Opinions and practice of stress ulcer prophylaxis in Australian and New Zealand intensive care units

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ABSTRACT

Background: Intensivists frequently prescribe proton pump inhibitors (PPIs) or histamine-2 receptor blockers (H_2RBs) to intensive care unit patients for stress ulcer prophylaxis (SUP). Despite the common use of SUP medicines, there is limited high-level evidence to support the choice between them.

Aim: To describe self-reported practice of SUP by Australian and New Zealand intensivists.

Method: An online questionnaire of intensivists between 13 January and 3 February 2014.

Results: Seventy-two intensivists responded to the survey: 61 (85%) practised in public metropolitan ICUs and 13/48 (27%) practised in paediatric ICUs. Fifty-two (72%) respondents indicated that PPIs were their preferred SUP medicine. Respondents estimated that an average of 84% of ventilated and 53% of non-ventilated patients received SUP medicines during their ICU admission. Seven respondents (9%) were concerned or very concerned about the possible increased risk of upper gastrointestinal bleeding associated with H_2RBs versus PPIs. Ten respondents (14%) were concerned or very concerned about the possible greater risk of *Clostridium difficile* infection, and 15 respondents (21%) were concerned or very concerned about the possible greater risk or ventilator-associated pneumonia with PPIs versus H_2RBs. Most respondents (64 [89%]) agreed or strongly agreed that there was insufficient evidence to support the choice of an optimal SUP medicine, and 58 respondents (81%) agreed or strongly agreed to patient enrolment in an RCT comparing PPIs with H_2RBs.

Conclusion: Most survey respondents felt that current evidence is insufficient to justify the preferential use of PPIs or H_2RBs for SUP and would enrol patients in a comparative SUP RCT.

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Intensive care unit patients are at risk of developing gastrointestinal (GI) ulcers, commonly known as stress ulcers, as a result of their illness.[1] ICU patients are typically prescribed prophylactic medicines to prevent the development of such stress ulcers.[1,2] Proton pump inhibitors (PPIs) and histamine-2 receptor blockers (H_2RBs) are the two most commonly prescribed classes of stress ulcer prophylaxis (SUP) medicines. These medicines may have important side effects, including an increased risk of developing ventilator-associated pneumonia (VAP) and *Clostridium difficile* infection (CDI).[1,3,4] Because PPIs may decrease the risk of stress ulcer-related bleeding (compared with H_2RBs[1,3]) but may also carry a greater risk of VAP[4-7] and CDI,[8,9] there is wide variation in the choice of class of SUP medication.[3] Such uncertainty, the frequent prescription of such medicines, and concerns about side effects all suggest the need for a large, multicentre, randomised controlled trial (RCT).[3] However, a better understanding of Australian and New Zealand reported practice and clinician concerns and preferences is crucial to the justification and design of such a study.

We surveyed Australian and New Zealand intensivists to study their attitudes and preferences in relation to SUP. In particular, we wanted to identify when intensivists initiated SUP and their level of concern about potential side effects associated with SUP therapy. Finally, we investigated the extent to which intensivists would be willing to enrol patients in a randomised trial comparing the safety and efficacy of PPIs versus H_2RBs for SUP in the ICU.

Methods

Human research ethics committee approval was obtained, and the survey was anonymous (approval 14/CEN/30).

Questionnaire

We used an anonymous, structured multichoice questionnaire to survey intensivists. The questionnaire consisted of eight questions in two parts. The first part sought basic demographic details for respondents, and the second part asked for information on:

- choice of SUP medicines
- frequency of SUP medicine use
- level of concern about upper GI bleeding and infection
- opinions on the evidence for optimal SUP therapy and willingness to enrol patients in an RCT of PPIs versus H_2RBs for ICU patients.

Target population and questionnaire administration

Australian and New Zealand intensivists were identified using the Australian and New Zealand Intensive Care Society Clinical Trials Group (ANZICS-CTG) database. This target population included paediatric and adult intensivists. Each intensivist was invited by email to respond to the

questions on an online survey site (SurveyMonkey). Two weeks after the initial email invitation, a single reminder email was sent. All responses were recorded during a 3-week period (13 January to 3 February 2014).

Data management and analysis

All responses are shown as a percentage of the total number of responses for that question. No imputation has been made, as the proportion of missing values was so low. All questions had one or no missing responses, except for the question about location of practice, which 24 respondents did not answer. Data collected from the survey were analysed using simple descriptive statistical procedures to calculate means and percentages. All quantitative analyses were performed using Excel 2007 (Microsoft).

