Improved compliance with a gentamicin prescribing policy after introduction of a monitoring form

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Objectives: Compliance with our local hospital policy for gentamicin administration and monitoring was found to be inadequate on audit. A gentamicin monitoring form was introduced with the aim of improving staff compliance with the policy thus minimizing the risks of toxicity while ensuring adequate dosing.

Patients and methods: The initial audit examined the prescribing, administration and monitoring of intravenous gentamicin given to 20 patients. The introduction of a gentamicin monitoring form was prompted by unsatisfactory initial dosing and subsequent monitoring and adjustment of gentamicin doses.

Results: Following introduction of the monitoring form, the proportion of appropriate starting doses had increased from 13 out of 20 to 18 out of 20 prescriptions. The timing of initial serum levels was significantly better: 18 timed correctly, compared with 12 in initial audit. Subsequent administration and monitoring appeared more compliant with fewer doses inappropriately omitted and more levels checked appropriately. No improvement was seen in the quality of dose adjustment.

Conclusions: In conjunction with the support and advice of the pharmacy and microbiology departments, the use of a gentamicin monitoring form can improve the quality of intravenous gentamicin use in the hospital setting.

Keywords: nephrotoxicity, pharmacists, algorithm

Introduction

Once-daily intravenous gentamicin¹ is now standard therapy for many infections. The side effects of gentamicin use, particularly nephrotoxicity and ototoxicity, are well documented. In an audit of aminoglycoside prescribing by divided doses, Shrimpton et al.² demonstrated that closer liaison between microbiologists, pharmacists and clinical staff was essential to improve clinical practice. Similarly, Buabeng et al.³ showed that compliance with a once-daily gentamicin antibiotic policy reduced the likelihood of toxicity-related side effects.

Following two adverse incidents in our Trust, involving incorrect gentamicin dosing, an audit was undertaken to compare the therapeutic use of gentamicin with the recommendations in our hospital antibiotic policy. Concerns about the results of the initial audit prompted the introduction of a gentamicin monitoring form with the aim of improving the quality of prescribing and therapeutic drug monitoring.

Patients and methods

Inpatients on once-daily gentamicin for more than 3 days were included in the initial audit. Patients in the intensive care unit, special care baby unit and renal unit were excluded as dosing regimens were already monitored closely within these departments. Twenty patients were identified from pharmacy records over a 3 month period in 2002 and included in the audit. The type of infections being treated comprised bone and joint, urinary tract, skin and soft tissue, vascular device, intra-abdominal site, lower respiratory tract, intra-cranial shunt and sepsis associated with immunocompromise.

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Our hospital antibiotic policy recommends the use of once-daily gentamicin for complicated urinary tract infection, life-threatening infection, bone and joint infection and intra-abdominal sepsis. We recommend starting with 5 mg/kg bodyweight of gentamicin if the creatinine clearance is >30 mL/min with subsequent dosage adjustment according to serum gentamicin levels. We do not recommend once daily dosing if there is moderate or severe renal impairment (creatinine clearance <30 mL/min or creatinine plasma concentration >200 µmol/L).

It has been suggested by Freeman et al. that 5–7 mg/kg bodyweight of gentamicin once daily is acceptable but that the optimum dosage has not been clearly determined. The 7 mg/kg regimen proposed by Nicolau et al. involves complicated dosing schedules (36-hourly, 48-hourly dosing) based on the patient’s creatinine clearance and requires the calculation of dosages based on actual body weight or ideal body weight if the patient is morbidly obese. We considered these estimations to be a potential cause of dosing error on our general wards. The possibility of endotoxin-like reactions with higher doses was deemed to be a further risk which could be minimized by using the lower dosing schedule.

According to our policy, the first pre-dose level should be taken before the second dose is administered. Doses should not be withheld while awaiting the result. If the first pre-dose level is <1 mg/L, we suggest measuring levels twice weekly thereafter. If the level is >1 mg/L but <2 mg/L, the dose should be reduced to 4 mg/kg and the level repeated before the third dose. Twice weekly levels can then be instituted if this brings the level to <1 mg/L. For patients with moderate to severe renal impairment or persistently high pre-dose levels, advice should be sought from a pharmacist or microbiologist.

Prescribing and monitoring information was gathered prospectively on daily ward rounds. Data collected included dose prescribed, date and time of administration, interval between doses, duration of therapy, timing of pre-dose levels, serum urea, creatinine and gentamicin levels.

A re-audit was carried out on a further 20 patients ~1 year later and 7 months after the hospital-wide introduction of a gentamicin monitoring form. A similar range of infections was represented. The form comprised a prescription and administration chart for daily prescribing of gentamicin with additional spaces to request and enter therapeutic drug monitoring levels. On the reverse was an algorithm outlining the estimation of creatinine clearance using body weight and serum creatinine level, calculation of the starting dose, measurement of serum levels and actions to take in response to reported levels.

### Results

The first audit demonstrated that calculation of the initial dose of gentamicin was frequently incorrect (more than ±1 mg/kg of ideal dose) and that monitoring of serum levels according to the policy was poor (Table 1). More than half of the patients had gentamicin doses omitted inappropriately. Often this was because gentamicin level results were being awaited before proceeding with the next dose (six patients). Lack of venous access was cited as another reason for omission. Some prescribed doses had no entry on the drug chart to determine whether the dose was actually given or omitted for a specific reason. Less than half of doses that required adjustment were adjusted correctly according to the policy.

