Survey of stress ulcer prophylaxis

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Background: No surveys of stress ulcer prophylaxis prescribing in the USA have been conducted since 1995. Since that time, the most comprehensive meta-analysis and largest randomized study to date concerning stress ulcer prophylaxis have been published.

Results: Three hundred sixty-eight surveys were sent to all members of the Section of Pharmacy and Pharmacology of the Society of Critical Care Medicine. One hundred fifty-three (42%) surveys were returned. Representatives from 86% of institutions stated that medications for stress ulcer prophylaxis are used in a majority (>90%) of patients admitted to the intensive care unit (ICU). Twenty-two per cent of institutions have recommendations for both ICU and non-ICU settings. Fifty-eight per cent of institutions stated that there was one preferred medication for stress ulcer prophylaxis, and in 77% of these histamine-2-antagonists were the most popular.

Conclusions: There are wide variations in prescribing practices for stress ulcer prophylaxis. Institutions should consult published literature and use pre-existing guidelines as templates for developing their own guidelines.

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Introduction

Stress-induced gastroduodenal erosions are a frequent occurrence in critically ill patients, but it is the incidence of clinically important complications resulting from these erosions that is important in deciding which patients should receive prophylaxis. Clinically important complications include bleeding that requires transfusion, bleeding associated with hemodynamic instability, and gastrointestinal perforations. Failure to document these complications in published studies limits the conclusions that can be drawn from much of the available literature. There have been inconsistent results in those studies that did record clinically important bleeding, depending on severity of illness or injury, and concomitant or underlying disease states.

Because the results of clinical investigations have led to different recommendations concerning stress ulcer prophylaxis, Cook *et al* [1] performed a meta-analysis of randomized trials to resolve the controversies associated with previous research in this area. They concluded that there was no clear agent of choice for prophylaxis based on efficacy considerations (ie ability to prevent clinically important bleeding), but sucralfate might have advantages in terms of adverse effects because it was associated with a lower incidence of pneumonia compared with histamine-blocking medications. Within 2 years of the publication of this meta-analysis, Cook *et al* [2] reported their findings from the largest randomized study conducted to date concerning stress ulcer prophylaxis. In that study, intravenous ranitidine 50 mg/8 h (with dose decreased for renal dysfunction) was associated with a lower incidence of clinically important bleeding compared with sucralfate 1 g/6 h (relative risk 0.44, 95% confidence interval 0.21–0.92, $P = 0.02$). There were no significant differences

ICU = intensive care unit.

between the medications with respect to pneumonia or mortality.

Given the recent publication of these important results, the present survey was conducted by members of the Research Committee of the Section of Pharmacy and Pharmacology of the Society of Critical Care Medicine. The survey was mailed to Section members who are well versed in medications used in the critical care area. The purpose of the survey was to determine current prescribing practices in light of recent publications concerning stress ulcer prophylaxis. The survey was also intended to assess institutional evaluations of stress ulcer prophylaxis. It is hoped that the results of this survey will provide clinicians with information as to how their prescribing and evaluation practices compare with those of practitioners in other institutions. Additionally, the survey might uncover institutional practices that are inconsistent with the available literature and that deserve further consideration.

Materials and methods

A survey was developed that contained questions regarding institutional prescribing and evaluation of stress ulcer prophylaxis. There were 11 questions on the survey, although several of the questions asked for additional information, depending on the initial response. The length of the survey was a compromise between asking enough questions to determine patterns of medication use and evaluation without discouraging completion of the survey by unnecessary length. The majority of questions were in a 'yes/no' format with further information required on the basis of the initial response. For example, one question was 'Does your institution have written guidelines for stress ulcer prophylaxis?' If the answer to this question was 'yes', then the responder was asked an additional series of questions concerning the details of these guidelines.

Several of the questions requested information that required answers as a percentage value. For example, 'What percentage of patients discharged from the intensive care unit to non-intensive care unit settings remain on stress ulcer prophylaxis?' For this type of question, the responder was requested to select from a range of percentages, such as 0–25%, 26–50%, 51–75%, or 76–100%. Most of the remaining questions allowed answers in either a check box or free text format.

