

Implementing inpatient, evidence-based, antihistamine-transfusion premedication guidelines at a single academic US hospital

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Allergic transfusion reactions (ATRs) are a common complication of blood transfusions. Advances in transfusion medicine have significantly decreased the incidence of ATRs; however, ATRs continue to be burdensome for patients and problematic for providers who regularly order packed red blood cells and platelet transfusions. To further decrease the frequency of ATRs, routine premedication with diphenhydramine is common practice and is part of “transfusion culture” in a majority of institutions. In this article, we review the history, practice, and literature of transfusion premedication, specifically antihistamines given the adverse-effect profile. We discuss the rationale and original academic studies, which have supported the use of premedication for transfusions for decades. However, despite the common use of premedication to prevent ATRs, recent literature has not conclusively validated its use. In addition, the existing premedication that is routinely prescribed often causes a number of adverse effects. These findings have motivated the Moores Cancer Center (University of California, San Diego) to change its current transfusion premedication practices, particularly with regard to ATRs and first-generation antihistamines. We outline the preliminary development of an evidence-based and patient-specific approach to transfusion premedication, including the challenges and steps taken to revise inpatient premedication protocols. We plan to expand this protocol to the outpatient setting at a later date. Future efforts require a prospective validation of our presented transfusion premedication guidelines.

Acute transfusion reactions such as allergic transfusion reactions (ATRs) have complicated the delivery of blood products since the establishment of transfusions. Although the true incidence of ATRs is not established, as there are wide variations in institutional reporting rates, the incidence of ATRs ranges from less than 1% up to 17%.¹ ATRs are responsible for the majority of transfusion interruptions and represent a major impediment to the delivery of needed transfusion support. As a result, ATRs result in additional blood-donor exposure and significant added health care expenditures.

ATRs range from mild (itching, hives) to anaphylaxis (bronchospasm, hypotension, and shock).² The pathophysiology of ATRs is unclear. Patient immunoglobulin E (IgE) antibodies have been classically elevated and associated with ATRs and postulated to be a main contributor in such reactions.³

Some donors are more frequently related to ATRs, indicating a possible relationship of the donor to the development of an ATR.⁴ Elevated levels of complement component, brain-derived neurotrophic factor, and chemokine (C-C motif) ligand 5 in platelet units have also been associated with ATRs.⁵ Prophylactic diphenhydramine, a first-generation antihistamine, has conventionally been empirically used for ATR prophylaxis.

In an effort to reduce ATRs, transfusion medicine physicians and researchers have developed new techniques, including clearer definitions of transfusion thresholds, plasma volume reduction, the washing of blood products, and storage in additive solution. These techniques have significantly decreased the incidence of ATRs. Although transfusion thresholds are regularly determined at the discretion of the ordering provider, studies show that lower-than-conventional thresholds can be safe.⁶ Setting

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clearly defined, clinically relevant transfusion thresholds and avoiding unnecessary transfusions are two often overlooked, but extremely important, means of decreasing all transfusion reactions and overall cost. Additionally, the concentration of blood products by plasma volume reduction, the washing of blood products, and the storage in additive solution all reduce rates of ATRs. Removal of most donor plasma in platelets has reduced the risk of ATRs from 5.5% to 1.7% in patients with prior history of multiple ATRs. Removing the donor plasma by washing platelets and packed red blood cells (PRBCs) has reduced the risk of ATRs to 0.5%.⁷ The transfusion of platelets stored in platelet-additive solution vs plasma, a storage technique recently approved by the US Food and Drug Administration (FDA), has also been shown to significantly decrease ATRs.⁸

Despite these major advances in transfusion medicine, ATRs continue to be a common complication of blood transfusions. Given the approximately 30 million blood components transfused in the United States each year,⁹ ATRs remain a challenge. In this article, we describe the data regarding routine premedication prior to blood transfusions and the risks associated with this practice, and present our evidenced-based and patient-specific approach to transfusion premedication, with particular emphasis on antihistamines.

