

## Research

# Stress ulcer prophylaxis in trauma patients

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Received: 17 May 2002

Revisions requested: 7 August 2002

Revisions received: 21 August 2002

Accepted: 25 August 2002

Published: 25 September 2002

*Critical Care* 2002, **6**:526-530 (DOI 10.1186/cc1831)

This article is online at <http://ccforum.com/content/6/6/526>

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## Abstract

**Introduction** A number of issues concerning stress ulcer prophylaxis remain unresolved despite numerous randomized, controlled trials and several meta-analyses. The role of stress ulcer prophylaxis, particularly in trauma patients, is further complicated by the lack of trials utilizing clinically important bleeding as an endpoint. Given the lack of consensus regarding stress ulcer prophylaxis in trauma patients, prescribing practices at Level I trauma centers in the United States were assessed.

**Materials and methods** A survey was developed that contained questions related to institutional prescribing and evaluation of stress ulcer prophylaxis. The survey was intended to delineate these practices at the 188 Level I trauma centers (at the time of the present survey) in the United States.

**Results** One hundred and nineteen surveys were returned, yielding a response rate of 63%. Eighty-six percent stated that medications for stress ulcer prophylaxis are used in a vast majority of trauma patients admitted to the intensive care unit. Sixty-five percent stated that there is one preferred medication. For these institutions, histamine-2-blockers were the most popular at 71%. Thirty-nine percent stated that greater than 50% of patients remain on stress ulcer prophylaxis following discharge from the intensive care unit.

**Conclusion** The lack of consensus with regards to appropriate stress ulcer prophylaxis is apparent in this survey of Level I trauma centers. For those institutions with a preferred agent, histamine-2-blockers were most common.

**Keywords** prophylaxis, stress ulcers, trauma

## Introduction

There are numerous randomized, controlled trials and several meta-analyses evaluating drug therapy for stress ulcer prophylaxis [1]. While these publications have shown significant benefit with using prophylaxis, a number of issues still remain unresolved. For example, Cook *et al.* performed a meta-analysis of published and unpublished research, and they concluded that sucralfate might be as effective as pH-altering medication in preventing stress-induced bleeding, with a lower incidence of pneumonia and mortality [1]. In a subse-

quent multicenter, randomized trial involving 1200 patients, Cook *et al.* found a lower incidence of clinically important gastrointestinal bleeding with ranitidine compared with sucralfate (relative risk, 0.44; 95% confidence interval, 0.21–0.92;  $P=0.02$ ), with no differences in pneumonia or mortality [2].

In contrast to the multiple, and often conflicting, studies of stress ulcer prophylaxis conducted in general medical and surgical populations, decisions concerning appropriate stress

ulcer prophylaxis in trauma patients are further complicated by a lack of randomized, controlled trials using clinically important bleeding (e.g. requiring transfusion, hemodynamic instability) as an endpoint. Furthermore, while many studies involving more heterogeneous patient populations included trauma patients, there were often insufficient numbers of these patients to draw any definitive conclusions. The relative lack of prospective studies involving trauma patients is somewhat surprising given the relationship between injury and gastrointestinal ulceration that was well described during the Korean and Vietnam wars [3,4].

Retrospective analyses of large numbers of trauma patients have found the incidence of stress-induced bleeding to range from 0.05 to 2.3% [5,6]. The lower figure was based on patients with clinically evident complications of bleeding such as perforation or blood loss requiring transfusion [5]. The higher figure was taken from an abstract in which gastrointestinal bleeding was not defined, so there is no way of knowing whether it led to any clinically important problems [6]. Both of these figures could, however, be misleading due to the difficulties in extracting such information from retrospective chart reviews or trauma registries.

A number of risk factors have been associated with stress ulceration in trauma patients, including sex, lung injury or pneumonia, renal or hepatic failure, sepsis, and severity of injury [5,6]. Two factors that appear to be independently predictive of bleeding are severe injury as defined by an Injury Severity Score greater than 16 and single-system injuries (e.g. head and spinal cord injuries) of the central nervous system [5]. However, the use of routine stress ulcer prophylaxis in these groups has both proponents [7] and opponents [8]. The diversity of opinion is partially explained by methodological problems of the available studies. For example, the incidence of clinically important bleeding is difficult to estimate since many of these studies did not distinguish between various types of occult (microscopic), overt (macroscopic), and clinically important bleeding [9–14].