Results

Cohort characteristics

Survey invitations were emailed to 587 intensivists. Seventy-two intensivists responded to the survey. Overall, 61 respondents (85%) practised in public metropolitan ICUs and 13 (27%) practised in a paediatric ICU (Table 1).

Table 1. Cohort characteristics and SUP medicine choice

Characteristic and SUP choice	Responses,* *n* (%)
Location of ICU predominantly worked in (72†)	
Public metropolitan	61 (85%)
Private metropolitan	2 (3%)
Public regional	9 (12%)
Private regional	0 (0%)
Type of ICU predominantly worked in (48†)	
Adult ICU	35 (73%)
Paediatric ICU	13 (27%)
Predominant medicine prescribed for SUP (72†)	
Proton pump inhibitor	52 (72%)
Histamine-2 receptor blocker	14 (19%)
No preference	6 (8%)
Estimated proportion of invasively ventilated ICU patients who received SUP (72†)	84%
Estimated proportion of non-ventilated ICU patients who received (71†)	53%

SUP = stress ulcer prophylaxis. ICU = intensive care unit. * Percentage of the total number of responses for that question. † Number of responses.

SUP agent

The average estimated proportion of invasively ventilated patients who received SUP during ICU admission was 84%, and of non-ventilated patients was 53%. Overall, 52 (72%) respondents indicated using PPIs in preference, 14 (19%) preferred H_2RBs, and the remaining six respondents (8%) reported not having a preference (Table 1).

The impact of enteral nutrition

For mechanically ventilated (MV) patients, the following rates of SUP were reported. If a patient had a contraindication to enteral nutrition (EN), the rates of SUP were: always, 53 respondents (74%); usually, 13 (18%); and sometimes or rarely, 6 (8%). When EN was commenced but had not reached the goal rate, the rates of SUP were: always, 31 respondents (43%); usually, 21 (29%); sometimes or rarely, 18 (25%); and never, two (3%). When EN had reached goal rate, the rates of SUP were: always, 13 respondents (18%); usually, 19 (26%); sometimes, 12 (17%); rarely, 24 (33%); and never, four (6%) (Table 2).

Concerns about SUP in ICU

Responses to questions about the possible increased risk of upper GI bleeding with H_2RBs were as follows: 46 respondents (65%) were not concerned or a little concerned, and seven (9%) were concerned or very concerned. Responses to questions about the possible increased risk of CDI with PPIs were as follows: 44 respondents (62%) were not concerned or a little concerned, and 10 (14%) were concerned or very concerned. Responses to questions about the possible increased risk of VAP with PPIs were as follows: 38 respondents (53%) were not concerned or a little concerned, and 15 (21%) were concerned or very concerned (Table 2).

Evidence supporting SUP in ICU

Twenty-three respondents (32%) strongly agreed that there is currently insufficient evidence to determine optimal choice of SUP medicines, and 41 respondents (57%) agreed. Thirty respondents (42%) strongly agreed that they would be prepared to enrol patients in an RCT comparing PPIs and H_2RBs, and 28 respondents (39%) agreed (Table 2). The responses of paediatric intensivists to the above questions were similar to those of the overall adult ICU intensivist cohort.

Discussion

Summary of major findings

We found that Australian and New Zealand intensivists are uncertain about the risks, benefits and choice of PPIs and H_2RBs for SUP in the ICU. They are concerned about the possible increased risk of GI bleeding, VAP or CDI, with one class of medicines compared with another, but indicate that

Table 2. Frequency of SUP in ICU patients on MV and EN, concern about SUP, and opinions on current evidence for SUP

