A Review of Dosing Recommendations for Overweight and Obese Patients

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Aim

• To evaluate the literature regarding medication dosage recommendations for overweight and obese patients

• To determine if these recommendations are reflected in standard reference texts
  - AMH, eTG, Micromedex, MIMs, RCHP
Method

• Extensive database searching:
  – The Cochrane Library, ACP Journal Club, Evidence Based Medicine, MEDLINE, Embase, CINAHL, BMJ Best Practice, Up-To-Date, CPG websites

• MESH search terminology:
  – obesity, overweight, dose response, drug therapy, dosing, dose
Method

- Limits: English language, full text, humans

- Citations selected based on title and abstract content

- Exclusions: anti-neoplastic agents and medications not registered in Australia
Results

• **30 articles** retrieved

• Recommendations for dosing **75 medications** or **classes**
Results: Therapeutic Categories

- Anaesthetic agents: 5%
- Anticoagulants: 10%
- Antiepileptics: 5%
- Anti-infectives: 38%
- Benzodiazepines: 7%
- Cardiovascular agents: 8%
- Methylxanthines: 3%
- Neuromuscular agents: 8%
- Opioids: 7%
- Other: 9%
Results: Study Population

• Adults: 68 medications/classes

• Paediatrics: 28 medications/classes
  – Of which 60% were extrapolated from adult data

• Unclear: 9 medications/classes
Results: Study Population

- Anti-infectives
- Neuromuscular agents
- Benzodiazepines
- Anaesthetic agents
- Cardiovascular agents
- Methylxanthines
- Antiepileptics
- Anticoagulants
- Opioids
- Other

Unclear
Paediatric
Adult
Results: Reference Texts

- 21 medications with recommendations matching standard reference texts = 29%
<table>
<thead>
<tr>
<th>Medication</th>
<th>Population</th>
<th>Recommendation</th>
<th>Micromedex</th>
<th>MIMs</th>
<th>AMH</th>
<th>eTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>Adult</td>
<td>IBW</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amikacin</td>
<td>Adult</td>
<td>ABW factor = 0.4</td>
<td>x</td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Atracurium</td>
<td>Adult</td>
<td>IBW</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisatracurium</td>
<td>Adult &amp; Paed</td>
<td>IBW</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daptomycin</td>
<td>Adult</td>
<td>TBW</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>Adult</td>
<td>Tm: TBW + anti-Xa up to 150kg</td>
<td>x</td>
<td>x</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>Adult</td>
<td>VTE prophylaxis: std dose, not higher</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Adult &amp; Paed</td>
<td>ABW factor = 0.4</td>
<td>x</td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Lepuridin</td>
<td>Adult</td>
<td>TBW up to 110kg</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>Adult</td>
<td>IBW</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midazolam</td>
<td>Paediatric</td>
<td>IBW</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenobarbitone</td>
<td>Adult</td>
<td>TBW + TDM</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Adult</td>
<td>IV load: ABW factor = 1.33</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remifentanin</td>
<td>Adult</td>
<td>IBW</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rocuronium</td>
<td>Adult &amp; Paed</td>
<td>IBW</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adult</td>
<td>1st dose TBW</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sugammadex</td>
<td>Paed (males)</td>
<td>TBW</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suxamethonium</td>
<td>Adult &amp; Paed</td>
<td>TBW</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Theophylline</td>
<td>Adult &amp; Paed</td>
<td>IBW</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobramycin</td>
<td>Adult &amp; Paed</td>
<td>ABW factor = 0.4</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Adult &amp; Paed</td>
<td>TBW + TDM</td>
<td>x</td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>Adult &amp; Paed</td>
<td>IBW</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>
Results: Conflicting Recommendations

- 25% within literature and between standard texts
  - 48 yo male, 160 kg, 195 cm, BMI = 42
  - Rocuronium intubation bolus: 0.6 mg/kg

<table>
<thead>
<tr>
<th>Dose adjustment recommendation</th>
<th>Calculated dose example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Literature, Micromedex: TBW</td>
<td>96 mg</td>
</tr>
<tr>
<td>MIMs: LBW</td>
<td>54 mg</td>
</tr>
<tr>
<td>Literature, AMH: IBW</td>
<td>53 mg</td>
</tr>
<tr>
<td>eTG: no recommendation</td>
<td>?assume use TBW</td>
</tr>
</tbody>
</table>
Results: Dose Adjustment Methods

- **IBW**: Ideal Body Weight
  - $\text{♂} = 50 \text{ kg} + 0.9 \text{ kg/each cm over } 152 \text{ cm}$
  - $\text{♀} = 45.5 \text{ kg} + 0.9 \text{ kg/each cm over } 152 \text{ cm}$

- **TBW**: Total Body Weight

- **ABW**: Adjusted body weight
  - DWCF: Dosing weight correction factor
  - $= IBW + \text{factor } \times (TBW - IBW)$
Results: Dose Adjustment Methods

• DW: Dosing weight
  \[ = IBW + 0.4 \times (TBW - IBW) \]

• LBW: Lean Body Weight
  \[ = (1.10 \times TBW) - (a \times BMI \times TBW) \]
  \[ (♂ a = 0.0128) (♀ a = 0.0148) \]

• Pharmacokinetic (PK) mass:
  \[ = \frac{52}{[1 + (196.4 \times e^{-0.025TBW} - 53.66) / 100]} \]
Limitations

• Search strategy

• Pharmacokinetics of drugs in obesity

• Study design
  – Most were small sample size, single centre
    • < 50 patients
    • Case report based on single patient
  – Different classifications of obesity
## BMI Classifications

<table>
<thead>
<tr>
<th>Classification</th>
<th>BMI Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overweight</td>
<td>25 – 29.9 kg/m²</td>
</tr>
<tr>
<td>Obesity class I</td>
<td>30 – 34.9 kg/m²</td>
</tr>
<tr>
<td>Obesity class II</td>
<td>35 – 39.9 kg/m²</td>
</tr>
<tr>
<td>Extreme obesity</td>
<td>≥ 40 kg/m²</td>
</tr>
</tbody>
</table>
Conclusions

- Lack of high quality information available regarding medication dosing in obesity
- Conflicting recommendations for the same medication
- Often no recommendation is provided in standard reference texts
- Where a recommendation is made, this frequently differs to recommendations found in the literature
- Further research is needed to guide clinicians in regards to dosing of medications for overweight and obese patients
References & Complete Results

• Available on request:
  – reeneh@bhs.org.au
  – eleanorv@bhs.org.au