The scope of the challenge

The history and rationale of transfusion premedication

In an attempt to prevent ATRs, physicians for decades have been prescribing transfusion premedication. In the 1950s, antihistamines – specifically chlorpheniramine – were injected into the blood products to decrease ATRs.¹⁰ Since then, transfusion premedication has evolved to include antihistamines such as diphenhydramine.

Physicians and nurses prefer premedication prior to transfusions for many reasons. Patients who receive blood products are often the most critically ill patients with multiple comorbidities. Complications including fever or rash that are attributed to a transfusion reaction may prevent or delay the completion of necessary transfusions. Furthermore, given that the blood products and infusion-center space are expensive and limited resources, medical providers prefer to err on the side of premedication rather than risk the possibility of a transfusion reaction. The significant cost, time, and resources required to work up a transfusion reaction are also incentives to premedicate.

The culture of transfusion premedication

Medical reasoning and cost aside, physicians who order blood products continue to give premedication regularly for transfusions in the belief that premedication will further decrease the incidence of ATRs. The practice of universal premedication to avoid blood transfusion reactions

is deeply ingrained in medical culture. It is still common to prescribe premedication, specifically acetaminophen and diphenhydramine, prior to the transfusion of all blood products without considering risk or prior transfusion reactions.¹¹ Although there has been discussion to change current routine premedication practices, there are challenges to changing this deeply established medical practice.^{11,12}

The leading reason for premedication may be the “culture of premedication.” Premedication has been ingrained in medical practice as “what we do.” Literature on ATRs often recommends premedication, perpetuating and authorizing its use.^{13,14} Premedication is frequently written into institutional transfusion protocols. Moreover, past generations of physicians, nurses, nurse practitioners, physician assistants, and even patients have communicated its utility to future generations. Because of these continued practices, premedication has become the standard of care.

Paucity of data

The most debatable topic, however, is the wide use of antihistamine premedication, despite very limited data to support its use (Table 1). Although 1950s data for premedication may have shown a decrease in ATRs, data over the past decade have challenged the utility of routine premedication for all blood products.¹⁵⁻²⁰ A small number of studies has examined the role of premedication for transfusions, but of the few that were published, the two prospective, randomized trials did not yield any significant difference in ATRs with premedication.^{16,17}

Furthermore, the available studies are limited by insufficient details outlining the adopted transfusion-reaction protocols. No standardized drug, dose, timing, or route of administration for antihistamines is provided. Although most facilities and studies use diphenhydramine as the choice antihistamine, a number of alternative antihistamines have fewer associated adverse effects. However, a PubMed literature search revealed no published studies comparing the efficacy of other antihistamines as a transfusion premedication. In addition, no guidelines for premedication exist for specialized products such as human leukocyte antigen-matched platelets, antigen-negative platelets, and antigen-negative PRBCs.

The dark side of routine transfusion antihistamine premedication

The use of conventional premedication does have known adverse effects. Diphenhydramine, the most commonly used antihistamine, has a large adverse-effect profile. Diphenhydramine falls in a class of antihistamines that inhibit target receptors (such as muscarinic and α -adrenergic receptors) and cross the blood-brain barrier. Consequently, its adverse effects include dry mouth, tachycardia, urinary retention, cognitive impairment, sedation, and delirium. Compared with patients who take nonsedating antihis-

TABLE 1 Summary of studies evaluating premedication for allergic transfusion reactions^a