A series of steps were taken in order to improve the validity and reliability of the instrument. After the initial survey construction at one site, the instrument was distributed to selected members of the Section of Pharmacy and Pharmacology of the Society of Critical Care Medicine for pretesting of the instrument. Additionally, a physician who practices in the critical care setting (but is not a member of the Section) was asked to review the instrument. Changes were made to the document on the basis of this input.

Table 1

Stress ulcer prophylaxis in ICU and non-ICU settings

Percentage of institutions stating that:	Percentage of patients			
	0–25	26–50	51–75	76–100
ICU patients received stress ulcer prophylaxis	0	7	17	76
Non-ICU patients received stress ulcer prophylaxis	34	44	19	3
Patients discharged from the ICU to non-ICU settings remained on stress ulcer prophylaxis	35	32	23	10

ICU, intensive care unit.

The survey was sent to all members of the Section of Pharmacy and Pharmacology of the Society of Critical Care Medicine in the fall of 1998. A stamped, self-addressed envelope was included in the mailing for returning the completed surveys. Descriptive statistics were used to analyze and report the data, because the answers were not amenable to inferential testing. Data were recorded and analyzed using Microsoft Excel version 4.0 (Microsoft Corporation).

Results

A total of 368 surveys were distributed and 153 were returned, yielding a response rate of 42%. Of the hospitals surveyed 62% had more than 400 beds, and 32% had between 200 and 399 beds. Sixty-one per cent of institutions had more than 40 intensive care unit (ICU) beds and 29% had between 20 and 39 beds. It is difficult to comment on the focus of the ICUs (ie surgical, medical, mixed or special) because of many respondents checking more than one item. Sixty-one per cent were classified as level I trauma centers. Of institutions 86% stated that medications for stress ulcer prophylaxis are used in a vast majority (>90%) of patients admitted to the ICU. Twenty-two per cent have recommendations for both ICU and non-ICU settings. These differences are provided in Table 1.

The majority of questions on the survey pertained to stress ulcer prophylaxis from an overall institutional standpoint. There were a few questions, however, that attempted to define specialized populations at the institutions that might be at particular risk for stress ulceration and related complications. With the exception of multiple trauma, these injuries can be considered as 'single-system' problems. The number of institutions that routinely institute stress ulcer prophylaxis in these specialized populations is listed in Table 2.

Twenty-seven per cent of institutions have written guidelines for stress ulcer prophylaxis, with approximately half of those stating that their guidelines have been reviewed

Table 2

Specialized populations where stress ulcer prophylaxis is routinely administered

Injury	Stress ulcer prophylaxis is given	Stress ulcer prophylaxis is not given	Do not have substantial numbers of this injury
Head injury	110	3	30
Spinal cord injury	99	4	39
Thermal injury	61	3	71
Multiple trauma	106	3	34
Hepatic injury with need for partial resection	67	9	62

Data are expressed as number of institutions responding to the question (not percentages).

Table 3

Description of the route of administration for each institutions preferred agent

Agent	Administration route	*n*
Histamine-2-antagonist	Intermittent IV	63
	IV infusion	13
	Oral	27
	Feeding tube	36
Sucralfate	Oral	13
	Nasogastric tube	20
Omeprazole	Oral	4
	Nasogastric tube	4
	Enteral tube	2
Other		0

Responders were permitted to check more than one administration route for their institution's preferred agent. IV, intravenous.

or updated within the past 2 years. Of responders 40% are either considering or developing guidelines for their respective institutions.

Fifty-eight per cent of institutions stated that there is one preferred medication for stress ulcer prophylaxis. For those institutions, histamine-2-antagonists were the most popular in 77%. Sucralfate was the agent of choice in 20%, whereas omeprazole was preferred in 3%. Antacids were not the agents of choice in any institution. A breakdown of the route of administration for each agent is listed in Table 3.

Ten per cent of institutions evaluated the incidence of clinically important bleeding, which was defined as the need for transfusion or hemodynamic changes that are associated with bleeding. It is unclear whether these institutions limited their evaluation to patients receiving stress ulcer prophylaxis due to the limited number of respondents who answered that question ($n = 13$). Twenty-three per cent routinely used gastric pH measurements (ie pH paper, pH sensor, gastric tonometry) for monitoring pH-altering agents when such measurements were feasible.