Once the decision is made to use stress ulcer prophylaxis, the clinician must decide between histamine-2 (H<sub>2</sub>)-antagonists, antacids, sucralfate, and proton pump inhibitors. There have been no prospective studies of adequate power involving trauma patients to determine whether there are important differences between these agents in preventing stress-induced bleeding complications. Some studies have attempted to determine whether there might be important differences in the adverse effect profiles of the medications, particularly nosocomial pneumonia. In general, there have been no significant differences in pneumonia between the various agents [15–17], although the appropriate diagnostic criteria for pneumonia in clinical investigations have been an issue of debate.

Given the lack of consensus on virtually every aspect of stress ulcer prophylaxis, a survey was developed to assess

current prescribing practices in Level I trauma centers in the United States. Additionally, the survey had questions concerning intra-institutional evaluations of prescribing practices.

## Materials and methods

A survey was developed that contained questions related to institutional prescribing and evaluation of stress ulcer prophylaxis. The survey was intended to delineate these practices at the 188 Level I trauma centers (at the time of the present survey) in the United States. The survey was limited to the front and back of one sheet of paper to encourage completion. There were 11 questions concerning stress ulcer prophylaxis, although several of the questions contained subparts. For example, one question evaluating institutional approaches asked 'Does your institution have written guidelines for stress ulcer prophylaxis?'. If the answer was yes, then the respondent was questioned on various aspects of these guidelines (i.e. have the guidelines been updated/reviewed in the past 2 years?, do they include recommendations for intensive care unit [ICU] and non-ICU settings?, etc.) A majority of the questions were in yes/no format; however, some questions requested information stated as a percentage value. For example, 'What percentage of patients discharged from the ICU to non-ICU settings remain on stress ulcer prophylaxis?'. The responses included 0–25%, 26–50%, 51–75% and 76–100%. The survey was approved by the human subjects committee (exempted from committee review).

The instrument was reviewed by several experienced trauma surgeons and pharmacists (who were not involved with this project) prior to mass distribution to assure validity and reliability. Changes to the instrument were then made accordingly. The survey was mailed to the trauma coordinator at each Level I trauma center. A self-addressed, stamped envelope was included to encourage return of the completed survey.

## Results

A total of 188 surveys were distributed to Level I trauma centers; 119 were returned, producing a response rate of 63%. Fifty-seven percent of the hospitals surveyed had more than 400 beds, and 29% of hospitals had between 200 and 399 beds. A further description of the hospitals surveyed, particularly a differentiation between the number of ICU beds versus trauma beds, is presented in Table 1.

Eighty-six percent of Level I trauma centers stated that medications for stress ulcer prophylaxis are used in a vast majority of trauma patients admitted to the ICU. The prescribing practices for stress ulcer prophylaxis are further described in Table 2. The most common type of injury where stress ulcer prophylaxis was routinely administered was a head injury, which is further described in Table 3.

Forty-five percent of the centers have recommendations for both ICU and non-ICU settings. Thirty-seven percent of institutions have written guidelines for stress ulcer prophylaxis,

**Table 1**

Description of the institutions surveyed*	Institutions (%) stating number of beds			
	<20 beds	20–29 beds	30–39 beds	>40 beds
Number of ICU beds	17	16	16	52
Number of trauma beds	47	24	7	23

\* The number of intensive care unit (ICU) beds refers to the total ICU beds for the hospital; the number of trauma beds was intended to delineate ICU trauma beds.

with approximately one-half of those stating that their guidelines have been reviewed or updated within the past 2 years. Forty-five percent of responders are either considering or developing guidelines for their respective institutions.

Sixty-five percent of institutions stated that there is one preferred medication for stress ulcer prophylaxis. For those institutions, H2 antagonists were the most popular at 71%. Sucralfate was the agent of choice for 25% of institutions, while omeprazole and antacids were preferred for 3 and 1%, respectively. A breakdown of the route of administration for each agent is presented in Table 4.

