

Summary of the project to develop the Patient Safety Alert on the safer use of intravenous gentamicin for neonates

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Contents

Introduction	2
1. The care bundle approach to improving patient safety	2
1.1 Explaining care bundles	2
1.2 Care bundles versus checklists and audits	2
1.3 Benefits of using the care bundle approach	3
2. Using the care bundle approach for intravenous gentamicin administration in neonates	3
2.1 Reasons for adopting the care bundle approach for intravenous gentamicin administration	3
2.2 Evidence to support a gentamicin care bundle	3
3. Developing and piloting the care bundle	11
3.1 Development	11
3.2 Pilot testing	11
3.3 Introducing the care bundle to the pilot sites	12
4. Post-pilot analysis of the gentamicin administration care bundle	12
4.1 Compliance and safety issues	12
4.2 User-friendliness of the care bundle	12
4.3 Conclusion	12
References	13

Introduction

The following is a summary of a project to develop a Patient Safety Alert about a care bundle for the safer use of intravenous gentamicin for neonates. Gentamicin is a broad spectrum antibiotic that is widely used in the treatment of neonatal infection. An NPSA telephone survey of 180 neonatal units in England carried out in 2007 indicated that 89 per cent used intravenous gentamicin. It is associated with a risk of adverse effects, specifically hearing impairment and kidney damage¹. Gentamicin has a narrow therapeutic range which necessitates its administration within an accurate timing regime and the careful monitoring of blood levels.

Data from the National Patient Safety Agency's (NPSA) Reporting and Learning System (RLS) from 1 April 2008 – 31 March 2009 identified 507 incidents, 15 per cent of all neonatal medication incidents, which related to the administration of intravenous gentamicin to neonates.

A Project Board was set up by the NPSA and its partners: the Royal College of Paediatrics and Child Health (RCPCH), the Royal College of Nursing, the Neonatal Nurses Association, the British Association of Perinatal Medicine and Bliss (the premature baby charity). An Expert Working Group (EWG) was established to develop the care bundle.

1. The care bundle approach to improving patient safety

1.1 Explaining care bundles

A care bundle is a 'structured way of improving processes of care and patient outcomes'². It consists of a number of clinical interventions that every patient should receive collectively during one clinical episode of care.

Each clinical intervention in the care bundle:

- must be proven to enhance patient outcome, that is, it must be supported by high-level evidence, be widely accepted as good practice and should be easily available;³
- is a 'must do' – without carrying out this intervention, patient care would be compromised;⁴
- must be simple to record as done or not done in one of three ways – action carried out, action not carried out, or action not carried out for a pre-defined reason (see below)².

A care bundle is not prescriptive. Clinical judgement by doctors and nurses is necessary in making the bundle work. The care bundle therefore may not include all the clinical interventions that may take place in the period of care the bundle is used. Essentially, the bundle acts as an *aide memoire* of what **must** be done³.

A clinical intervention that forms part of a care bundle could be contraindicated in some patients. Organisations should take a clinical decision as to which patients and under what circumstances the care bundle may be contraindicated².

1.2 Care bundles versus checklists and audits

Care bundles are not the same as either checklists or audits. Tasks in a checklist are not necessarily evidence-based or must-do processes. Checklists may also have a large number of elements, whereas a care bundle usually has three to five interventions only. Also, checklists may not specify which patients it applies to and when it applies, but in a care bundle these elements are clearly stated, thus increasing accountability and compliance².

The care bundle approach differs from an audit because compliance with the care bundle involves carrying out **all** the interventions every time. An audit could consider just one intervention or look at efficacy rather than compliance.

1.3 Benefits of using the care bundle approach

To measure whether the care bundle is being effectively applied, clinical teams using the bundle should record, on a continued basis, how many patients receive all elements of the bundle, with the aim of achieving 100 per cent compliance. The care bundle approach to therapeutic interventions is advocated as one of the Institute of Innovation and Improvement's high impact changes as outlined in the report; 'Increasing the reliability of performing therapeutic interventions through a Care Bundle approach'⁵.