Author, year Study type	No. of transfusions	Aims	Products evaluated evaluated (patients)	Medications administered	Reactions evaluated
Kennedy, 2008 ¹⁶ Prospective, randomized	4,199 (315)	Compare the risk of transfusion reactions in hematology/oncology patients who receive acetaminophen with diphenhydramine or placebo before transfusion.	Leukoreduced PRBCs and leukoreduced platelets (single-donor apheresis); products irradiated for BMT patients	Acetaminophen 500 mg plus diphenhydramine 25 mg vs placebo administered 30 minutes before first transfusion	FNHTR, ATR
Wang, 2002 ¹⁷ Prospective, randomized	98 (51)	Evaluate the efficacy of acetaminophen and diphenhydramine as premedication for transfusions in hematology/oncology patients.	Leukoreduced platelets (single-donor apheresis)	Acetaminophen 650 mg plus diphenhydramine 25 mg IV vs placebo	NHTR, ATR
Sanders, 2005 ¹⁸ Prospective	7,900 (385)	Evaluate the effectiveness of premedication with acetaminophen and/or diphenhydramine in FNHTR and ATR.	Leukoreduced, irradiated PRBCs and platelets (single-donor apheresis)	Acetaminophen and/or diphenhydramine (doses unspecified)	FNHTR, ATR
Patterson, 2000 ¹⁹ Retrospective	3,472 (716)	Compare the rates of transfusion reactions before and after pretransfusion guidelines.	Nonleukocyte reduced, pooled, random-donor platelets	Acetaminophen and/or antihistamine (doses unspecified)	FNHTR, ATR
Szelei-Stevens, 2006 (abstract) ²⁰ Retrospective	301,210 (31,665)	Investigate whether premedication with acetaminophen and diphenhydramine decrease FNHTR and ATR.	PRBCs, platelets (single-donor apheresis), and FFP/cryoprecipitate (unknown if leukoreduced)	Acetaminophen and/or diphenhydramine (doses unspecified)	FNHTR, ATR

ATR, allergic transfusion reaction; BMT, bone marrow transplant; CI, confidence interval; FFP, fresh frozen plasma; FNHTR, febrile nonhemolytic transfusion reaction; NHTR, nonhemolytic transfusion reaction; PRBCs, packed red blood cells

^aAdapted from Fry et al.¹⁵

Limitations	Result
<ul style="list-style-type: none"> ■ Low event rates ■ Plasma transfusions were not evaluated ■ Lack of methodology of transfusion protocol 	<p>No difference in FNHTRs ($P = .08$) or ATRs ($P = .90$) based on one-sided P value. No difference in number of transfusions until first reaction ($P = .39$).</p>
<ul style="list-style-type: none"> ■ Platelet transfusions only ■ Lack of methodology transfusion protocol 	<p>No difference in NHTRs ($P = .94$); NHTRs occurred more often in patients with history of NHTR than in those with no history ($P = .06$).</p>
<ul style="list-style-type: none"> ■ Retrospective study ■ Pediatric population ■ Lack of methodology of transfusion protocol ■ Doses unspecified 	<p>No difference in FNHTRs ($P = .22$) or ATRs ($P = .054$).</p>
<ul style="list-style-type: none"> ■ Observational study ■ Platelet transfusions only ■ No standardized premedication dosing, drugs ■ Lack of methodology of transfusion protocol 	<p>No difference in FNHTRs or ATRs. With 73% of patients premedicated, 30% (95% CI, 28% \pm 33%) of transfusions were complicated by FNHTRs and ATRs. With 50% of patients premedicated the following year, 26% (95% CI, 24% \pm 29%) of transfusions were complicated by FNHTRs and ATRs.</p>
<ul style="list-style-type: none"> ■ Retrospective study ■ Lack of methodology of transfusion protocol ■ Doses unspecified 	<p>No difference in FNHTRs ($P = .31$). No difference in ATRs; of the 154 patients premedicated with diphenhydramine, 49.3% had ATRs; of the 90 patients not premedicated, 39% had ATRs</p>

tamines, those who receive diphenhydramine have an increased risk of serious injury and increased risk of cognitive changes in attention, working memory, and motivation.^{21,22} Given the usual population receiving blood transfusions (older, more seriously ill patients), these adverse effects may be heightened and potentially more dangerous. Therefore, the routine use of diphenhydramine may place patients at an even higher risk of unintentional injury, especially when it is used in the outpatient setting from which patients have to drive home.

