

Acute stress ulceration prophylaxis: point prevalence surveys in intensive care units in Victoria, 1997 and 2005

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Most critically ill patients develop some form of gastrointestinal dysfunction, often as part of the systemic response to injury or infection. In the upper gastrointestinal tract, the major manifestation of this response is acute stress-related mucosal damage and ulceration, which is associated with increased mortality and morbidity related to bleeding or perforation.^{1,2} Endoscopy studies have shown some evidence of stress-related gastric mucosal damage in most seriously ill patients within 24 hours of admission to an intensive care unit.^{3,4} Despite the frequency and significance of acute stress-related gastric mucosal damage, the underlying pathogenesis remains uncertain. Altered gastric acid and pepsin production, decreased mucosal blood flow with resultant mucosal ischaemia, and altered gastric mucosal permeability have all been implicated as potential causative factors, but evidence supporting these theories is lacking.^{3,4}

Historically, acute stress ulceration (ASU) with severe bleeding, once established, was difficult to manage and associated with a high mortality. Thus, management has traditionally focused on prophylaxis to prevent ASU and the complications of bleeding and perforation.

We conducted a structured telephone survey of stress ulcer prophylaxis practices in adult ICUs in Victoria, Australia, on two occasions 8 years apart. The survey aimed to assess three main areas:

- the proportion of Victorian ICUs that had a formal written protocol or guideline for management of stress ulcer prophylaxis;
- the changes in management of stress ulcer prophylaxis in the 2 years before the first survey (1997) and between the two surveys (1997 and 2005), plus the stability of current practice and the inclusion of new evidence that became available between 1997 and 2005; and
- the point prevalence of stress ulcer prophylaxis in patients currently in the ICU on the survey days in 1997 and 2005.

Methods

A comprehensive list of all ICUs in both private and public hospitals in Victoria was compiled from data obtained from the Australian and New Zealand Intensive Care Society, the Department of Human Services Victoria and local knowledge. The list compiled in 1997 was reviewed and updated for the survey in 2005.

ABSTRACT

Objective: To assess current practice in acute stress ulceration (ASU) prophylaxis in adult intensive care units in Victoria, Australia, in 1997 and 2005.

Methods: Point prevalence surveys using a structured telephone questionnaire of ASU prophylaxis practices were performed in adult ICUs in Victoria on 11 November 1997 and 13 April 2005.

Results: All Victorian ICUs identified on each study day participated, comprising 30 ICUs in 1997 and 35 ICUs in 2005. Presence of a clinical protocol or guideline for ASU prophylaxis increased significantly from 23% in 1997 to 54% in 2005 ($P=0.01$). Overall provision of ASU prophylaxis to ICU patients also increased significantly from 67% in 1997 to 86% in 2005 ($P<0.001$). H₂-receptor antagonists were the preferred first-line agent in at least 50% of ICUs, and were also the most commonly used agents in both point prevalence surveys, with no change over 8 years. Use of proton-pump inhibitors increased significantly, both as first-line ASU prophylaxis agents and in clinical use, from 13% in 1997 to 45% in 2005 ($P<0.001$). Use of sucralfate and antacids for ASU prophylaxis ceased between 1997 and 2005.

Conclusions: Use of ASU prophylaxis for patients admitted to Victorian ICUs increased significantly from 1997 to 2005, with an associated increase in the presence of protocols or guidelines for ASU prophylaxis. Although agents currently used for ASU prophylaxis in Victorian ICUs are consistent with available evidence, we are concerned that ASU prophylaxis is given to all patients admitted to the ICU rather than targeted to patients in high-risk categories.

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Initially, a letter explaining the survey and requesting that the unit participate was sent to the nominated director of each ICU. The letter listed the five questions to be asked in the survey (Table 1, Questions 1–5) and included a recent report of a similar survey conducted in the United Kingdom.⁵ The letter was followed by a confirmatory telephone call to each ICU during which we reviewed the date, time and information to be sought for the planned point prevalence survey, and identified a contact person in each

Table 1. Structured interview for point prevalence survey of acute stress ulcer prophylaxis in Victorian ICUs

1. Does your intensive care unit have a protocol for stress ulcer prophylaxis?
2. Which agent is most commonly used for prophylaxis in your unit?
3. How many adult ICU patients are in your unit today?
4. How many of these patients are receiving H₂-receptor antagonist, sucralfate, omeprazole, or no prophylaxis?
5. Has your stress ulcer prophylaxis practice changed in the past 2 years?
6. Are any patients in your unit currently being treated for active stress ulcer bleeding?
7. When does your unit discontinue stress ulcer prophylaxis?