Other benefits are that care bundles encourage collaborative working and provide an impetus for regular updating of guidelines so that they are in keeping with current best evidence-based practice. They also act as a tool to both educate staff about and empower them to implement that best practice.²

2. Using the care bundle approach for intravenous gentamicin administration in neonates

2.1 Reasons for adopting the care bundle approach for intravenous gentamicin administration

The NPSA and its collaborating organisations, the Royal College of Paediatrics and Child Health (RCPCH), the Royal College of Nursing, the Neonatal Nurses Association, the British Association of Perinatal Medicine and Bliss (the premature baby charity), considered adopting the care bundle approach for gentamicin administration in neonatal units after considering the available evidence as detailed in section 2.2.

2.2 Evidence to support a gentamicin care bundle

In general, guidelines include a hierarchy of evidence to support them, with randomised control trials (RCTs) considered to be the highest grade of evidence. However, it has been suggested that reliance on 'high level' evidence may not be helpful in many areas of clinical practice; for example where the benefits of practices are obvious (such as hand washing) or where there are contextual complexities⁶. Also, for rarely occurring conditions, an RCT is unlikely to find evidence that is statistically significant.

The GRADE* rating process, which is now commonly used in the UK, includes recommendations that are based on the quality of the evidence and other factors, such as the balance between desirable and undesirable effects, the values and preferences of patients and the cost of an intervention⁷.

Evidence to support the efficacy and acceptability of the gentamicin care bundle elements were synthesised from multiple evidence sources including:

- data from the RLS;
- root cause analyses of gentamicin incidents;
- a national survey of neonatal units in England on the use gentamicin;

* The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) process for developing evidence based guidelines classifies the quality of evidence in one of four levels (high, moderate, low, and very low) and the strength of recommendations as strong or weak.

- evidence from published literature;
- expert opinion from the working group.

2.2.1 RLS data

Data from the RLS was analysed for the period 1 April 2008 to 31 March 2009. A total of 21,487 neonatal incidents were identified as having occurred during this period, of which 3,379 (16 per cent) were medication-related, and 507 (15 per cent of all neonatal medication incidents) related to the administration of intravenous gentamicin. These 507 incidents were individually reviewed and categorised into the following error types: administration error, prescribing error and blood monitoring error.

Some incident reports contained two categories of error, for example where there was a prescription error that then led to a subsequent error in administration, or errors or omissions in blood level monitoring that led to a subsequent administration error.

Table A and Figure 1 (below) indicate error type by incident report.

Table A: Type of error by incident.

Type of error	Frequency	Percentage*
Administration	296	58
Prescribing	77	15
Prescribing and administration	52	10
Monitoring	42	8
Administration and monitoring	40	8
Total	507	100