**Table 2**

**Stress ulcer prophylaxis in intensive care unit (ICU) and non-ICU settings**

	Institutions (%) stating percentage of patients			
	0–25%	26–50%	51–75%	76–100%
ICU trauma patients received stress ulcer prophylaxis	8	4	11	77
Non-ICU trauma patients received stress ulcer prophylaxis	39	21	28	12
Patients discharged from the ICU to non-ICU settings remained on stress ulcer prophylaxis	33	28	25	14

**Table 3**

**Injuries where stress ulcer prophylaxis is routinely administered\***

Injury	Yes	No	Do not have substantial numbers of this injury
Head injury	106 (90%)	5 (4%)	7 (6%)
Spinal cord injury	100 (85%)	6 (5%)	11 (10%)
Thermal injury	62 (57%)	6 (6%)	40 (37%)
Multiple trauma	102 (88%)	10 (9%)	4 (3%)
Hepatic injury with need for partial resection	77 (69%)	12 (11%)	23 (20%)

\* Data are expressed as the number of institutions responding to the question (percentage of responders).

**Table 4**

Description of the route of administration for each institution's preferred agent*	
Histamine-2 antagonist	
Intermittent intravenous	40
Intravenous infusion	27
Oral	15
Feeding tube	16
Sucralfate	
Oral	18
Nasogastric tube	24
Omeprazole	
Oral	2
Nasogastric tube	2
Enteral tube	3
Other (antacid)	1

\* Responders were permitted to check more than one administration route for their institution's preferred agent.

Twenty-seven percent of institutions evaluated the incidence of clinically important bleeding, defined as the need for transfusion or hemodynamic changes associated with bleeding. Fifteen percent of those institutions limited their evaluation to patients receiving stress ulcer prophylaxis, and 69% included both ICU and non-ICU patients. Twenty-nine percent of institutions routinely used gastric pH measurements (i.e. pH

paper, pH sensor, gastric tonometry) for monitoring pH-altering agents when such measurements were feasible.

## Discussion

One hundred and nineteen surveys were returned from Level I trauma centers, yielding a total response rate of 63%. The results obtained from the present survey indicated that prophylaxis is used in a high percentage of patients at Level I trauma centers, particularly in the ICU. Part of the explanation for this widespread prescribing may be due to the lack of well-defined risk factors for stress-induced bleeding in trauma patients. Another explanation for the widespread prescribing of medications for stress ulcer prophylaxis in trauma patients may be the lack of intra-institutional data concerning the incidence of clinically important bleeding. Only 27% of the institutions surveyed evaluated the incidence of clinically important bleeding. Of those institutions, the majority (85%) evaluated all ICU patients for potential bleeding, irrespective of whether the patients were receiving stress ulcer prophylaxis.

While a number of institutions had a preferred medication for prophylaxis, there were usually no restrictions placed on the choice of medication. It is difficult to state that there is a clear agent of choice for stress ulcer prophylaxis in any population based on available research in general medical/surgical patients, and even less reason to recommend a particular agent in trauma patients. The largest randomized, controlled trial to date was conducted by Cook *et al.* [2] This study, which involved a heterogeneous group of patients at risk for stress ulcer prophylaxis, found ranitidine to be more effective than sucralfate. However, an earlier meta-analysis by some of those authors suggested no substantial differences in efficacy between the available agents [1].

The present survey revealed that H<sub>2</sub>-antagonists were the preferred agent in Level I trauma centers, followed by sucralfate and, finally, omeprazole. A limited number of institutions have reviewed their guidelines within the past 2 years, therefore it is unclear whether H<sub>2</sub>-antagonists have always been the preferred agents or whether guidelines have been changed due to the recent findings of Cook *et al.* [2]. Given the lack of consensus as to the most appropriate agent for prophylaxis, it seems reasonable to make the decision at the local level based on cost, convenience, and adverse effects.

The number of patients receiving stress ulcer prophylaxis in non-ICU settings is a cause for concern. Forty percent of institutions stated that non-ICU trauma patients receive stress ulcer prophylaxis more than 50% of the time. In the overwhelming majority of published studies concerning stress ulcer prophylaxis, the prophylactic medication was discontinued when a patient was transferred out of the ICU. The present report showed that 39% of institutions have greater than one-half of their patients discharged from ICU to non-ICU settings remaining on stress ulcer prophylaxis. While there have been few controlled studies of stress ulcer pro-

phylaxis in non-ICU settings, indirect evidence (i.e. routine discontinuation of prophylaxis in published investigations) suggests that most experts believe the risk of clinically important bleeding is too low to justify continued prophylaxis.