Two patients had existing renal impairment at the start of gentamicin therapy. One had mild impairment (creatinine 129 µmol/L) which subsequently improved during therapy with a 5 mg/kg dose (creatinine 95 µmol/L). The other patient received an appropriate initial dose but did not have levels checked after the first dose. On testing after the second dose, he was found to have toxic levels (trough gentamicin level of 3.0 mg/L) and deteriorating renal function (creatinine 134 µmol/L to 176 µmol/L). Gentamicin was discontinued at this point.

Finally, the duration of therapy was considered inappropriately long in 20% of cases. Only one patient was prescribed and administered gentamicin in strict concordance with the antibiotic policy.

The re-audit revealed that the gentamicin monitoring form was in use throughout the prescription in all but two patients. Correct prescribing of the initial dose appeared to have improved and there was a significant improvement in timing of initial serum gentamicin levels (Table 1; \( P = 0.0735 \) and \( P = 0.0366 \), respectively by Fisher’s Exact test). Subsequent administration of gentamicin and measuring of serum levels appeared more compliant (not statistically significant). The duration of treatment again appeared to be a cause for concern with a large proportion of patients receiving unnecessarily prolonged courses of the agent. The monitoring form had no beneficial effect on the adjustment of inappropriate doses with a reduction in the proportion of correctly altered prescriptions being observed.

During the re-audit, again two patients had evidence of impaired renal function prior to commencing gentamicin. One patient’s renal function gradually normalized despite high serum gentamicin levels after an appropriate starting dose (trough gentamicin level 2.8 mg/L; creatinine 209 µmol/L to 90 µmol/L). The other patient’s serum urea level initially deteriorated, corresponding to high trough gentamicin levels (2.6 mg/L), but subsequently normalized as gentamicin levels fell to within the therapeutic range (creatinine normal; urea 13.7 to 19.6 to 4.7 µmol/L). Her initial dose had not been outwith the accepted range. A third patient had normal renal function before receiving gentamicin but having been given too high a starting dose, developed some impairment (creatinine 117 to 144 µmol/L). Doses were omitted because of high serum levels and on restarting at a lower dose, renal function normalized. No reports of ototoxicity were received for either audit although they were not actively sought.

### Table 1. Results of audits

<table>
<thead>
<tr>
<th></th>
<th>First audit (no. of patients)</th>
<th>Second audit (no. of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of patients in audit</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Gentamicin monitoring form used throughout</td>
<td>0</td>
<td>18</td>
</tr>
<tr>
<td>Initial dose correct</td>
<td>13</td>
<td>18</td>
</tr>
<tr>
<td>Dosing interval correct</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Renal function monitored</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Initial serum gentamicin level correctly timed</td>
<td>12</td>
<td>18</td>
</tr>
<tr>
<td>Subsequent serum gentamicin levels checked appropriately</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>No doses omitted inappropriately</td>
<td>9</td>
<td>14</td>
</tr>
<tr>
<td>Dose adjusted correctly if required</td>
<td>4/9</td>
<td>2/8</td>
</tr>
<tr>
<td>Duration of gentamicin therapy appropriate</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>Fully compliant with policy</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

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**Gentamicin monitoring audit**

Nicolau et al. has not been clearly determined. The 7 mg/kg regimen proposed by Nicolau et al. involves complicated dosing schedules (36-hourly, 48-hourly dosing) based on the patient’s creatinine clearance and requires the calculation of dosages based on actual body weight or ideal body weight if the patient is morbidly obese. We considered these estimations to be a potential cause of dosing error on our general wards. The possibility of endotoxin-like reactions with higher doses was deemed to be a further risk which could be minimized by using the lower dosing schedule.

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Discussion

The initial audit demonstrated that the prescribing of gentamicin on the general wards in our hospital fell below the expected standard for patient care set by the antibiotic policy. This occurred despite the antibiotic policy being widely available on the hospital intranet and issued to every new doctor. Ward-based pharmacists also reviewed patients’ medication daily. Given the degree of poor compliance with the policy, urgent consideration was given to improving the application of a once-daily gentamicin regimen.

A gentamicin monitoring form to be attached to the patient’s drug chart was instituted as a result. With the new form, responsibility for gentamicin prescribing would remain with the clinicians, thus prompting regular review of the clinical indication for each prescription. The form comprised a user-friendly format for writing daily gentamicin prescriptions with specific guidance on calculating the correct starting dose, monitoring levels and adjusting doses. A contact telephone number for pharmacy advice was also provided on the form.

The form was well received by clinicians and utilized for the majority of subsequent gentamicin prescriptions. Minor improvements were observed in initial dosing and monitoring of serum levels although subsequent dosage adjustment remained sub-optimal. Closer monitoring by ward-based pharmacists may be a means of addressing this. There was an increase in the number of patients whose gentamicin regimen was compliant with the local prescribing policy, although this total remained low. Neither audit showed evidence of gentamicin nephrotoxicity as defined by Freeman et al.1 The overall effect of the introduction of the monitoring form appeared beneficial. However, some inadequate or inappropriate prescribing continued. Although no formal education on gentamicin use accompanied the introduction of the form, increased awareness about safe gentamicin prescribing may also have contributed. The provision of education along with continued advice and support from the microbiology and pharmacy departments may be required to ensure the risk of adverse incidents is minimized.

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References