Finally, the true cost benefit of premedication has not been fully analyzed. Although premedications alone are relatively inexpensive, there are a number of indirect costs in administering them, including costs for nursing, pharmacy, infusion-center, and inpatient resources. For example, hypotension or delirium associated with diphenhydramine may require clinical evaluation and work-up, and may therefore occupy necessary and expensive infusion-center and inpatient space. Altogether, these less-obvious costs may be more expensive than those from rationally dosed premedication.

Approach to developing recommendations

After reviewing the current literature on transfusion premedication, we decided to revise the transfusion premedication practices at our institution to better reflect evidence-based practices. Our blood bank distributes approximately 27,000 units of blood components yearly. For the scope of this article, we narrowed the focus to the inpatient bone marrow transplant (BMT) unit, which utilizes approximately 20% to 25% of all transfusions at our institution. Furthermore, we focused on ATRs and antihistamine use given the anticholinergic effects, as well as the impact on patient quality of life and medical cost. All transfused blood products that are ordered through our blood bank for hematology/oncology/BMT patients are leukoreduced and irradiated, and platelets are single-donor apheresis platelets.

To initiate the revision of transfusion premedication, the director of transfusion medicine, the clinical director of the BMT program, a supportive oncology physician, and a physician assistant from the cancer center's infusion center formed a "Transfusion Premedication Utilization Committee." The committee met several times to identify the current challenges with transfusion-premedication practice at our institution, to review the pharmacology and current costs of premedication, and to develop an evidenced-based protocol for inpatient transfusion premedication with the plan to initiate these measures in the hospital first and then to expand to the outpatient setting.

Identifying the current problems

The first challenge with the current transfusion-premedication protocol was the established electronic order set.

Our institution utilizes computerized, provider-order entry to order all inpatient transfusions. This order set includes a drop-down menu for premedication and blood products with modifiers. When we focused on antihistamines, we found that the previous BMT inpatient order set was limited to oral diphenhydramine 25 mg. Unless the provider selected to discontinue the diphenhydramine, the diphenhydramine would be ordered automatically. If the provider wanted an alternative premedication, she or he needed order it outside the order set, which required extra steps. Thus, most prescribers selected the preordered premedication without changing or discontinuing these default options. Therefore, our committee desired to modify the computerized premedication order set in order to encourage selective ordering of premedication for transfusion.

Another challenge facing the existing protocol was the adverse-effect profile of premedication, specifically diphenhydramine. Our team was contacted repeatedly by the inpatient nurses to assess patients with hypotension and/or tachycardia who had been premedicated with diphenhydramine. Many patients also experienced sedation after receiving diphenhydramine, which placed them at risk for falls. In the outpatient arena, the adverse effects of sedation required patients to be observed for a longer period of time in the infusion center, and prohibited the patient from driving home from treatment. A handful of patients reported a paradoxical restlessness and agitation associated with diphenhydramine, which then required low-dose lorazepam; the lorazepam, however, further potentiated the sedative effects of diphenhydramine. Compared with oral administration, intravenous diphenhydramine was also associated with a higher propensity for headaches, drowsiness, ataxia, and restlessness. Patients often asked to discontinue diphenhydramine because of its adverse effects and because they planned to drive home. It was important to identify those who might be at higher risk of ATRs and to administer the appropriate premedication, but many of these patients had no history of ATR, which put into question the benefits of premedication in the first place. The adverse-effect profile of diphenhydramine became such an issue that empirical switches from diphenhydramine to second-generation antihistamines were common practice, especially if the patient had any prior history of hypotension, tachycardia, drowsiness, or restlessness with diphenhydramine. Occasionally, antihistamines were discontinued altogether. These experiences in the inpatient setting and infusion center further emphasized the need to consider alternative antihistamine transfusion premedication.