Discussion

As indicated by the results of this survey, stress ulcer prophylaxis is used in the majority (86%) of critically ill patients. Although it is difficult (if not impossible) for any survey to elucidate the reasons why physicians prescribe the way they do, it is possible to hypothesize from the results of our questionnaire. For most clinicians, it appears that the presumed benefits of prophylaxis outweigh its associated risks and costs. Consistent with a small percentage of individuals returning the surveys, however, there are clinicians who believe the value of prophylaxis is overstated and question its widespread use. This opinion is based on the perception that the incidence of bleeding is rare, and when it does occur it is readily amenable to endoscopic or medical therapies [3].

The number of patients receiving stress ulcer prophylaxis in non-ICU settings is concerning. Of institutions surveyed 22% stated that stress ulcer prophylaxis is given to patients in non-ICU settings more than 50% of the time. Also, patients discharged from ICU to non-ICU settings remain on stress ulcer prophylaxis more than 50% of the time in 33% of institutions. Given the lack of published literature in non-ICU settings, along with the low risk of clinically important bleeding, many experts believe that routine prophylaxis is not warranted.

The incidence of stress-induced bleeding has varied considerably, depending on the definition of bleeding and the population under study. Both microscopic and macroscopic (ie overt) bleeding are relatively common findings in published studies, but there is no well documented relationship between such bleeding and the incidence of clinically important bleeding complications (eg hemodynamic instability, perforation, need for transfusion). Unfortunately, the actual incidence of clinically important bleeding associated with many published investigations is not available, particularly in those published before 1990. In randomized trials conducted since 1990 that enrolled at least 100 general medical/surgical ICU patients, the incidence of clinically important bleeding associated with no prophylaxis has ranged from 3.5 to 22.9% [4,5]. In this survey, only 10% of the surveyed institutions evaluated the incidence of clinically important bleeding.

Certain types of defined or single-system injuries appear to be associated with a higher incidence of bleeding, on the basis of retrospective data. In the present study, the great majority of patients with head, spinal cord, thermal, or hepatic injuries were routinely given prophylaxis. Using

thermal injury as an example, however, only one randomized trial has been conducted, the results of which were published in 1976 [6]. In that trial, 29.2% of patients not receiving prophylaxis had clinically important bleeding, compared with 4.2% of patients receiving antacid prophylaxis ($P < 0.02$). Using adult patients with head injuries (Glasgow Coma Scores ≤10) as another example, one trial published in 1993 ($n = 167$) [7] found no instances of clinically important bleeding with either saline placebo or ranitidine, whereas another trial published in 1995 ($n = 34$) [8] found that 27.8% of patients receiving no prophylaxis had clinically important bleeding compared with none of the patients in the ranitidine group ($P \leq 0.05$).

Some of the variation in bleeding rates in published studies may be attributable to the definition used for delineating patients at risk for stress-induced complications. Two risk factors have been found to be predictive of clinically important bleeding using multivariate analytic techniques in a large sample of mixed medical/surgical patients [9]. These risk factors are respiratory failure requiring mechanical ventilation, and coagulopathy. It is unknown whether these findings are applicable to more homogeneous, specialized populations (eg patients with burns or trauma, or patients undergoing central nervous system surgery) because of lack of study inclusion or insufficient enrolment numbers.

Once the decision is made to use prophylaxis, there are several medications available. In the present investigation, 77% of the institutions surveyed used histamine-2-antagonists as the agent of choice, whereas 20% used sucralfate. These percentages are similar to the findings in another survey of stress ulcer prophylaxis in which histamine-2-antagonists were used in 67% of patients compared with 24% of patients receiving sucralfate [10]. The majority of published studies using clinically important bleeding as an end point have involved histamine-2-antagonists and sucralfate. The most comprehensive meta-analysis [1] found no substantial differences in clinically important bleeding between the latter agents, whereas the most recent and largest randomized trial [2] suggested that ranitidine was more efficacious than sucralfate (at least with the doses used in the trial). Trials involving other agents such as the proton pump inhibitor omeprazole have either not used clinically important bleeding as an end point or lacked sufficient power to detect potential differences in bleeding between other agents or when compared with placebo. Given the similar type of action (inhibition of acid release) between histamine-2-antagonists and proton pump inhibitors, it seems likely that the pump inhibitors would have similar efficacy.

