Objectives:

- Discuss the current recommendations for venous thromboprophylaxis
- Identify patients as ‘high risk’ for venous thromboprophylaxis
- Discuss why ‘one size fits all’ may not be the best approach for venous thromboprophylaxis
- Review the reasoning/rationale for weight-based dosing of enoxaparin in obese patients
Research?

It doesn’t have to make you feel like this guy

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### Where Do I Start?

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Who to target?</td>
<td>What intervention do</td>
</tr>
<tr>
<td>Who to include?</td>
<td>you want to study?</td>
</tr>
<tr>
<td>Who to exclude?</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td>What will you</td>
<td>What is the primary</td>
</tr>
<tr>
<td>compare?</td>
<td>outcome?</td>
</tr>
<tr>
<td>What are your</td>
<td>Secondary outcomes?</td>
</tr>
<tr>
<td>groups?</td>
<td></td>
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</tbody>
</table>
What we asked ourselves:

- Why is incidence of VTE, especially DVTs, still so rampant?
- Is what we are doing adequate?
- Should all patients really be getting the same dose of enoxaparin for DVT prophylaxis?
- So we reviewed the literature and came up with a clinical question

Is weight-based dosing of enoxaparin for DVT prophylaxis in obese trauma patients efficacious, as assessed by anti-Xa levels and incidence of VTE?
Elements & Concepts

The Research Question

What is the research question you are trying to answer?

Be as SPECIFIC as possible!
Elements & Concepts

Null Hypothesis

Restate the research question as a null hypothesis

What is the NULL HYPOTHESIS??

A general statement or default position that states there is no relationship between two measured phenomena.

Generally, you are trying to prove an alternative hypothesis is true

*P-value!
Elements & Concepts

Significance

- Why does this research matter?
- What is known or unknown about this topic?
  - A comprehensive literature review is key!
- How does it relate to your work, and patient care/outcomes?
- What is the potential impact of this work?
Elements & Concepts

Design

- Prospective vs. retrospective
- Randomized vs. cohort
- Observational vs. experimental
Elements & Concepts

Subjects

Selection criteria
- Who are the subjects and how will they be selected?
- Inclusion and exclusion criteria

Sampling Design
- Consecutive: all patients seen in concession
- Convenience: all patients seen during business hours
- Chart review: review of medical records
Elements & Concepts

Variables

Predictor variables
- What measurements will be made before and after the study?
- i.e. MOI, age, gender, ISS

Outcome variables
- List your main outcome variables
- i.e. mortality, LOS, cost
Elements & Concepts

Statistics

Statistical and analytical issues...

- How large is the study?
- How will it be analyzed?
- Power?
- GET HELP!
Elements & Concepts

Next steps…

- Anticipated problems or barriers?
- Create a list of bite-size goals
- IRB (internal review board)
- Look for a journal for submission
- Write and submit your abstract
- Keep track and collect all your references
- Write a manuscript...the time sucker
How we did it...

1. Created new trauma team protocol, approved by attending surgeons
2. IRB approval
3. Collected and analyzed data
4. Chose a meeting/journal for submission
5. Wrote and submitted an abstract
6. Abstract accepted
7. Wrote a manuscript
8. Podium presentation
9. Manuscript publication process
10. Manuscript in print!
PUBLISHED!
American Journal of Surgery

QuickTime™ and a decompressor are needed to see this picture.
Weight-Based Enoxaparin Dosing For Venousthromboembolism Prophylaxis in the Obese Trauma Patient

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Venous Thromboembolism (VTE)

Deep venous thrombosis

*Blood clot formation within a deep vein, commonly in the leg or pelvis*

*Virchow’s Triad*

- 1. Blood hypercoagulability
- 2. Venous stasis/immobility
- 3. Vessel wall injury

Pulmonary embolism

*Blood clot travels to lung and lodges in one or more pulmonary arteries*
VTE
Incidence and Risks

- Nearly 6 million cases of serious VTE are reported in the U.S. each year
- Significant short- and long-term complications and a tremendous financial burden

Risk Factors
- Surgery
- Trauma
- Obesity
- Cancer
- Inherited thrombophilia
VTE In Trauma

Incidence (without chemoprophylaxis)
- DVT: 28-65%
- PE: up to 9%
- VTE: up to 70% in critical trauma pts

PE is most common cause of preventable hospital death

NEJM study identified independent risk factors
- Age
- LE (femur or tibia) injury
- Spinal cord injury
- Blood transfusion in first 24 hrs of trauma
VTE and Obesity

- Obesity is a critical risk factor for developing VTE
  - Relative risk of 2.50!
- Mayo clinic autopsy series of 8000+ surgical patients revealed obesity alone as an independent risk factor for fatal postop PEs
- In gastric bypass surgery, the number one cause of unexpected early and late postoperative death is PE
- Obesity is associated with increased prothrombotic factors
Sequential compression devices alone have not shown benefit in preventing DVT.