Pharmacology and costs

These anecdotal cases moved the committee to reconsider the choice of diphenhydramine and evaluate other antihistamines commonly used as premedication for transfusions, and to decide whether an alternative antihistamine

(when appropriate) would be beneficial. There are 4 known histamine receptor subtypes; the H₁ subtype is associated with allergic inflammation resulting in pruritus and smooth-muscle contraction.²³ Both first- and second-generation antihistamines elicit their pharmacologic effects by competitive antagonism of histamine for the H₁ receptors present in smooth muscles, nerve endings, and glandular cells.²⁴ H₁ antihistamines downregulate allergic inflammation through the H₁ receptor. However, H₁-receptor antagonism may potentially cause central nervous system adverse effects, which manifest as dizziness, hypotension, and sedation. Antihistamines can also affect H₁ receptors through the muscarinic, α -adrenergic, and serotonin receptors as well as the cardiac ion channels, which cause dry mouth, urinary retention, sinus tachycardia, and cardiac arrhythmias.²⁵

Benefits of second-generation antihistamines include a lower incidence of central nervous system adverse effects, given that they are not considered to cross the blood-brain barrier. Second-generation antihistamines are specific and selective to H₁ receptors vs other receptors, such as muscarinic and α -adrenergic receptors. Both the literature and institutional experience dictated a more desirable safety profile for H₁-specific antihistamine premedication. After review of the typical antihistamines, cetirizine appeared to be the favored choice, based on a number of factors (Table 2). Cetirizine is a second-generation antihistamine with decreased risk for sedation, tachycardia, hypotension, and urinary retention. Its cost is minimally different from that of diphenhydramine, as cetirizine is available as a generic and is the least expensive second-generation antihistamine. Cetirizine also has a more potent and faster onset of action than do both fexofenadine and loratadine.²⁶ Thus, a proposal to change the premedication antihistamine to cetirizine was outlined and presented to the committee.

Changes in protocols

At a follow-up meeting, the committee reviewed information from the institutional evaluation as well as data from the published studies. A stepwise approach was taken to revise the transfusion premedication protocol. Because inpatients are under direct supervision for longer periods of time than are outpatients, we focused our initial efforts on the inpatient transfusion guidelines, with the goal of expanding these guidelines to the outpatient setting.

To reflect evidence-based standards, the inpatient BMT transfusion order set was changed so that the previously automatic default of predetermined oral diphenhydramine 25 mg would be omitted. Now, if the medical provider wishes to administer any premedication, he or she needs to actively select, through a drop-down menu, either an antihistamine (oral cetirizine 10 mg as the first choice antihistamine) and/or an oral acetaminophen (Figure 1). Recognizing that each patient's risk for a reaction may not be equivalent, the

TABLE 2 Summary of antihistamines

Generation (class)	Antihistamines	Crosses blood-brain barrier	Onset of action, min	Half-life, h	Elimination	Notable adverse effects	Cost, US \$
First (ethanolamines)	Diphenhydramine (oral)	Yes	120	9.2	Renal	Antimuscarinic effects and -adrenergic receptor blockade, tachycardia	0.04
First (ethanolamines)	Diphenhydramine (IV)	Yes	2-3	8.5	Renal	Antimuscarinic effects and -adrenergic receptor blockade, tachycardia	0.78
First (piperazines)	Hydroxyzine (oral)	Yes	30	20	Renal	Sedation	0.22
Second (piperidines)	Cetirizine (oral)	No	30-60	6.5-11	Renal	NA	0.16
Second (piperidines)	Fexofenadine (oral)	No	120	14.4	Bile	NA	1.51
Second (piperidines)	Loratadine (oral)	No	120	7.8	Renal	NA	0.30

