Show Me the Evidence: Is the Routine Use of Premedication for Transfusion Really Necessary?

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The newly created EBP committee looked for their first project

- Blood draw waste volumes
- Premedication for blood products
- Heparin for CVC’s
- Potassium infusion rates
The newly created EBP committee found their first project

• Blood draw waste volumes- completed an ongoing project

• Premedication for blood products

Practice Issues Identified

• Current premedication standard
  • Acetaminophen 650mg PO
  • Diphenhydramine 25-50mg PO
  • 30 minutes prior to starting transfusion.
• Toxicities associated with the premeds
  • Are we exposing the patient to potential side effects unnecessarily?
  • Is there any alternative from the "same old, same old"?
  • Are premedications even necessary?

Side Effects of Pre-medication

<table>
<thead>
<tr>
<th>Risks of Benadryl</th>
<th>Risks of Tylenol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Falls</td>
<td>Liver Toxicity</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>Drug interactions</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>Busulfan</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>Cytoxan</td>
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<tr>
<td>Cognitive impairment</td>
<td></td>
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<tr>
<td>Sedation</td>
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<tr>
<td>Delirium</td>
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<tr>
<td>Restless Legs Syndrome</td>
<td></td>
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<tr>
<td>Anxiety</td>
<td></td>
</tr>
</tbody>
</table>
### Is there an alternative?

- Claritin as a second generation antihistamine
  - Decreased risk for sedation, tachycardia, hypotension, and urinary retention.
  - Little evidence that utilizes direct comparison of Claritin vs. Benadryl as premedication and prevention of reaction to blood products in hematology/oncology patients

### Transfusion Reactions

- Transfusion reactions can range from
  - Mild (itching, hives)
  - Anaphylaxis (bronchospasm, hypotension, and shock)
- How often and how severe?

### Reactions are common: Fact or fiction?

- There have been many improvements in transfusion medicine, blood typing, and donor screening in the modern world.
  - Leuko-reduced (the reaction is in the WBC exposure mostly)
  - Irradiated reduces GVHD and reactivation
  - Human leukocyte antigen-matched platelets (HLA)
- Antigen-negative platelets
- Antigen-negative PRBCs
- Has the technology of transfusion medicine advanced to the point that quite possibly we do not need to pre-medicate patients anymore prior to blood product transfusions?
A project was Born!

PICO Question

- **P**=Population
- In the adult oncology patient
- **I**=Intervention
- does the prophylactic use of acetaminophen and diphenhydramine
- **C**=Comparator/Control
- versus no premedication
- **O**=Outcome
- affect the incidence of blood transfusion reactions?

Search Strategy

- PubMed (MEDLINE), CINAHL (Cumulative Index to Nursing and Allied Health Literature), Medline, Elton B. Stephens Company (EBSCO), Ovid, and Scopus to gather established information for the literature search.
- Keywords used were: Blood Products, Transfusions, Reactions, Tylenol, Benadryl, Steroids, Platelets, Packed Red Blood Cells, Transfusion Medicine
### Integration and Synthesis of the Evidence

#### Study 1

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Wang (2002)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Prospective/Randomized/Double-blind/Placebo-controlled</td>
</tr>
<tr>
<td>Purpose</td>
<td>Evaluate the use and effectiveness of Acetaminophen and Diphenhydramine vs. placebo when used as premedication for transfusions in Oncology Patients</td>
</tr>
<tr>
<td>Limitations</td>
<td>Studied platelet transfusions only, Low number of transfusions</td>
</tr>
<tr>
<td>Results</td>
<td>No statistical difference in reactions between the two groups.</td>
</tr>
<tr>
<td>Significance</td>
<td>The study reflected no difference in the premedication vs. placebo groups but it also showed something significant that the researchers were not looking for. The study demonstrated that patients with a history of reactions will be more likely to have reactions with or without pre-medication.</td>
</tr>
</tbody>
</table>

#### Study 2

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Sanders (2005)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Retrospective-examined 7,900 transfusions</td>
</tr>
<tr>
<td>Purpose</td>
<td>Evaluate the effectiveness of premedication with acetaminophen and/or diphenhydramine in febrile non-hemolytic transfusion reactions and allergic transfusion reactions.</td>
</tr>
<tr>
<td>Limitations</td>
<td>Retrospective, Pediatric Population, No doses specified</td>
</tr>
<tr>
<td>Results</td>
<td>No difference noted between the types of reactions</td>
</tr>
<tr>
<td>Significance</td>
<td>This data clearly demonstrates that pre-medicating patients prior to transfusions show no marked benefit. Utilized only Single donor apheresis for platelets and leukocyte reduced and irradiated PRBCs consistent with our current practices</td>
</tr>
</tbody>
</table>

#### Study 3

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Patterson (2000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Prospective with 3 large hospitals</td>
</tr>
<tr>
<td>Purpose</td>
<td>Examine the rates of reactions that patients experienced when given premedication prior to transfusion and comparing it with the rate of reactions exhibited after premed guidelines initiated - note a drop in use of premeds by 50% with little change in reactions.</td>
</tr>
<tr>
<td>Limitations</td>
<td>Observational, No standard dose of premedication</td>
</tr>
<tr>
<td>Results</td>
<td>Platelet reactions had little significant change from baseline when pre-medications were administered</td>
</tr>
<tr>
<td>Significance</td>
<td>These prospective studies document a high rate of plt transfusion rxn in onc pts and indicate that the reduction in routine use of premed doesn’t increase occurrences of transfusion related reactions. The study also validates the use of leukoreduced and/or plasma reduced of platelet products reduces the incidence but does not completely eliminate reactions. Reaction rate reduction of 10% when leuko and/or plasma reduced platelets were given</td>
</tr>
</tbody>
</table>
We have a Case for Change!