*percentages have been rounded to nearest whole number

Figure 1

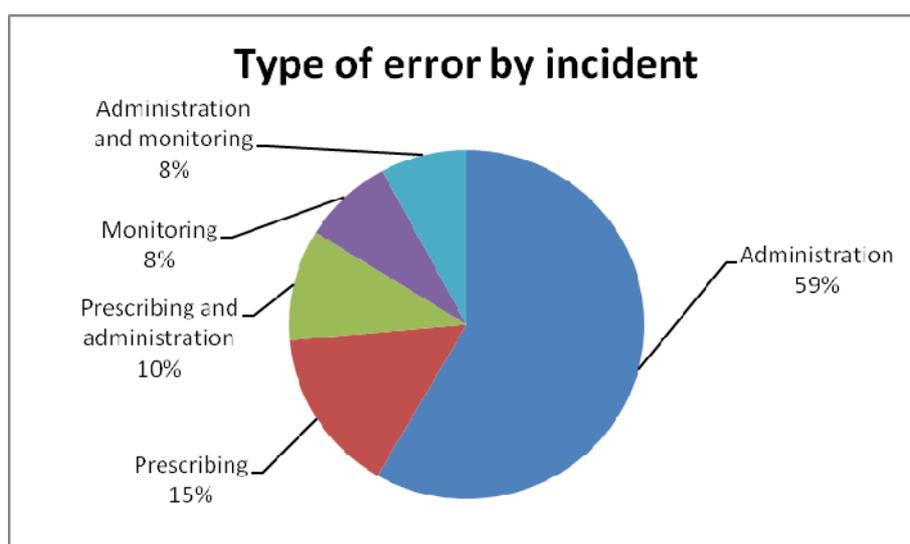


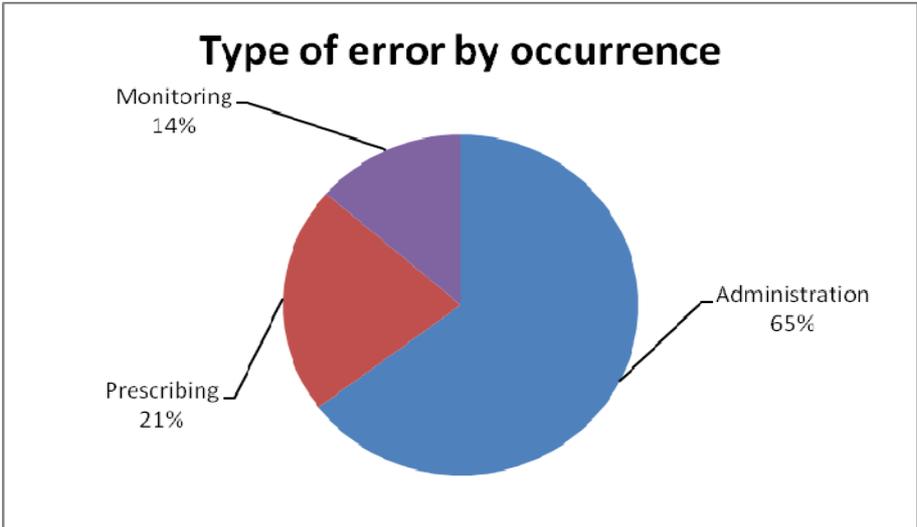
Table B and Figure 2 indicate error type by occurrence. (N.B. as some reports contained two categories of error, the total number of occurrences exceeds the total number of incident reports.)

Table B: Type of error by occurrence

Type of error	Frequency	Percentage*
Administration	388	65
Prescribing	129	22
Monitoring	82	14
Total	599	100

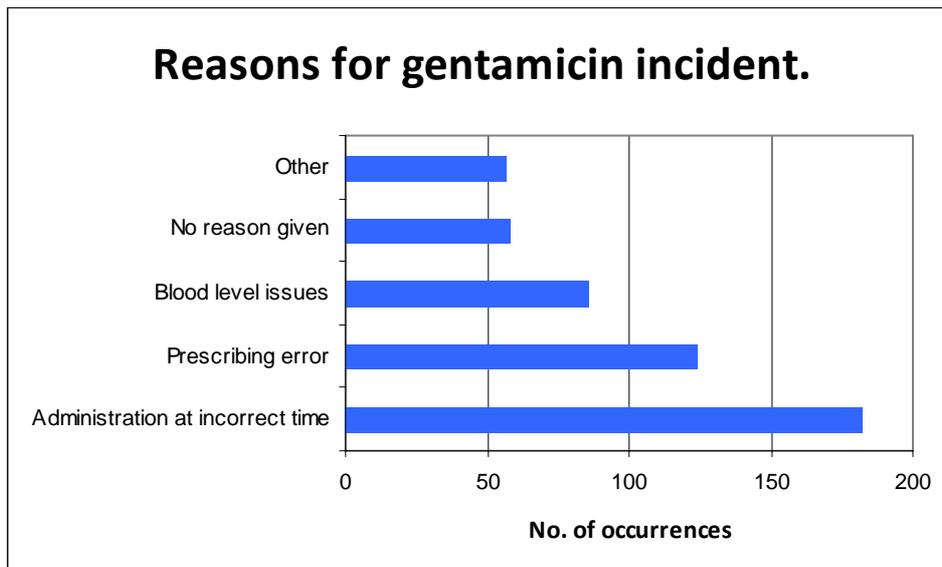
*percentages have been rounded to nearest whole number

Figure 2



The incidents were then analysed to determine if there were any apparent reasons within the text of the incident report to indicate why the incident had occurred. In 182 incidents (36 per cent), the primary reason for the error was related to the administration of the drug dose at an incorrect time. In 124 cases (24 per cent) a prescription error led to the incident; in 86 incidents (17 per cent) the reason for the error was linked to issues relating to blood levels; and in 58 incidents (12 per cent) it was not possible to identify a reason for the error. The remaining 57 incidents (11 per cent) were categorised as being due to a variety of 'other' issues (Figure 3).

