and bleeding, particularly in vulnerable populations such as patients with diabetes and children. Not surprisingly, there was substantially more concern relating to perioperative hyperglycaemia in patients with diabetes than in those without. However, the current literature in this field is sparse and does not currently support this concern. In a subset of the dexamethasone, light anaesthesia, and tight glucose control trial (DeLit), a single 8 mg preoperative dose of dexamethasone produced a small but significant increase (1.6 mmol/l) in blood glucose concentrations, but only in patients without diabetes. Conversely, in 200 females without diabetes undergoing elective gynaecological surgery, Murphy et al did not identify any differences between either intra- or postoperative blood glucose concentrations. They compared the early and late effects of dexamethasone 4 mg and 8 mg to saline placebo on blood glucose concentrations. The lower level of awareness of other potential risks amongst our respondents probably reflects the uncertainty in the literature on this topic. The concern relating to these side-effects may in part explain why a 4 mg dose of dexamethasone is more likely amongst those expressing concern in relation to hyperglycaemia and perioperative infection. Hence, although it would appear that the fellows of ANZCA consider perioperative dexamethasone administration as not being without risk, the prevalence of its administration indicates that the risks are considered to be low.

This survey has several weaknesses which may limit the conclusions that can be drawn from it and which might significantly bias any interpretations that can be based upon the responses received. Firstly, the low response rate of 33% may have introduced bias into the results. The respondents may have self-selected as being those with a particular interest in the field of PONV or in relation to additional benefits or potential risks associated with the use of dexamethasone. Hence, the results may not necessarily be representative of the practice of the entire fellowship of ANZCA. This response rate, however, is consistent with previous surveys of the fellowship of ANZCA. Moreover, it is possible and even likely that the responses are representative of the wider fellowship, in which case the findings could be extrapolated more broadly. Secondly, we asked a limited number of questions in a field that spans many anaesthesia sub-specialties. We tried to achieve a balance between a survey that was sufficiently short to be non-onerous and encourage completion, whilst affording the maximum yield in terms of the information we were seeking—which was primarily in relation to the use of dexamethasone. This limits more sophisticated interrogation of the answers to questions not related to dexamethasone. Thirdly, as we were parsimonious in our question set, we did not collect information on the demographics of the respondents, principal surgical specialties for which they anaesthetise, their case-mix, the nature of their principal workplace or at what stage they were at in their careers.

Conclusion

In conclusion, this survey has permitted us to determine whether PONV prophylaxis strategies employed by the fellows of ANZCA who responded to the survey, are consistent with published guidelines. It is clear that PONV prophylaxis amongst the respondents is more liberal than that recommended.
Dexamethasone dosing strategies are consistent with the literature on this agent and the recommendations. Given that up to 46.6% of patients in a subset of institutions in Australia and New Zealand receive prophylactic dexamethasone perioperatively and 80% of respondents admit to concern relating to possible adverse effects, further studies to establish safety would be timely and likely to impact practice. The perioperative administration of dexamethasone and infection trial, which has recently secured $4.6 million funding from the National Health and Medical Research Council of Australia, is a large (8800 participants) non-inferiority safety study designed to comprehensively answer these questions.

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