Clinical scenarios and response options	Responses, *n* (%*)
Frequency of initiation (or continuation) of SUP for patient on invasive MV when EN is contraindicated (72†)	
Always	53 (74%)
Usually	13 (18%)
Sometimes	3 (4%)
Rarely	3 (4%)
Never	0 (0%)
Frequency of initiation (or continuation) of SUP for patient on invasive MV when EN has not reached goal rate (72†)	
Always	31 (43%)
Usually	21 (29%)
Sometimes	11 (15%)
Rarely	7 (10%)
Never	2 (3%)
Frequency of initiation (or continuation) of SUP for patient on invasive MV when EN has reached goal rate (72†)	
Always	13 (18%)
Usually	19 (26%)
Sometimes	12 (17%)
Rarely	24 (33%)
Never	4 (6%)
Level of concern about increased risk of upper gastrointestinal bleeding with use of H_2RBs instead of PPIs for SUP (71†‡)	
Not concerned	21 (30%)
Neutral	18 (25%)
A little concerned	25 (35%)
Concerned	6 (8%)
Very concerned	1 (1%)
Level of concern about increased risk of *Clostridium difficile* infection with use of PPIs instead of H_2RBs for SUP (71†)	
Not concerned	24 (34%)
Neutral	17 (24%)
A little concerned	20 (28%)
Concerned	9 (13%)
Very concerned	1 (1%)
Level of concern about increased risk of ventilator-associated pneumonia with use of PPIs instead of H_2RBs for SUP (71†‡)	
Not concerned	18 (25%)
Neutral	18 (25%)
A little concerned	20 (28%)
Concerned	14 (20%)
Very concerned	1(1%)
Level of agreement that there is currently insufficient evidence to determine the optimal medicine for SUP in the ICU (72†‡)	
Strongly agree	23 (32%)
Agree	41 (57%)
Neutral	4 (6%)
Disagree	4 (6%)
Strongly disagree	0 (0%)
Level of agreement for patients to be enrolled in a randomised trial of PPI v H_2RB for SUP in the ICU (72†‡)	
Strongly agree	30 (42%)
Agree	28 (39%)
Uncertain	7 (10%)
Disagree	4 (6%)
Strongly disagree	3 (4%)

SUP = stress ulcer prophylaxis. ICU = intensive care unit. MV = mechanical ventilation. EN = enteral nutrition. H_2RB = histamine-2 receptor blocker. PPI = proton pump inhibitor. * Percentage of the total number of responses for that question. † Number of responses. ‡ Percentages may not total 100 due to rounding.

the evidence is insufficient to justify a specific choice. They also support patient enrolment in an RCT of SUP medicines.

Comparison with previous studies

The views expressed by Australian and New Zealand intensivists are not surprising and are consistent with the literature. The findings of two surveys of members of the Society of Critical Care Medicine,[10,11] conducted 10 and 15 years ago, respectively, show similar variation in SUP choices, prescription and concerns.

Recently, a retrospective pharmacoepidemiological study assessed SUP in 35 312 MV critically ill patients.[2] After correcting for confounding factors and performing multivariate regression modelling, patients who were administered PPIs, when compared with H_2RBs, had a greater risk of GI bleeding, VAP and CDI. These findings were also identified as contradicting the current Surviving Sepsis Campaign guidelines,[12] which favour PPI use. The incidence of adverse clinical outcomes validates the concerns raised by our cohort.

Prospective practice data on SUP in intensive care are few.[4,13] Findings from a 2009 point-prevalence program study of 678 patients from 51 Australian and New Zealand ICUs showed that 90% of patients (IQR, 78%–100%) were routinely prescribed SUP medicines.[14] Thus, routine SUP in Australian and New Zealand ICUs, with clinical equipoise from our respondents, suggests that a prospective randomised trial is important and could be successfully conducted.

Clinical implications

No definitive RCT comparing SUP medicines has been conducted for ICU patients.[2,3] Given the number of ICU patients treated each year with SUP worldwide, there is the potential for even a small absolute difference in effect size to have substantial public health benefits. The presence of clear equipoise in most Australian and New Zealand intensivists justifies the importance and feasibility of conducting a RCT.

Strengths and weakness

The strengths of our study are: it is the largest sample of Australian and New Zealand intensivists surveyed in relation to their SUP practices reported to date; and it included intensivists who work in paediatric and adult ICUs, which increased generalisability.

Limitations associated with the conduct of this study are: responses included those from clinicians involved in trial execution and design, potentially resulting in a biased sample; responses were self-reported and so may not reflect actual practice; the clinical scenarios may not have provided enough information to make a definitive clinical judgement; and electronic surveys with email invitations often have low response rates,[15,16] so our response rate was typical of others using this technique. The low response rate, the general uncertainty associated with choice of SUP medicine, and the strong willingness to participate in an RCT mean that the findings of our survey are likely to reflect non-responders.

Conclusion

Australian and New Zealand intensivists who responded to our survey are uncertain about SUP risks and benefits and about the choice between PPIs and H_2RBs in the ICU; they agree that the evidence is insufficient to justify a specific choice; and they support patient enrolment in an RCT of SUP.

Competing interests

None declared.

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