ICU to provide this information. Question 6 was added to the survey after discussion with staff from the participating ICUs in 1997, and Question 7 was added for the 2005 survey.

The point prevalence surveys were conducted by telephone on a single day in each year by one investigator (MSR in 1997; SJW in 2005). The telephone interviews followed a structured format and comprised the questions listed in Table 1.

Results

1997 survey

The initial point prevalence survey was conducted on Tuesday 11 November 1997, and all identified ICUs in Victoria participated. The hospitals comprised five tertiary hospitals, six metropolitan hospitals, nine regional hospitals and seven private hospitals (all of the last group were in the metropolitan area). The Alfred Hospital had three separate ICUs (general, trauma and cardiothoracic surgery units) and the Royal Melbourne Hospital had two separate ICUs (general and cardiothoracic units), giving 30 ICUs in 27 hospitals.

Of the 30 ICUs surveyed in 1997, 23% (7/30) had a written protocol or guideline for the management of stress ulcer prophylaxis. H₂-receptor antagonists were the preferred prophylactic agents in 50% (15/30) of ICUs, with sucralfate preferred in 40% (12/30), antacids in 7% (2/30), and no routine prophylaxis in one ICU.

Ten ICUs reported that they had changed their stress ulcer prophylaxis in the preceding 2 years. Seven ICUs had begun using sucralfate as their preferred agent, two had added proton-pump inhibitors (PPIs) to their stress ulcer prophylaxis, but not as a first-line agent, and two ICUs reported limiting stress ulcer prophylaxis to patients considered to be at high risk.

The participating ICUs had a total of 155 adult inpatients on the survey day. Two thirds of these patients (103/155)

were receiving ASU prophylaxis, including seven who had upper gastrointestinal tract bleeding reported during their ICU stay. H₂-receptor antagonists were the most commonly used agents on a patient basis (63%; 65/103 patients), as well as on an ICU basis, with sucralfate second (26%; 27/103), and PPIs used infrequently (13%; 13/103). Two patients were receiving combined prophylaxis with sucralfate and an H₂-receptor antagonist or a PPI. Although antacids were first-line ASU prophylaxis in two ICUs, no patients were receiving these as ASU prophylaxis on the survey day.

2005 survey

The second point prevalence survey was conducted on Wednesday 13 April 2005, and 35 ICUs participated. These included eight ICUs that were not identified or not operational during the 1997 survey (one metropolitan hospital, two regional hospitals and five private hospitals, the last in either metropolitan or regional areas). The separate ICUs at the Royal Melbourne Hospital and the Alfred Hospital had been consolidated into a single ICU at each site. Thus, 35 ICUs in 35 hospitals were surveyed in 2005, comprising five tertiary hospitals, seven metropolitan hospitals, 11 regional hospitals and 12 private hospitals.

Of the 35 ICUs surveyed, 54% (19/35) had a protocol or guideline for the management of stress ulcer prophylaxis, which was significantly more than found in the previous survey ($P=0.01$). H₂-receptor antagonists remained the preferred prophylactic agents in 60% (21/35) of ICUs, and there was a significant increase in the number of units using PPIs as first-line prophylaxis (40%, 14/35; $P<0.001$). No ICUs reported using either sucralfate or antacids for ASU prophylaxis in the 2005 survey. Consistent with these findings, 24 ICUs (69%) reported that they had changed their ASU prophylaxis in the preceding 8 years.

Participating ICUs had a total of 208 adult inpatients on the survey day. Overall, 86% (179/208) of these patients were receiving stress ulcer prophylaxis, which was a significant increase since 1997, when 67% of patients were receiving stress ulcer prophylaxis ($P<0.001$). Only one patient in the 2005 survey was reported with active upper gastrointestinal tract bleeding presumed due to stress ulceration, which was significantly lower than the proportion reported in 1997 (1/208 versus 7/155; $P=0.01$).