Low-molecular-weight heparin (LMWH) is more efficacious than unfractionated heparin (UFH) in preventing VTE after major trauma.

Despite chemoprophylaxis, DVT rates still up to 31%:
- 6% to 15% proximal
Can One Size Fit All?

Enoxaparin has a high volume of distribution

- Affected by fat tissue and fluid accumulation

Fixed-dose LMWH may not provide adequate VTE prophylaxis in obese patients or in trauma patients
LMWH is recommended for VTE prophylaxis in major trauma

No definitive recommendations for or against weight-based dosing in obese patients


Routine coagulation monitoring not recommended

- Exceptions include pregnancy, obesity, and renal dysfunction
  - Plasma anti-Xa activity
OUR STUDY
WEIGHT-BASED ENOXAPARIN DOSING FOR VENOUS THROMBOEMBOLISM PROPHYLAXIS IN THE OBESE TRAUMA PATIENT

Purpose

Is a weight-based dosing regimen of enoxaparin for VTE prophylaxis in obese trauma patients efficacious?

- Primary outcome = plasma anti-Xa level
- Secondary outcome = incidence of VTE

Is it safe?

- Bleeding complications
Our Study...

**Inclusion criteria**
- Obese (BMI ≥ 30kg/m²)
- Adult (≥18 years)
- Admitted to level I trauma center, January 2011-July 2012

**Exclusion criteria**
- Acute traumatic intracranial hemorrhage
- Active internal bleeding
- Renal insufficiency (CrCl<30mL/min)
- Pregnancy
- Epidural anesthesia
- Coagulopathy (factor deficiencies)
- Thrombocytopenia (plts<50K or drop>50% baseline)
- Heparin allergy or h/o HIT
Dosing & Monitoring
Prospective

**Dosing**

*Enoxaparin 0.5 mg/kg subcutaneously twice daily*

- Total body weight on admission

**Monitoring**

- Peak anti-Xa levels, drawn 4 hours after 3\textsuperscript{rd}/4\textsuperscript{th} dose
  - Target range: 0.2-0.6 IU/mL
- Bilateral lower extremity duplex ultrasound
- Computed tomography of chest if PE suspected
<table>
<thead>
<tr>
<th>Anti-Xa level (IU/mL)</th>
<th>Dose adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.2</td>
<td>Increase total daily dose by 20 mg</td>
</tr>
<tr>
<td>0.2-0.6</td>
<td>No change</td>
</tr>
<tr>
<td>0.61-1.0</td>
<td>Decrease total daily dose by 20 mg</td>
</tr>
<tr>
<td>&gt;1.0</td>
<td>Decrease total daily dose by 50%</td>
</tr>
</tbody>
</table>

*Repeat peak anti-Xa level after the adjusted dose*
Results
Demographics

86 patients met study criteria
60 (70%) males, 26 (30%) females
Mean age 52 ± 1.78 years
Median BMI 35.3 kg/m², IQR of 9.8
Median weight 113.3 kg, IQR of 30
Median ISS 14, IQR of 12

*BMI = body mass index  *IQR = interquartile range  *ISS = injury severity score
Results
Primary Outcome Measure

74 patients (86%) reached target anti-Xa level
  • Mean = 0.42 ± 0.01 IU/mL

12 patients were out of range: 8 above and 4 below
  – Dose adjustments achieved target anti-Xa levels
  – No significant differences in age, weight, or BMI between those above and those below target anti-Xa range
  – No dramatic weight gain/loss during hospitalization.
No correlation was found between weight and anti-Xa level

$r^2 = -0.01$
Results
Secondary Outcome Measures

_Incidence of VTE?_

18 patients (21%) diagnosed with DVT

In 16 patients, DVT was present **prior to** or on the day of starting weight-based LMWH

<table>
<thead>
<tr>
<th></th>
<th>DVT group</th>
<th>non-DVT group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>52.4 (3.8)</td>
<td>51.3 (2.03)</td>
<td>0.40</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>102.6 (8.02)</td>
<td>120.4 (3.63)</td>
<td>0.016</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>34.5 (1.02)</td>
<td>39.7 (1.3)</td>
<td>0.021</td>
</tr>
<tr>
<td>Injury severity score</td>
<td>23.9 (3.1)</td>
<td>12.7 (0.77)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

- No cases of PE identified
Conclusions

One size does NOT fit all

Weight-based enoxaparin for VTE prophylaxis in obese trauma patients works

- Majority reached target anti-Xa levels
- Nomogram for dose adjustments led to appropriate levels 100% of the time
Conclusions

Controlling for obesity with weight-based dosing leads to equal and adequate prophylaxis

- No correlation between weight and anti-Xa

DVT incidence should not be attributed to inadequate prophylaxis

- Majority diagnosed prior to start of LMWH
Conclusions

Lack of data regarding the relationship between weight-based dosing and/or anti-Xa levels with VTE incidence

Larger randomized trials are needed
THANK YOU!
? QUESTIONS ?
References


References