IV, intravenous; NA, not applicable

committee recommended that patients who were at higher risk of reaction (including multiple mild allergic reactions; unexplained hypotensive reaction with prior transfusion; moderate to severe allergic reaction; known preexisting anti-IgA antibodies; and haptoglobin deficiency) be considered for more-aggressive premedication, such as cetirizine, an H₂ blocker such as ranitidine, as well as corticosteroids prior to transfusion. The efficacy of either corticosteroids or H₂ blockers has not been evaluated prospectively in blood transfusions. They have, however, been used in the treatment and prevention of other severe allergic reactions, including contrast allergies.^{27,28} Furthermore, in a high-risk allergy setting, the physician members of the committee strongly advocated administering steroids and H₂ blockers. In addition to the existing default blood-component specifications (ie, leukocyte-reduced, irradiated blood), the committee determined that these high-risk patients should ideally be considered for plasma volume reduction, washed blood products, and/or additive solution platelets, if available.^{7,29} The committee developed a detailed algorithm for the revised recommendations for BMT inpatient-transfusion premedication, with a particular focus on antihistamine use (Figure 2).

Preliminary results

In the year prior to and following the institutional change, the total BMT inpatient premedication orders decreased from 4,017 to 2,993. This was in the setting of an overall increase in blood products (PRBCs, platelets, cryoprecipi-

tate, fresh frozen plasma, and granulocytes) ordered, with 2,866 orders in the year prior to the change, and 3,266 orders in the year after the change. The use of diphenhydramine dropped from 85.9% to 34.2%, whereas the use of cetirizine increased from 3.3% to 55.9% (Table 3).

Challenges and limitations

With this premedication policy change, several challenges emerged. Staff and patient education regarding the change was one of the biggest challenges. As expected, most staff were unfamiliar with the evidence-based data surrounding premedication for transfusions, and therefore were skeptical of changing the routine practice. We were and are constantly educating and reeducating the staff regarding the new protocol and rationale behind the change. Furthermore, because there is a constant change in nursing staff, education about the change in premedication policy is not always successful, and some nurses continue to page physicians and midlevel practitioners to question the lack of premedication orders. Additionally, patients are wary of discontinuing premedication that they believe is preventing allergic reactions. Patients occasionally still ask for premedication, regardless of our new policy.

To complicate matters, a number of non-hematology/oncology physicians moonlight on the BMT service. If blood transfusions are ordered through the adult, non-BMT transfusion-order set, the order set still includes a drop-down menu with preordered diphenhydramine.