Given the inconsistent results of published investigations, it is perhaps not surprising that almost all aspects of stress ulcer prophylaxis remain controversial. Until some of the issues are resolved through further study, there are a few recommendations that seem in order. First, it seems that clinicians should aim for some form of consistency based on intra-institutional guidelines using the most current, best evidence of prophylactic benefit with histamine-2-receptor antagonists. A majority of institutions surveyed (73%) had no guidelines in place. Of those that did have guidelines, almost half (48%) had not been updated in the 2 years before receiving the survey. This finding is of concern, because the most comprehensive meta-analysis [1] and largest randomized study [2] to date concerning stress ulcer prophylaxis were published in the 2 years preceding the survey. This finding could be misleading, however, because it is possible that the results of these recent publications did not require an alteration in the institution's guidelines.

Institutions contemplating the development of stress ulcer prophylaxis guidelines should take advantage of existing information. One organization, the American Society of Health-System Pharmacists, has recently promulgated guidelines for stress ulcer prophylaxis that could be used as a template for the intra-institutional development process [11]. The American Society of Health-System Pharmacists guidelines have an economic model that can be modified using local efficacy, toxicity, and cost information.

There is another large survey that has been published concerning stress ulcer prophylaxis [10]. That survey, however, was conducted in October 1995, which was before the publication of the largest meta-analysis [1] and largest randomized controlled trial [2] to date. The present survey was conducted in the fall of 1998, with one intention of determining how those reports may have influenced prescribing habits. A second difference relates to the sample of clinicians being surveyed. The previous study [10] selected a random sample of the members of the Society of Critical Care Medicine who identified anesthesiology, surgery, or internal medicine as their specialty area. The survey response rate was 26%. Our survey was sent to the entire Section of Pharmacy and Pharmacology of the Society of Critical Care Medicine, and had a response rate of 42%.

Another recommendation is to review stress ulcer prophylaxis prescribing periodically, as well as any guidelines that are in place. Both published literature and local evaluations may necessitate a change in the guidelines. There are examples in the literature of where guideline changes relative to stress ulcer prophylaxis have resulted in lowered institutional costs without compromising the quality of patient care [12].

A final recommendation applies to those individuals who have the capabilities of performing clinical studies concerning stress ulcer prophylaxis. Although it seems

unlikely that another study involving general medical/surgical patients would resolve the debate concerning the need for prophylaxis, randomized studies involving specialized populations (eg trauma patients) could be of potential value, given the relative lack of controlled investigations. Also, comparative studies involving newer medications and different routes of administration are needed that use clinically important bleeding as an end point.

Although the results of this survey describe some of the current prescribing practices of physicians in the USA relative to stress ulcer prophylaxis, there are important limitations to the information presented. Some of the limitations concern questionnaires in general. For example, there are concerns regarding the number and type of questions. If the instrument contains an excessive number of questions, the responder may be less willing to complete and return the material. This survey was limited to one page, front and back, in an attempt to increase compliance. Another concern in common with all questionnaires relates to the reliability and validity of the instrument, although attempts were made to reduce such problems during the instrument construction process.

Other limitations of these results pertain to the topic at hand (ie stress ulcer prophylaxis). Physician prescribing and guideline development are affected at different times and to varying degrees by published trials. The largest randomized trial comparing ranitidine and sucralfate for stress ulcer prophylaxis was published in March 1998 [2]. This survey was mailed approximately 6 months after that publication. Therefore, physician prescribing and institutional guidelines may not have changed as a result of that trial at the time of the present survey. Additionally, the responses to the survey questions are a function of the person completing the survey. Because the individuals completing the survey were members of the Section of Pharmacy and Pharmacology of the Society of Critical Care Medicine, it was presumed that they were well versed in the area of stress ulcer prophylaxis issues at their institutions.

Conclusion

There are wide variations in prescribing practices with regard to stress ulcer prophylaxis, although such prophylaxis is used in the majority of ICU patients. Histamine-2-antagonists, sucralfate, and proton pump inhibitors are commonly used agents, with histamine-2-antagonists being the most commonly preferred agent among the institutions surveyed. Published literature and available guidelines should be used as a template for institutions that are constructing their own guidelines.

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