The 2005 point prevalence survey of clinical management again demonstrated that H₂-receptor antagonists were the most commonly used prophylactic agent (99/179; 55%), with PPIs used in the remaining 80 patients (45%) who were receiving prophylaxis, while no patients received combined prophylactic therapy. Thus, although the use of H₂-receptor antagonists did not change significantly, PPI use increased significantly compared with the 1997 survey data ($P<0.001$).

The final question posed in the 2005 survey related to cessation of stress ulcer prophylaxis in ICU patients: 19 (54%)

ICUs had clear stopping criteria, while 16 (46%) either did not cease prophylaxis or did not have clearly established stopping criteria. Criteria stated for ceasing prophylaxis included patient established on enteral feeding (12/35; 34%), patient discharged from ICU (11/35; 31%), extubation and resolution of respiratory failure (1/35 each; 3%).

Discussion

This study confirms that the provision of stress ulcer prophylaxis has increased significantly in ICUs in Victoria, from 67% of ICU patients in 1997 to 86% in 2005 ($P < 0.001$). Despite a significant increase in the use of PPIs since 1997 ($P < 0.001$), the 2005 survey demonstrated that H₂-receptor antagonists, particularly ranitidine, remained the most commonly used agents for stress ulcer prophylaxis. No Victorian ICU surveyed in 2005 reported continuing use of either sucralfate or antacids. In contrast, sucralfate was the second most common prophylactic agent on the survey day in 1997, used in 26% of patients.

The more extensive provision of ASU prophylaxis in 2005 may reflect both local and international trends in intensive care practice. A Department of Human Services quality initiative specifically aimed at ICUs was launched in Victoria in 2002 and promoted universal use of several prophylactic regimens in ICU patients, including ASU prophylaxis. Both clinicians and leading nursing staff from many Victorian ICUs participated in this ICU collaborative project, with the aim of rapidly improving compliance with specified standard management protocols. This may have contributed to the increased use of ASU prophylaxis noted in 2005. In addition, an international focus of quality and safety of health care provision, particularly with the widespread adoption of clinical guidelines and protocols, may also have increased both clinician awareness of the importance of ASU prophylaxis and compliance with ASU prophylaxis prescription in the clinical setting.

Alternatively, the increased use of ASU prophylaxis in 2005 compared with 1997 may reflect less discerning prescribing practices and an increase in inappropriate use. Cook et al showed that the incidence of clinically significant ASU bleeding had fallen to 1.5% in ICU patients admitted in 1990–1991,⁶ a marked decrease in reported incidence since the initial studies describing ASU were published in the 1970s and early 1980s.^{1,2,7,8} In particular, they identified two high-risk groups for the development of clinically significant bleeding related to ASU in the modern ICU setting: patients who received mechanical ventilation for more than 48 hours (odds ratio [OR], 15.6), and those with a coagulopathy, defined as a platelet count $< 50\,000$ cells/mL, an international normalised ratio > 1.5 , or an activated partial thromboplastin time more than twice the control level (OR, 4.3).⁶ In patients with one or more of these risk factors, the incidence of

clinically significant bleeding was reported as 3.7% (95% CI, 2.5%–5.2%) compared with 0.1% (95% CI, 0.02%–0.5%) in patients with no risk factors.⁶

Our study did not document the indications for ASU prophylaxis, but a recent audit of ASU prophylaxis practice among 519 intensivists in North America reported that 28.6% of respondents commenced ASU prophylaxis in all ICU patients, despite no clear clinical indication for its use.⁹ Although H₂-receptor antagonists and PPIs are relatively safe, with low adverse event profiles, indiscriminate use of any pharmaceutical treatment modality should not be accepted as optimal clinical practice. A targeted, evidence-based practice in ASU prophylaxis prescribing is likely to be both safer and more cost-effective.