Anecdotally, however, the new policy seems to be

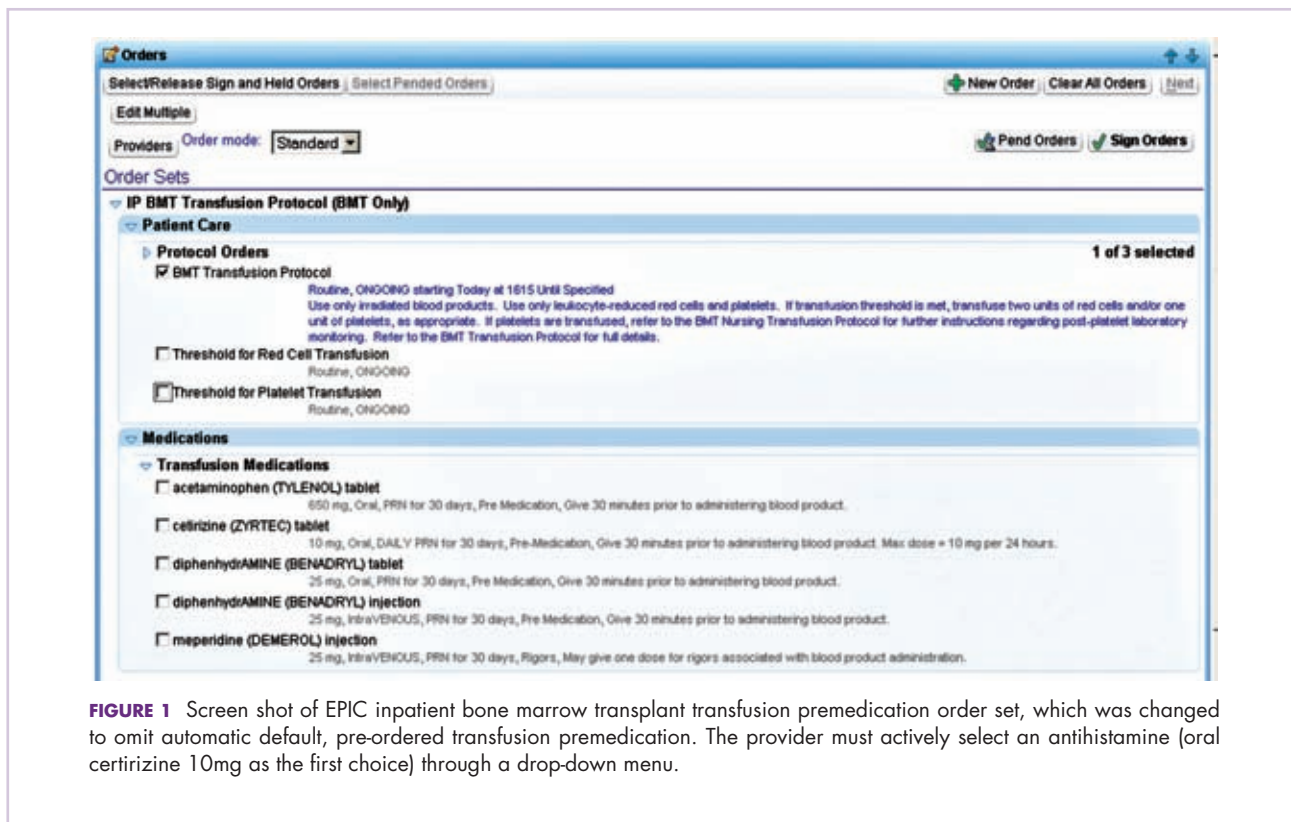


FIGURE 1 Screen shot of EPIC inpatient bone marrow transplant transfusion premedication order set, which was changed to omit automatic default, pre-ordered transfusion premedication. The provider must actively select an antihistamine (oral cetirizine 10mg as the first choice) through a drop-down menu.

having a positive effect. For example, the early adapting nursing staff has observed a reduced time to transfusion, as well as decreased sedation and delirium in patients. In addition, because of the notable decrease in sedation, many of the physicians have omitted premedication in their outpatients, which has allowed patients to be observed for a shorter period at the infusion center and permitted patients to drive themselves home. A few patients who previously requested either to hold or to switch antihistamines were supportive of the change in protocol.

Our retrospective review is limited in several ways. We restricted our scope to antihistamine premedication, and

did not collect any data regarding acetaminophen premedication use in febrile, nonhemolytic transfusion reactions. Furthermore, we did not compare the number of ATRs during this period to the number of reactions in patients who did and did not receive premedication; unfortunately, we were unable to obtain these data because of multiple electronic-charting systems at our institution. For example, medications are dated, charted, and filed in an order through our computerized system, but blood bank reactions (including febrile reactions and ATRs) are charted in a progress note. Therefore, transfusion reactions are not easily accessible or retrievable. For the same reason, there was no clear method to identify patients who received plasma-reduced or washed platelets. By identifying these retrospective limitations, our institution would like to implement changes to the electronic system in order to provide improved data for prospective validation. Furthermore, ATRs will now be charted as an allergy, which is easily retrievable. Our plan is to prospectively track each transfusion reaction, and to document premedication and type of blood product.

