THROMBOCYTOPENIA IN THE ICU

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May 31, 2014

OVERVIEW

- Platelet basics
- Epidemiology
  - Time course
  - Prognostic significance
- Causes and differential diagnosis
  - Sepsis
  - Drug-induced
  - HIT
- Investigation
- Treatment

FUNCTION OF PLATELETS

- Hemostasis and thrombus formation
- Modulation of platelet and receptor function
  - Secretion of pro-coagulant factors
    - Platelet activating factors
    - Complement proteins
  - Secretion of pro-inflammatory factors
    - Cytokines
    - Oxidants
  - Antigen presentation


DISCLOSURES

- I have nothing to disclose.
CONSEQUENCES OF PLATELET ACTIVATION

- **Beneficial**
  - Wound healing and vascular remodeling
  - Enhanced integrity of endothelial membranes
  - Reduction in vascular permeability
  - Mediation of inflammatory processes and host defense

- **Harmful**
  - Impairment of microcirculatory flow
  - Propagation of inflammatory and coagulation cascades

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**WHY IS PLATELET PATHOLOGY HARMFUL?**

- Contribution to organ dysfunction
- Bleeding or thrombosis
  - Complications of treatment
- Influence on patient management
  - Avoidance of invasive procedures
  - Avoidance of thromboprophylaxis
  - Investigation of cause
- Marker of illness severity
**THROMBOCYTOPENIA IN THE ICU**

- Platelet count < 150,000/μL
- The most common hemostatic disorder in critically ill patients
  - Incidence approaches 50%
- Association between thrombocytopenia and
  - Mortality
  - Poor ICU outcomes

**A MARKER OF ILLNESS SEVERITY AND A PREDICTOR OF MORTALITY**

- Patients with thrombocytopenia have:
  - Higher admission APACHE II, SAPS II, MODS II scores
  - Higher mortality within the same APACHE II or SAPS II quartiles
  - Higher ICU (39% vs. 24%, p<0.0005) and hospital (56% vs 48%, p<0.0005) mortality
  - Longer duration of mechanical ventilation (11 vs. 5 days, p<0.0005)
  - Receive more PRBC, FFP, platelet transfusions

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**Thrombocytopenia in Critically Ill Patients Receiving Thromboprophylaxis**


**Platelet Count Decline* An Early Prognostic Marker in Critically Ill Patients With Prolonged ICU Stays**

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**Mechanisms of thrombocytopenia**

- Blood loss or hemodilution
- Decreased production
  - Infection
  - Toxins (including drugs)
  - Inflammatory mediators
  - Bone marrow disorders
  - Liver disease
- Increased destruction
  - Consumption
  - Immune-mediated
- Sequestration
  - Spleen
  - Liver
  - Lungs (ARDS)
- Pseudothrombocytopenia

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**Variation based on patient population**


**Time course of platelet counts in critically ill patients**

**Differential diagnosis in the ICU**

- **Infectious**
  - Sepsis
  - HIV
  - HCV
  - Other viral infections

- **Drug-induced**
  - Liver disease
  - DIC
  - Massive transfusion (dilutional)
  - Rheumatologic disease
  - Idiopathic/unknown

- **Hematologic disease**
  - TTP/HUS
  - ITP
  - Bone marrow disorders
  - Macrophage activation syndrome

- **Liver disease**

- **DIC**

- **Massive transfusion (dilutional)**

- **Rheumatologic disease**

- **Idiopathic/unknown**

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**Sepsis**

- Represents hematologic system dysfunction in sepsis
- Results from activation of the host inflammatory response
- Mechanisms of thrombocytopenia in sepsis
  - Pseudothrombocytopenia
  - Bone marrow suppression
  - Non-immune mechanisms
    - Consumption
    - DIC
  - Immune mediated mechanisms

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**Drug-induced thrombocytopenia**

- Antibiotics
  - PCN
  - β-lactamase inhibitors
  - Carbapenems
  - Cephalosporins
  - Quinolones

- Anti-epileptics
  - Valproate
  - Carbamazepine
  - Phenytoin

- Alcohol
- Acetaminophen (overdose)
- Anti-platelet agents
- NSAIDs
- Heparin
- H2 blockers
- Chemotherapy
- Herbs
- Snake venom

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**Heparin-induced thrombocytopenia**

- Uncommon cause of thrombocytopenia in the ICU
- Formation of antibodies against PF4-heparin complexes → activation of platelets
- Detection is more complicated in ICU patients
- Seroprevalence of Anti-PF4 is high in ICU patients
  - 10.8% on admission → 29.4% on day 7
  - Not all develop TCP or thrombosis!
**Clinical Features of HIT**

- Fall in platelet count > 50%
- Platelet count nadir 50-80,000
- Associated with thrombotic complications
  - Patients with vs. without HIT have OR 12-41 for developing thrombosis
- Onset 5-14 days after starting heparin
  - Within 24h if previous exposure (within 90 days)


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**When Should We Investigate?**

- Platelet count < 100,000
- > 30% decrease in platelet count
- Rapid decline in platelet count (24-48 hours)
- Failure to rebound after 5-7 days
- Decline in platelet count after initial recovery
- Other appropriate clinical situations

INITIAL INVESTIGATION

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TREATMENT

- Target of treatment is the underlying process
- Supportive care may include
  - Platelet transfusion
  - Anticoagulation
  - Etiology-specific treatments

3 QUESTIONS TO GUIDE TREATMENT...

- Is this condition pro-hemorrhagic?
- Is this condition pro-thrombotic?
- Are additional therapies or specialized studies necessary?
BLEEDING AND THROMBOCYTOPENIA

• Thrombocytopenic patients:
  – Bleed more often
  – Receive more transfusions

• There is still controversy surrounding the practice of prophylactic platelet transfusion

FOR FURTHER REVIEW...


CONSENSUS RECOMMENDATIONS FOR TREATMENT

Decision to transfuse should be based on:

– Platelet count
– Presence of active bleeding
  • Site
  • Severity
– Etiology
– Risk of thrombosis
– Risk of hemorrhage
  • Platelet function
  • Invasive procedures or surgery
– Associated treatment

**CONCLUSIONS**

- Platelets have diverse roles in coagulation, inflammation, and the immune response
- Thrombocytopenia is common in the ICU
- Mild decrease in platelet count early in the ICU stay is predictable and physiologic
- The most common causes of thrombocytopenia in the ICU are
  - Sepsis
  - Drug-induced
  - Liver disease
  - Dilutional
- Diagnosis of HIT should be made using a combination of clinical and laboratory data

**Questions?**

**CONCLUSIONS**

- Certain features of thrombocytopenia should prompt investigation
  - < 100,000 or decrease > 30%
  - Rapid decline
  - Failure to rebound after 5-7 days
  - Decline after initial recovery
- Initial investigation should include peripheral smear and other labs as clinically indicated
- Decision to transfuse depends on platelet count, etiology, bleeding risk, thrombotic risk, other factors
- Consider anticoagulation and other etiology-specific treatments depending on clinical scenario

**REFERENCES**

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