Figure 3



Further analysis of all administration errors (including prescribing and administration errors, and monitoring and administration errors) indicated that in 146 incidents (38 per cent) the outcome was that the dose had been given early; in 108 cases (28 per cent) the drug was omitted; in 54 cases (14 per cent) an incorrect dose was given, and in 60 incidents (15 per cent) the dose was given late. In a further seven cases (two per cent), the report indicated that the dose had been given at the incorrect time, but did not specify if this was early or late, and 13 incidents (three per cent) were due to a variety of other reasons.

Analysis of the 77 reported prescribing errors indicated that 26 incidents (34 per cent) were due to an incorrect timing interval being prescribed. Other issues included:

- problems with the signature, route or date on the prescription – 17 incidents, (22 per cent);
- prescription of the incorrect dose – 11 incidents (14 per cent);
- drug required but not prescribed – six incidents;
- use of the incorrect weight in calculating the dose – six incidents.

The remaining 11 incidents were due to a variety of other reasons.

Analysis of the 42 reported blood monitoring incidents highlighted that the majority of the reported incidents, 52 per cent, consisted of 22 incidents related to levels not being taken. Other reasons for monitoring incidents included:

- levels taken at the incorrect time – four incidents;
- levels acted on inappropriately – three incidents;
- levels not acted on – three incidents;
- delay/failure to review levels – two incidents;
- delay in taking levels – two incidents;
- delay in receiving levels – two incidents
- other reasons – four incidents.

Ninety-six per cent of the incidents were categorised as no harm or low harm and four per cent moderate harm. However, it should be noted that the incidence of long-term hearing or renal damage a result of gentamicin toxicity is often not known until a much later stage.

2.2.2 Examples of incidents

Administration of medication at the incorrect time:

'Gentamycin was prescribed 36-hourly however the second dose was given after 24 hours. Error picked up by the pharmacist 16 hours later while checking patient charts.'

'X checked when next dose of IV Gentamicin should be given and found that the last dose of Gentamicin had been given 12 hours too early. Parents informed by Dr. Gentamicin level repeated, medical staff to decide on administration of next dose.'

'IV Gentamycin was given 12 hourly instead of 36-hourly.'

'Second dose of gentamycin given after 12 hours instead of 24. Prescription states that dose is 24-hourly. Times written are 12-hourly.'

Prescribing errors:

'High pre-dose gentamicin level on 36-hourly dosing. Intention to change prescription to 48-hourly but prescription re-written in such a way that was given interval of 24 hours.'

'Gentamicin dose was not given at 18.00. Found out at 11.00 by the pharmacist. The drug was not prescribed. Third dose not written therefore missed.'

'IV Gentamicin prescribed to be given 36-hourly but due dose boxed wrongly in the medication chart.'

'X was prescribed and given double dose of Gentamycin intravenously. Found by SpR on ward round this morning. Drug error made last night on the night shift. Consultant advised to withhold antibiotics for now and to do Gentamycin level.'

'I was preparing to give medication and on checking the dose against the neonatal protocol found the dose prescribed was too high. The dose had previously been given on x. Drs informed and the dose for today was not given. Gentamicin levels taken and awaiting results until new dose to be prescribed.'

Blood level issues:

'This baby was on Gentamicin. Gentamicin and creatinine blood results were tested. The results were not chased for two days, but Gentamicin was still given. When the results came back the levels of both Gentamicin and Creatinine were very high. Gentamicin was stopped.'

'The patient was receiving gentamycin. Blood levels were also being checked before and after gentamycin was to be given. Both the 06.00 and 14.00 gentamycin was given before gentamycin level results were known.'

'Gentamycin level was due prior to drug administration on X. No record found of level being taken on this date.'

'Gentamicin dose not given as bloods not processed in lab.'