Discussion and future directions

ATRs continue to be a challenge in blood transfusions. New blood-bank techniques and approaches, such as plasma reduction, have decreased ATRs. As plasma reduction, the washing of blood products, and platelet additives be

TABLE 3 Antihistamine dose counts before and after implementation of inpatient transfusion premedication protocol

Drug	Dose count, no. (%)	
	Jul 2010-Jun 2011	Jul 2011-Jun 2012
Cetirizine	131 (3.3)	1,672 (55.9)
Diphenhydramine	3,453 (85.9)	1,025 (34.2)
Loratadine	433 (10.8)	296 (9.9)
Total	4,017 (100)	2,993 (100)

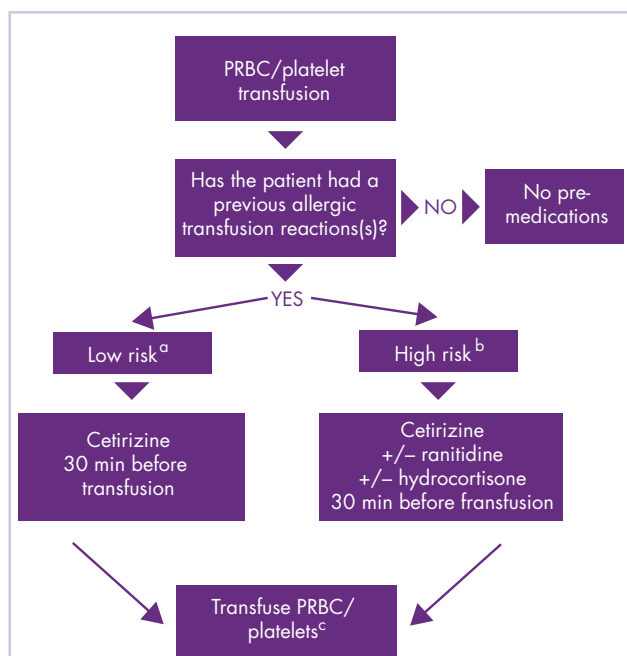


FIGURE 2 Algorithm for premedication for inpatient bone marrow transplant-related allergic transfusion reactions.

PRBC, packed red blood cells

^aLow-risk allergic reactions = one or no mild allergic reactions. Mild allergic reactions are reactions with only mucocutaneous signs and symptoms that respond quickly to treatment. ^bHigh-risk allergic reactions = multiple mild allergic reactions, unexplained hypotensive reaction with transfusion, moderate to severe allergic reaction, IgA deficiency, pre-existing anti-IgA antibodies, haptoglobin deficiency. ^cLeukoreduced, irradiated PRBCs: if there is a history of multiple allergic reactions, consider volume-reduced PRBCs, or washed PRBCs and/or 'additive solution' PRBCs if available. Leukoreduced, irradiated apheresis platelets: if there is a history of multiple allergic reactions, consider volume-reduced platelets, and/or washed platelets or 'additive solution' platelets if available.

come more readily available, these approaches may decrease ATRs even further. Avoiding unnecessary blood transfusions and developing clear, clinically relevant transfusion parameters are the most fundamental of these approaches to limiting ATRs.

We propose that universal premedication to decrease ATRs should not be a default institutional practice. We believe that the use of antihistamines should be selected based on risk, including the patient's prior history of ATR. We aimed to create an evidence-based, selective inpatient-transfusion premedication protocol in order to update our institutional transfusion practices, based on the available published data and patient-specific needs. Our first changes included avoidance of preordered premedication, specifically diphenhydramine, in the BMT inpatient transfusion order set. This change resulted in a dramatic decrease in the inpatient use of diphenhydramine and the subse-

quent increased use of cetirizine. We now plan to expand these guidelines to the outpatient setting, focusing on our infusion center. Although the aim of our changes to premedication is to practice more evidence-based medicine, the larger motive is to improve quality of life for our patients. The outpatient population would be a target population to measure quality-of-life changes before and after the change of premedication practices.

ATRs continue to be a major difficulty with transfusions. However, the role of premedication in the era of concentration of blood products is unclear. As the literature on transfusion premedication is limited, prospective studies evaluating the impact of rationally administered transfusion premedication are essential to appropriately avoid transfusion-related toxicity and to mitigate cost. We hope that the description of our experience will encourage other institutions to reevaluate and challenge the culture of routine transfusion premedication.

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