The medications used for stress ulcer prophylaxis have associated costs and adverse effects that must be considered when contemplating the continuation of prophylaxis. The drug-related costs are not always obvious. For example, since sucralfate acts locally it would be expected to have few systemic adverse effects, but it may result in clogged feeding tubes that need to be replaced. In this example, there is the cost of the medication, the cost of the feeding tube, and the cost of the personnel time required to replace the tube. Second, the most popular medication class and route of administration for stress ulcer prophylaxis, according to our survey, are H<sub>2</sub>-antagonists by intravenous injection. The additional costs of intravenous tubing, infusion pumps, and personnel time must be considered when addressing the total cost of therapy.

Of those institutions that have substantial numbers of single-system type injuries such as burns, central nervous system damage, or hepatic damage, stress ulcer prophylaxis is routinely implemented. It is difficult to argue, at least in the ICU setting, against such use given the paucity of randomized investigations conducted in these populations using an endpoint of clinically important bleeding. However, it is reasonable to set local guidelines based on some type of severity of injury scale, since the risk of bleeding appears to be correlated with severity of injury [5]. In one of the largest prospective trials to date, respiratory failure (i.e. mechanical ventilation for >48 hours) and coagulopathy (i.e. platelet count <50,000 mm<sup>3</sup>, or an International Normalized Ratio >1.5 or a partial thromboplastin time >2 times the control value) were found to be independent predictors of clinically important bleeding in a heterogeneous population of medical/surgical patients [18]. Although this requires further study, it is possible that respiratory failure and coagulopathy may serve as adequate predictors of bleeding in trauma patients as well as in these mixed populations.

The lack of consensus with regards to appropriate stress ulcer prophylaxis is apparent in this survey of Level I trauma centers. Given the limitations of the survey instrument, it cannot be stated with certainty that the 63% of centers responding to the survey represent Level I trauma centers as a whole with regards to size, to geographic location, and to survey responses. It does seem unlikely, however, that the basic results would change substantially with such additional information given that the one area of consistency in responses was the high percentage of trauma patients in the ICU who were thought to be in need of prophylaxis. Most other aspects of prophylaxis, including the choice of medication, the route of administration, and the discontinuation of prophylaxis upon ICU discharge, varied among institutions.

### Key messages

- There is a lack of consensus regarding stress ulcer prophylaxis in trauma patients
- Many patients in non-ICU settings still receive stress ulcer prophylaxis
- H2-blockers are the preferred agent for many institutions

The varying prescribing patterns noted with this survey of trauma centers are consistent with the results obtained from another survey involving a more heterogeneous group of critical care physicians. Lam *et al.* surveyed members of the Society of Critical Care Medicine who listed anesthesiology, internal medicine, or surgery as their primary specialty [19]. The survey was sent to 1268 physicians, and had a response rate of 26%. The diversity of the practice areas of the physicians under study was evident in the respondents' reasons for initiating stress ulcer prophylaxis. Using a checklist of 12 possible reasons for prophylaxis (plus an 'other' category), at least 20% of respondents chose each listed risk factor as sufficient justification for prophylaxis. Several reasons were given for the choice of agent, including ease of administration, clinical effectiveness, cost-effectiveness, and formulary considerations. Despite the different response rates and physician groups surveyed, the major results and conclusions of Lam *et al.* [19] were similar to those reported in this evaluation (i.e. a lack of consensus regarding stress ulcer prophylaxis prescribing).

The number of institutions performing evaluations of stress ulcer prophylaxis was less than 50% of those surveyed. Medications, however, do not guarantee prevention of stress-induced bleeding. Additionally, the medications have potential adverse effects and associated costs of administration. Therefore, periodic examination of prescribing and bleeding patterns is indicated. For those institutions developing or revising stress ulcer prophylaxis guidelines, comprehensive recommendations have been developed that may facilitate this process [20].

### Competing interests

Since completing this research project, JFB has served as a speaker for Wyeth.

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