Quantifying Gentamicin Toxicity in NHS Greater Glasgow and Clyde

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Background (1)

• Restrictions on 4C antibiotics introduced across NHS GGC from June 2008 onwards

• Short term gentamicin use promoted in
  – Sepsis: unknown cause, Uro, Intra-abdominal, Severe SSTI, HAI
  – Surgical prophylaxis

• Agreement with board senior clinicians (including renal) representing all hospital sites

• Concerns relating to anticipated renal and VIII nerve toxicity discussed
Measures to reduce toxicity

- Dosing and monitoring guidelines
- Calculator
- “Best guess” for urgent administration
- Limit to 72 hours
- Education regarding toxicity

![Gentamicin Dose Calculator](image)
Renal Toxicity

• Question: Has gentamicin been associated with increase in need for dialysis?
• “Gentamicin-associated AKI” = AKI associated with the initiation of gentamicin between 1 and 10 days prior to the requirement for renal replacement therapy
• Retrospective study of patients receiving emergency RRT in renal units and ICUs across GGC (6mths pre and post)
  – Pts with CKD stage 5, already RRT and outside (GGC) transfers excluded
Results

- 191 patients who received emergency RRT identified during Period 1 and 184 during Period 2.

- No significant difference in patient age, length of hospital stay, incidence of sepsis, or mortality between the 2 periods.

- No increase in gentamicin as a contributing factor in RRT
  - 43% received gentamicin at any time during their admission in both populations.
## Baseline characteristics and selected AKI risk factors

<table>
<thead>
<tr>
<th>Variable</th>
<th>Gentamicin-associated AKI group n=60</th>
<th>all other AKI group n=315</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of stay (days)</td>
<td>24.0 (14.0-42.5)</td>
<td>19.0 (8.0-34.8)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Duration of stay for those who survived to discharge (days)</td>
<td>37.0 (26-74)</td>
<td>25.0 (16-44.8)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Duration of gentamicin use (days)</td>
<td>2.0 (1.0-7.0)</td>
<td>4.0 (1.0-9.0)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>ITU admission %</td>
<td>83.6</td>
<td>70.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Sepsis %</td>
<td>95.1</td>
<td>70.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Surgery %</td>
<td>44.3</td>
<td>19.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Immunosuppressed %</td>
<td>16.4</td>
<td>7.3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Mortality (inpatient) %</td>
<td>52.5</td>
<td>49.0</td>
<td>0.72</td>
</tr>
<tr>
<td>Mortality (1 year) %</td>
<td>57.4</td>
<td>55.4</td>
<td>0.81</td>
</tr>
</tbody>
</table>
Multivariate binary logistic regression analysis of factors associated with in-hospital mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITU admission</td>
<td>4.87</td>
<td>2.65, 8.23</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Age(^a)</td>
<td>1.44</td>
<td>1.22, 1.70</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Prior ACE-I/ARB</td>
<td>0.45</td>
<td>0.24, 0.82</td>
<td>0.01</td>
</tr>
</tbody>
</table>

\(^a\) Per 10 year increase in age
Conclusions

• No evidence of an increase in gentamicin-associated AKI requiring RRT despite doubling of gentamicin use in the hospital population.

• Lesser degrees of AKI are associated with significant morbidity and mortality and so further audit into AKI not requiring dialysis is necessary.
Has increase in Gentamicin lead to increase in ototoxicity?

• Concerns raised by ENT surgeons
  – Reported incidence of toxicity varies; 1.16 – 45 %
  – Variation observed within class

• Gent ototoxicity is cumulative and not predicted by TDM
Has increase in Gentamicin lead to increase in ototoxicity?

- ICD-10 codes relating to hearing or vestibular disorder identified and applied to ENT IP and OP database of clinical episodes (all GGC sites)
- Patients receiving gentamicin identified via gentamicin TDM record (North Glasgow Hospitals)
June 2008

ENT IP and OP Database (n= 25853)

Gentamicin population (n=1363)

Sep 2009

Sep 2010
Results

- 62 (4.5%) patients matched both databases
- 61 case notes retrieved and reviewed
- 2 identified with possible gentamicin associated ototoxicity.
  - Patient 1: ENT concluded age related decline of hearing function and not associated with gentamicin.
  - Patient 2: ENT concluded vestibular toxicity following 5 days of gentamicin for neutropenic sepsis.
Retrospective Audit Results

- 4.5% of those who had received at least one dose of Gentamicin were reviewed within at least one year in an ENT clinic with an ICD-10 code relating to hearing or vestibular impairment.
- 0.07% were considered to have had gentamicin-associated ototoxicity.
Limitations

• Retrospective
• Required recognition of problem and referral to ENT
• Patients who had not had a gent level were excluded
• Patients who had not had an ICD-10 code were excluded
Conclusions and follow up

• Possibly under-estimating ototoxicity?
• All ENT surgeons alerted to contact AMT with suspected cases of ototoxicity and to complete DATIX reports in parallel
• In last one year one reported case by ENT in NHS GGC
  – Prolonged gent use for Pseudomonas in bronchiectasis exacerbation
Ongoing initiatives

- **Education**
  - FY1/2 Induction programmes
  - Antimicrobial ward rounds (WIG/ GGH/ VIC/ SGH)
  - Nurse IV training course
  - Infection management guidelines

- **Limit gentamicin**
  - To 72 hours
  - Liaise with microbiology / infectious disease

- **Continued discussion**
  - With ENT colleagues
Acknowledgements

- Renal study: Aileen Helps, Colin Deighan
- Ototoxicity: Fiona Robb, Myles Gilpin, Ysobel Gourlay, Fiona Kinnaird, Eleanor Hughes

Gentamicin and acute kidney injury requiring renal replacement therapy in the context of a restrictive antibiotic policy

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