- Despite the common use of premedication to prevent transfusion reactions, recent literature has not conclusively validated its use.
- Current standing orders for blood product transfusions include the premedication medication already pre-printed. Physicians may be unknowingly ordering premedication because of this.
- The routine ordering of premedication to prevent transfusion reactions was not adequately supported by current evidence-based research.
- The standard of care and routine ordering of premedication for blood products should be reevaluated and revised to better reflect current evidence-based practices.

Comparing Apples to Oranges?

- We felt the need to establish a baseline
- Linking the research to our current practice and supplying actual numbers to substantiate a change in practice.
- Let’s see if it changes if we change...

Plan For Change: Establishing a baseline

- Collected Data from 137 patients transfused pts at Siteman Cancer Center outpatient oncology/BMT/Heme infusion center from
  - January 1, 2014 through April 1, 2014.
- Data collection included:
  - Patient Initials
  - Disease
  - Service (Med Oncology/BMT/Hematology)
  - Type of Blood product given (Packed Red Blood Cells (PRBC), Single Donor Platelets (SDP, PLT)
  - Type of Premedication used - Tylenol, Benadryl, Claritin, Solu-Cortef
  - Did reaction occur? (Yes/No)
  - Was a transfusion Reaction form filled out?
  - When did it occur? (during/after)
  - Did we proceed with remaining once symptoms resolved?
  - Description of reaction
Of the 137 transfusions, 61 platelets, 76 PRBCs
Only 4 reactions occurred: In all cases the patients had been premedicated with acetaminophen 650mg and Benadryl 25mg p.o.
In all cases additional Benadryl 25mg-50mg was administered IV and the patients were able to continue with treatment – consistent with previous study findings
3 of the reactions that occurred were itching/urticaria/hives
One reaction included back pain and decreased oxygen saturation
Demographics of patients who had reactions:
2 patients with Sickle Cell Disease reacted to PRBCs
1 patient with AML reacted to platelets
1 patient with MDS reacted to platelets
None of the patients sampled were hospitalized due to allergic reactions
All responded to treatment

Research Findings

Premedication before giving transfusions seem to be the standard for many reasons.
We are creatures of habit but so much has changed in transfusion medicine
A blood transfusion reaction can delay treatment and completion of transfusions.
Blood Transfusions take a lot of time...... lets do the math.
Time = money
Reactions = more time
More Time = longer chair time/less pt
Sedation and dizziness = patient safety risk
Sometimes we just like to take a sledgehammer to an ant hill in an attempt to reduce the risk and the possibility of a reaction.
The significant cost, time, and resources required to work up a transfusion reaction are also incentives to pre-medicate and a barrier to change.
Staff and patient education regarding the change
Conclusions?

- No comparison between no premeds to those premedicated
  - Only 6/137 did not receive premeds
- 2/4 patients who did have a reaction were SSD
- Specific data was not collected regarding leukocyte reduction or irradiation of blood products,
  - SOC for patients to receive leukocyte reduced, apheresis, single donor platelets.

Feasibility of Change

- We propose that routine pre-medications for blood products be discontinued unless the patient has had a prior allergic reaction.
  - Presented at BMT QI
    - Much discussion and worry about “the fever issue”
    - Compromised: NO benadryl
  - Presented to Med/Onc
    - Accepted

Barriers: Perceived and Reality

- BMT not willing to take the leap for Tylenol
- Will patients want to change?
- Will staff buy into and suggest the change
We Did It!

• The EBPC with the assistance of our APRN and a dedicated medical assistant developed a plan for evaluating this practice change.
• MA placed a Yellow EBP screening sheet in the patient chart asking the patient’s RN to offer the patient the option of joining in our EBP project.
• A consistent script was developed for the nursing staff to allow the patient to make an informed decision.
• Patients with documented previous reaction risk were excluded from our EBP research as part of our compromise.
• When patients agreed, a new standing order set was written by the APRN.

Evaluating the Change

• Retrospective data on 48 patients from October 8, 2014 to January 15, 2015.
  – 98 units of PRBCs transfused
  – 40 units of platelets
  – MM, AML, ALL, MDS, Lymphoma
  – Rectal, Sarcoma, Brain, Renal, Head and Neck, Gastric, Lung
• When offered, pts were very willing to opt out of premedication with diphenhydramine and avoid the associated drowsiness and restless leg syndrome.

Breaking down the Findings

• 1/48 enrolled had infusion reaction
  • BMT patient
  • Urticaria
  • Symptoms resolved with additional administration of IV diphenhydramine and famotidine and the patient was able to be discharged home.
• Another patient had a fluid volume overload reaction.
  • This patient had not taken his antihypertensive or diuretic on this day.
  • Was given Lasix and was able to finish the blood product.
The role of premedication has been challenged.

Literature on the benefit to transfusion premedication is limited and predates the change in technology. Transfusion medicine/processing has made reactivity less likely by using techniques such as plasma reduction, leukocyte reduction, irradiation and the washing of blood products.

Additional prospective studies evaluating the impact of rationally administered transfusion premedication is needed.

Do we really need to do this on those who had prior reaction?

Avoiding unnecessary medications and developing clear EVIDENCE-Based standards when selecting pre-medication is essential when providing quality healthcare to our patients.

Go against the grain!

Thanks to all those who helped

- EBP Committee
  - Ashlee K
  - Megan C
  - Jim W
- Katie L
- The staff in the Siteman Cancer Treatment center
- The patients willing to participate
- Chris Rinkus

Questions are guaranteed in life; Answers aren’t.