Root cause analysis:

Root cause analysis was undertaken of 15 incidents in a tertiary neonatal unit. As a result of this and the expert working group experience it was concluded that incidents occur because of:

- poor prescribing practice;
- a lack of clearly assigned responsibility relating to blood levels;
- a lack of clearly assigned responsibility during the preparation, checking and administration phase (failure to identify administration frequency and dosing errors);
- poor communication between medical and nursing staff;
- interruptions, particularly during the preparation and administration phase (this from RCA and EWG experience);
- poor monitoring.

2.2.3 Survey of neonatal units in England

In 2007, all 180 neonatal units in England took part in a telephone survey. The survey found that:

- Gentamicin was used in 89 per cent (166/180) of neonatal units.
- Prescribing regimens varied considerably and not all units complied with the recommendations of the *British National Formulary for Children*. recommendations. The extended interval dose regimen was more commonly used than multiple daily dose regimens.
- There was also variation in practice in undertaking pre and/or post dose monitoring and in assigning responsibility for obtaining the results of levels from the laboratory.
- Eighty-two per cent (147 units) had visiting paediatric pharmacists, but only 38 units (23 per cent) had formal arrangements for pharmacists to check doctors' competency in prescribing. (Some units may have had alternative methods for assessing doctors' competency in prescribing.)
- No unit (of those surveyed in England) had a dose calculator or computerised medication prescribing facility.

2.2.4 Evidence from published literature

Gentamicin is a broad spectrum aminoglycoside antibiotic, which is widely used in the treatment of neonatal infection. It is not absorbed intestinally and therefore is given by injection. It is associated with a risk of kidney damage and hearing impairment. Adverse effects are particularly associated with patients with poor renal function, and where higher gentamicin blood levels and longer duration of therapy have been used¹.

In order to reduce the risk of adverse effects, it is important that gentamicin concentrations are kept within the accepted therapeutic range. Serum levels of gentamicin can be monitored through the measurement of both peak and trough gentamicin blood levels. A peak level is the amount of drug that is in the blood shortly after administration.

Peak aminoglycoside levels correlate with efficacy, as the rate and extent to which an aminoglycoside achieves bacterial killing is a function of its concentration. The trough blood level of a drug is the amount of drug that is in the blood just before the next dose is due. Trough levels reflect renal clearance. If the kidney is unable to excrete the dose of aminoglycoside within the dosing interval, nephrotoxicity may occur⁸.

Impaired renal function will affect the ability of the kidney to excrete aminoglycosides. In addition, high trough blood levels of gentamicin have also been associated with hearing loss⁹. Hearing loss in neonates may not be detected whilst they are on the neonatal unit and therefore evidence of harm may not be apparent until some time after discharge. It is also important to note that high blood levels of gentamicin may be due to the patient's condition and not dosing error.

Prolonging the time interval between doses of gentamicin has been advocated to provide more time for clearance of gentamicin, resulting in less accumulation, and lower trough levels which can minimise toxicity¹⁰.

i) Medication error

It is not straightforward to define or measure medication errors. As a consequence assessing the impact of interventions to reduce medical error is problematic, particularly in complex medication administration processes. Direct observation is viewed as the most effective method of measuring medication error; other methods include chart and record reviews, incident reporting, and nurse and pharmacist clinical intervention data.

Studies of medication errors in children have found rates ranging from to 1.2 per cent¹¹ to 11 per cent¹² of medication administrations, and children are said to be at three times greater risk of a medication error than adults¹². Medications such as gentamicin require complex dose calculations because of the wide range of patient weights and gestation. Neonates are particularly vulnerable if medication errors occur because they have underdeveloped renal, immune and hepatic functions.

ii) Interruptions

Interruptions by patients, staff and visitors are a common source of distraction to those involved in drug administration. A study observing 38 medication rounds on an acute surgical ward found 11 per cent of the time was spent dealing with interruptions. Sources of interruptions were doctors, other nurses, patients, telephone enquiries and relatives, with 21 per cent of interruptions initiated by the nurses themselves¹³.

