TxMD NEWS

ACCELERATE CHANGE. IMPROVE OUTCOMES. REDUCE COSTS. Volume 22

Tips for Transfusionists: Premedications before a blood transfusion. Where's the evidence?

Physicians commonly prescribe premedications – acetaminophen (AKA Tylenol) and diphenhydramine (AKA Benadryl) – prior to the administration of a blood transfusion.[1] For good reason, premedicating before a blood transfusion was more widespread and likely effective when most blood products were not leukocyte-reduced (e.g. contained white blood cells). But even now in the era of universal leukoreduced blood products, which is known to lower the incidence of transfusion reactions,[2-3] there is over-use of pretransfusion medications that may be as high as 50%.[4]

What is the rationale for prescribing premedication prior to a blood transfusion?

Allergic and febrile non-hemolytic transfusion reactions are common complications of transfusion, comprising nearly 75% of all transfusion reactions reported to the transfusion service.[5]

Most allergic reactions are defined by cutaneous symptoms of rash and itching, and when more severe include respiratory complications (such as cough, wheezing, difficulty breathing) and hypotension. Many minor allergic reactions are the result of an allergen or plasma protein present in the transfused product. The recipient's immune system recognizes the allergen and triggers the release of histamine and other chemical substances which leads to the patient's symptoms. Diphenhydramine, an antihistamine, works by blocking histamine from binding to receptors, and when given as a premedication, would theoretically prevent or diminish the patient's symptoms.

Febrile non-hemolytic transfusion reaction (FNHTR) is defined as more than 1°C (or 2°F) rise in temperature above baseline with or without chills or rigors. While the cause of FNHTR is likely multifactorial, the release of cytokines from transfused white blood cells or accumulation of pro-inflammatory mediators in the product appear to play a major role in the development of the patient's symptoms. Prophylactic use of acetaminophen prior to transfusion is perceived to prevent the development of any fever and/or chills if there is a cytokine release.

But, do these drugs really help prevent reactions in patients without any history of previous transfusion reaction and is it worth the risk and cost?

What is the risk of giving these drugs?

Acetaminophen and Diphenhydramine, although available over-the counter, are not benign medications. Tylenol can cause hepatotoxicity and should not be given in patients with underlying hepatic dysfunction. Benadryl, on the other hand, is a potent anticholinergic and has been associated with dry mouth, urinary retention, altered mental status, drowsiness, and in some patients, agitation. In fact, use of Benadryl should be avoided in patients with neurologic disorders and its use is strongly discouraged in the elderly patient population.[6]

These medications can have a financial impact on the institution as well. The cost for these medications at one tertiary care center was estimated at $40,000 annually in addition to pharmacy and nursing time for preparation and administration.[7]

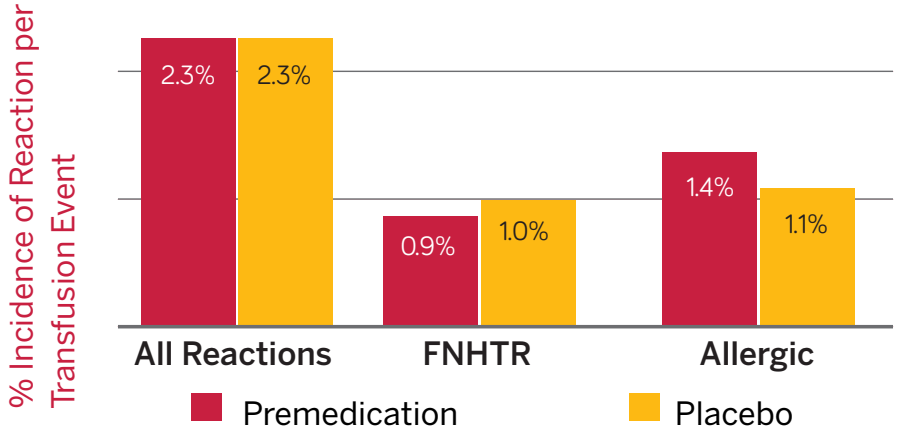
What evidence is there for use of premedications?

A recent systematic review evaluated the efficacy of premedication for the prevention of reactions (allergic and FNHTR) in both adults and children receiving allogeneic blood transfusion.[8] Three randomized controlled trials provided quality evidence. A total of 517 patients receiving 4,444 transfusions (2,013 RBC transfusions and 2,431 platelet transfusions) were randomized to receive either premedication or placebo (or no treatment) prior to transfusion. Premedication consisted of 650mg or 500mg oral acetaminophen and 25mg oral diphenhydramine in adults or weight-based dosing if pediatric patient. The patients enrolled in the three trials had hematologic or oncologic diagnoses, and nearly all patients (490 of 517) had no prior history of transfusion reaction.

Regardless of intervention, the results showed no difference in transfusion reaction rates. In transfusions with use of premedication, 49 of 2133 (2.3%) led to a nonhemolytic reaction, compared with 53 of 2311 (2.3%) transfusions in the control group. All blood products transfused in the three trials were leukoreduced, which likely reflected the overall low rate of reactions seen. The incidence of allergic and FNHTRs were similar regardless if the patient received premedication or not.

The findings from this systemic review argue against the routine use for pretransfusion medication. Such practice fails to reduce nonhemolytic transfusion reaction in patients with no prior history of transfusion reaction. The impact of premedication on patients with history of reaction remains unknown though, and further research is needed in this area.

Incidence of Transfusion Reactions with and without Premedication–Summary of 3 Studies[8]



Patient Care Recommendations:

- In the era of universal leukoreduction, use of premedication for transfusion is not effective in decreasing the incidence of FNHTR. Similarly, premedication does not reduce the incidence of allergic reaction.
- For patients without a history of transfusion reaction, premedication is not recommended and may place the patient at risk for side effects of the drugs.
- If a patient has a history of transfusion reaction, the decision to premedicate should be made on a case-by-case basis. Type of prior reaction should dictate the specific medication needed – acetaminophen or diphenhydramine.

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