From 1997 to 2005, H₂-receptor antagonists remained the most commonly used agents for ASU prophylaxis in Victorian ICUs, with around 60% of patients who received ASU prophylaxis being treated with these agents. The role of H₂-receptor antagonists for ASU prophylaxis was confirmed in the definitive article by Cook et al in 1998, which reported the results of a multicentre, randomised controlled clinical trial to compare the efficacy of ranitidine and sucralfate for preventing clinically significant ASU bleeding in critically ill patients requiring mechanical ventilation.¹⁰ This study of 1200 patients demonstrated that ranitidine was significantly more effective in preventing clinically significant upper gastrointestinal bleeding in this patient cohort than sucralfate.¹⁰ Published soon after our first survey was completed, this study undoubtedly contributed to the cessation of sucralfate use for ASU prophylaxis, which was subsequently shown in our 2005 survey. This change in clinical practice evident in 8 years represents a surprisingly rapid and complete translation of research into clinical practice, and the high level of evidence-based care provided in Victorian ICUs.

The increased availability of PPIs, particularly in parenteral forms, together with their demonstrated superiority over H₂-receptor antagonists in the treatment of peptic ulcer disease and gastro-oesophageal reflux¹¹ are likely to have contributed to the significant increase in PPI use as prophylaxis for ASU, from 13% in 1997 to 45% in 2005 ($P < 0.001$). However, there is little evidence, from relatively small studies, to support the preferential use of PPIs over H₂-receptor antagonists for ASU prophylaxis,^{12–17} and it is unlikely that further studies of adequate size and quality will now be completed, given the current low rate of ASU-related clinically significant bleeding, plus the already widespread use of PPIs for ASU prophylaxis. Single daily administration, easy access to parenteral formulations, marketing by pharmaceutical suppliers and the cost effectiveness of PPI ASU prophylaxis will probably lead to further increases in their use for first-line ASU prophylaxis. Our study showed that over the 8 years from 1997 to 2005, PPIs became

established as first-line ASU prophylaxis in 40% of Victorian ICUs surveyed, a significant increase in their clinical role ($P < 0.001$). We did not identify patients who were taking PPI agents on admission to the ICU, so it is possible that some of the increased PPI use in the ICU reflects widespread use in the community and continuation of regular medications after ICU admission.

Finally, our study demonstrated that the presence of clinical protocols or guidelines for ASU prophylaxis more than doubled in Victorian ICUs, from 23% in 1997 to 54% in 2005 ($P = 0.01$). Similarly, 54% of ICUs surveyed had clear stopping criteria for ASU prophylaxis, while almost half the ICUs stated they either did not cease ASU prophylaxis, continuing it on patient discharge from ICU, or had no clear rules as to when it should be ceased. This reflects a marked lack of evidence in this area and general uncertainty as to the duration of risk for clinically significant bleeding that needs to be covered by ASU prophylaxis, in addition to the duration of efficacy of such prophylaxis.

The findings of our study represent two single snapshots of clinical practice in 1997 and 2005, and as such may not truly represent clinical practice at either time point or the change in clinical practice over 8 years. However, the surveys were simply structured and circulated before each study date, and the survey data were collected by a single physician on each occasion. In addition, all ICUs identified in Victoria at the time of each point prevalence survey participated. Prior notification of the surveys with a letter and telephone call may have altered the results by increasing physician awareness of ASU prophylaxis on the survey days, but prior notification also probably increased participation resulting in a comprehensive sample. It is also possible that while the survey may demonstrate Victorian practice, this may not reflect current practice in all Australian ICUs. Finally, our study population may have included patients who were receiving acid-suppressant therapy for reasons other than ASU prophylaxis, such as continuation of previous long-term PPI therapy.

Conclusions

Our study shows that the provision of ASU prophylaxis for patients admitted to Victorian ICUs increased significantly from 1997 to 2005, with an associated increase in the presence of protocols or guidelines for ASU prophylaxis. H_2 -receptor antagonists remain the preferred first-line agents for ASU prophylaxis in 60% of ICUs surveyed, and, on the day of each survey, H_2 -receptor antagonists were prescribed in over 55% of all patients receiving ASU prophylaxis. Since the 1997 survey, use of sucralfate and antacids for prophylaxis has ceased in 40% of Victorian ICUs. Thus, although the agents currently used for ASU prophylaxis in Victorian ICUs are consistent with available evidence, we are concerned that

it appears the norm to provide ASU prophylaxis to all patients admitted to the ICU, rather than to target prophylaxis to patients in well-documented high-risk categories.

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