A study of medication errors in a children's hospital by Conroy et al¹⁴ found that 13 out of 14 medication administrations on a neonatal intensive care unit were interrupted. Methods to prevent or reduce interruption include the wearing of a special apron or tabard to signify that the wearer is checking medications and should not be interrupted¹⁵ and having a designated area for checking. These interventions are reported to have good effect, but no formal evaluations have been reported.

iii) Calculating doses

The problems of calculation errors have been highlighted in a number of studies¹⁶. Wong et al¹⁷ tested nurses' ability to calculate doses of gentamicin for children and neonates using four questions found that only 11 out of 51 (21 per cent) answered all four questions correctly. Independent checking of dose calculation is recommended by the Council of Europe¹⁷ and others.

iv) Calculating dosing intervals

The problems that nurses have calculating the correct time to administer gentamicin, in particular when the dose regimen is 36-hourly, was highlighted in the RLS data (see page 3). Conroy et al¹⁵ reported that inappropriate timing of doses was found in 10 out of 81 pharmacist interventions and 4 out of 34 of nurse interventions. The expert working group experience suggested that the use of the 24-hour clock was good practice to avoid confusion over timing, although this has not been formally evaluated in a research setting.

v) Double-checking

An Australian study found that the error rate was significantly lower when two nurses rather than one administered medication¹⁸ and a decrease in the number of pharmacy errors following the introduction of double-checking has been reported¹⁹. The Institute for Safe Medication Practices in Canada compared two methods of double-checking, a flow sheet and verbal feedback, in a skills testing area²⁰. Both methods were found to be effective at detecting error, but the verbal feedback method was preferred by staff. Another study using simulation tested two methods of double-checking²¹. One of the new methods resulted in significant improvement in error detection, but the other had little effect on error detection. It was concluded that different approaches to double-checking were required for different clinical environments.

Other studies (for example Jarman et al²²) did not find significant differences in error when comparing single and double-checking. Factors associated with the failure of double-checking to detect error have been explored with reference to lessons learnt from the aviation and other hazardous industries where double-checking is established practice. The problem of automaticity when undertaking routine tasks prevents people from giving appropriate attention to the task²³. In addition, diffusion of responsibility and deference to authority may limit the effectiveness of double-checking processes²⁴. Studies that have examined the evidence of errors due to poor checking have noted the lack of assigned responsibility^{11,25}.

vi) Training, education and communication

Errors usually occur when human and system factors interact in a chain of often complex events. When designing systems to prevent errors, it is important to include the team, environment, and existing culture²⁴. A literature review by Conroy et al, entitled *Interventions to reduce dosing errors in children* identified three studies which showed that educational/risk management programmes reduce medication errors in children¹¹.

Morey et al's evaluation of the effectiveness of training and institutionalised teamwork behaviours on emergency department staff found a significant improvement in the quality of team behaviour with a fall error rate from 30.9 per cent to 4.4 per cent²⁶. In addition, Ginsburg et al's study examining the effect of a training intervention on nurse leaders' perceptions of safety culture found that leadership support for improvement significantly enhanced safety culture measures²⁷.

2.2.5 Interventions considered suitable for the gentamicin care bundle by the Expert Working Group (EWG)

i) When prescribing gentamicin the 24-hour clock format should be used.

RLS data highlighted that 36 per cent of gentamicin incidents related to the administration of the drug at an incorrect timing interval. The EWG experience suggested that the use of the 24-hour clock was good practice to avoid confusion over timing although this has not been formally evaluated in a research setting.

ii) Interruptions during the preparation and administration of gentamicin should be minimised by the wearing of a coloured apron by staff.

Interruptions by patients, staff and visitors are a common source of distraction to those involved in drug administration and there are a number of studies to support this. Methods to prevent or reduce interruption such as the wearing of a coloured apron are reported to have good effect but no formal evaluations have been reported.

iii) A double-checking prompt should be used during the preparation and administration of gentamicin.

Root cause analysis identified that incidents occurred because of a lack of clearly assigned responsibility during the preparation, checking and administration of gentamicin. There are a number of studies to support the use of double-checking, and the assignment of responsibility to one checker within the checking process. Double-checking is also advocated by the Nursing and Midwifery Council²⁸.

iv) The prescribed dose of gentamicin should be given within an hour either side of the prescribed time.

Gentamicin has a narrow therapeutic range and the potential for toxicity or non efficacy if prescribed timing intervals are not adhered to. RLS data highlighted that 36 per cent of gentamicin incidents related to the administration of the drug at an incorrect time. In addition, the survey of neonatal units indicated variation in practice of blood level monitoring and in assigning responsibility for obtaining the results of levels from the laboratory. Lack of clarity about blood level monitoring may contribute to administration delays or omissions.

Although education and training was not included as a specific care bundle component, the EWG felt it should be considered vital to the implementation of the care bundle.

3. Developing and piloting the care bundle

3.1 Development

The EWG first reviewed the evidence regarding the efficacy of various interventions that have been/are being used to minimise errors with gentamicin administrations, by extensive literature reviews, a national survey to ascertain current practice, root cause analysis of gentamicin-related incidents and analysis of gentamicin patient safety incidents (see section 2 for results).

The EWG then developed a care bundle made up of four simple interventions to optimise the safe use of gentamicin in neonates and undertook a risk assessment of each element of the bundle. The care bundle was tested by a small-scale pilot in neonatal units.

3.1.1 Impact assessment

The most powerful outcome measures would have been a measurement of hearing and kidney damage caused by gentamicin prescribing and administration errors. However, as these are not measurable at the time of the incident, the EWG agreed that the feasibility of the care bundle implementation would be evaluated by measuring care bundle compliance, together with feedback from the units on the practicalities of implementing the bundle and about safety issues in general.

3.2 Pilot testing

Five units tested the gentamicin care bundle. A designated local champion coordinated communication with staff, and six additional units (similar levels of care) served as comparison sites. Although not part of usual care bundle methodology, the EWG felt that data from non-implementing sites would aid understanding of the gentamicin prescribing issues. Comparison sites were not asked to change practice in any way.

3.3 Introducing the care bundle to the pilot sites

Prior to starting the pilot, participating units were asked for information about the unit's gentamicin prescribing regimen, monitoring criteria and governance framework, and the number of gentamicin incidents reported in the previous year to gather pre-implementation data.

The project coordinator visited the sites to educate staff, giving a presentation about care bundle methodology, a background to gentamicin and description of the components of the bundle and supporting evidence, followed by a discussion of the practicalities of implementing and collecting data, and making parents aware of the significance of the coloured apron.

The units collected data for eight weeks while implementing the care bundle. Comparison sites continued to record their data for this period. To implement the bundle, the units obtained a supply of disposable coloured aprons, conforming to local infection control requirements, and 24-hour format clocks (both through NHS Supplies), and a laminated version of the double-checking prompt.

4. Post-pilot analysis of the gentamicin administration care bundle

4.1 Compliance and safety issues

Compliance in the five units for all elements of the care bundle ranged from 92.2 to 96.3 per cent.

Across the five units, 16.9 per cent of gentamicin doses were associated with patient safety incidents in the pre-implementation period and 18.3 per cent during the implementation period. This increase may have been due to increased awareness of patient safety incidents following implementation. The 'need to clarify the prescription' was the most frequent patient safety incident reported; in 27.6 per cent this was a query about the gentamicin level (e.g. levels not available, not measured, or level abnormal).

4.2 User-friendliness of the care bundle

Four of five units ranked the care bundle information provided as good or very good. All sites reported that the bundle was easy to implement. In general, staff were enthusiastic about the bundle, particularly the use of a coloured apron to prevent interruptions. Three units are now using the aprons for the administration of all intravenous drugs. Giving the dose on time was the element most pilot sites found difficult to comply with. The 24-hour clock had very few safety issues associated with it.

Other positive impacts included increased awareness of the risk of medication errors and the need to ensure gentamicin levels were obtained, although there were concerns about the time required to document compliance. The completion of incident forms for the safety issues took time.

4.3 Conclusion

There was a widespread acknowledgement amongst neonatal units that patient safety issues existed relating to the administration of intravenous gentamicin to neonates due to its complex dosing regime and the need to monitor blood levels. The care bundle was generally well received by the pilot sites as a means by which staff could focus on carrying out a fixed, small number of evidence-based interventions in a way that effectively enhanced patient outcomes.

Good planning, communication and the involvement of all levels of clinical staff are all vital in ensuring acceptance by and engagement of all practitioners with the care bundle. Finally, the elements of this care bundle can provide a foundation for the development of safe administration practices of all medications for newborn babies.

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