Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Gentamicin dosing regimens in infants of 34 weeks gestation or more, requiring antibiotics for a 72 hour rule-out sepsis evaluation.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study consisted of neonates with 34 or more week’s gestation requiring antibiotics for a 72-hour rule-out sepsis evaluation.

Setting
The setting was hospital. The economic evaluation was carried out in Colorado, USA.

Dates to which data relate
The years during which the effectiveness and resource use data were collected were not specified. The price year was 1998.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken retrospectively and not on the same patient sample as that used in the effectiveness study.

Study sample
Consecutive neonates at two University of Colorado neonatal intensive care units, who met the inclusion criteria, were considered for enrollment in the study. Inclusion criteria were:

1. gestational age greater or equal to 34 weeks;
2. postnatal age inferior to 7 days;
(3) Apgar scores greater than 4 at 1 minute and greater than 6 at 5 minutes;

(4) urine output greater than 0.5 mL/kg/h in the first 24 hours or greater than 1 mL/kg/h in the second 24 hours of life; and

(5) absence of inotropic support.

Patients were assigned to one of two groups: TDD or ODD. Assignment to a particular study group was dependent on the intensive care site, with monthly rotation of dosing regimens. Inclusion criteria ensured that the initial study sample was appropriate for the clinical study question. Power calculations were not used to determine the sample size. A total of 55 patients were evaluated with 28 randomised to the TDD group and 27 to the ODD group. Patients’ (parents) refusing to participate and the number of patients excluded from the study were not reported.

Study design
The study design was a non-blinded randomised controlled trial. Two centres were involved in the study. The duration of follow up was 72 hours. Allocation to the arms of the study was based on the month and location of birth of the patient, this is not considered to be a truly random allocation method. The study was not blinded. There was no loss to follow up.

Analysis of effectiveness
The analysis of the clinical study was based on intention to treat (there was no loss to follow up). The primary health outcome used in the analysis was the proportion of patients in each dosing group within a target serum gentamicin concentration (SGC), established as a peak of 5 to 10 microgrammes/mL and a trough less than or equal to 2 microgrammes/mL. Side effects, such as nephrotoxicity, were not reported. Patients’ characteristics at study entry were shown to be comparable.

Effectiveness results
43% of patients within the TDD group had serum concentrations inside the accepted target range compared with 93% in the ODD group (p<0.5).

Clinical conclusions
Once daily gentamicin therapy of 4mg/kg in neonates with 34 weeks or more gestation resulted in improved serum drug concentrations compared with conventional twice-daily therapy of 2.5 mg/kg/dose. Higher doses administered less often to this patient population provided an attractive therapeutic alternative to traditional 12-hour dosing.

Measure of benefits used in the economic analysis
The outcome measure used in the economic analysis was the fraction target SGC in each dosing group.

Direct costs
Costs were not discounted due to the short time span of the study (72 hours). Quantities and costs were not reported separately. Costs included were drug acquisition costs, equipment, drug preparation and administration (labour) and serum concentration analysis. The boundary adopted was that of the hospital. The estimation of quantities was based on information collected in 15 questionnaires distributed to paediatric pharmacists across the United States and Canada. Labour time was determined by time-in-motion observations of gentamicin associated tasks by pharmacy and nursing personnel at a single institution (University Hospital). Cost information other than labour was collected via the questionnaires, although the methods used by the respondents to establish costs were not reported. Mean hourly wage was used to calculate labour costs. The period during which the quantity of resources was measured was not reported. The price year was 1998.
Statistical analysis of costs
A statistical analysis of costs was not conducted.

Indirect Costs
Indirect costs were not reported.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was conducted on costs. Additional cost-effectiveness analyses were conducted excluding labour costs, using the lowest SGC analysis cost ($28) and excluding SGC analysis costs.

Estimated benefits used in the economic analysis
43% of patients within the TDD group had serum concentrations inside the accepted target range compared with 93% in the ODD group (p<0.5). The difference in effect was 0.5. The duration of follow-up was 72 hours. Side effects of treatment were not included in the analysis.

Cost results
The cost results were as follows:

The total mean (standard deviation) cost of drug acquisition was $1.98 (0.96) in the TDD group and $0.99 (0.48) in the ODD group.

The total mean (standard deviation) cost of materials and equipment was $26.58 (13.2) in the TDD group and $21.6 (11.1) in the ODD group.

The total mean (standard deviation) cost of labour was $14.46 (1.5) in the TDD group and $7.23 (0.75) in the ODD group.

The total mean (standard deviation) cost of SGC analysis was $132.16 (74.62) in the TDD group and $132.16 (74.62) in the ODD group.

In the TDD group, the mean cost per patient (with labour) was $175.18 compared to $29.82 in the ODD group.

The mean difference in cost was $145.36 less in the ODD group compared to the TDD group.

The duration of the intervention quantities and costs was 72 hours.

Costs of adverse effects were not included in the analysis.

Synthesis of costs and benefits
Costs and benefits were combined into incremental cost-effectiveness ratios. The ODD strategy was found to be dominant (higher effectiveness and lower costs) over the TDD strategy, in all cases (with and without labour costs included, with lowest SGC cost used, and without SGC analysis). The incremental cost-effectiveness ratio of ODD compared to TDD was -$290.72.

Authors' conclusions
The authors concluded that ODD of gentamicin at 4 mg/kg in neonates with 34 or more weeks' gestation is the
preferable treatment strategy. This is based on a significantly improved SGC performance compared with TDD, the elimination of the need for routine SGC collection in infants on short courses of therapy, significant antibiotic associated hospital cost-savings when compared with conventional therapy of TDD and SGC analysis.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparator was justified, as the twice-daily dosing regimen was the standard practice.

**Validity of estimate of measure of benefit**
The randomised controlled trial study design was appropriate for the hypothesis. The study sample was representative of the study population. The patient groups were shown to be comparable at analysis. However, the method of randomisation, based on the month and the location, is not considered to be true randomisation. Moreover, such a study design precludes blinded analysis, which may lead to bias in the results. The measure of health benefit was proxied directly by a single measure of effectiveness (the proportion of patients in the target SGC ranges); this choice was justified. However, possible complications of gentamicin therapy such as nephrotoxicity were not included. Moreover, the authors warn that the results should not be extrapolated for longer courses of therapy or to older infants.

**Validity of estimate of costs**
All categories of cost relevant to the perspective adopted were included in the analysis and for each category of cost, all relevant costs were included. Moreover a sensitivity analysis was performed on some of the costs and the price year was reported. Some problems with the validity of the estimates of costs were that quantities and costs were not reported separately, and details of the questionnaires on which some of the resources and costs were based were not given, so it was not possible to know how the estimates were derived by the respondents. A statistical analysis of costs was not performed.

**Other issues**
The authors made appropriate comparisons of their findings with those from other studies, although it was not stated whether a systematic review of the literature was conducted. The issue of generalisibility to other settings was addressed. The authors did not appear to present their results selectively. The study enrolled neonates with 34 weeks or more gestation and this was reflected in the authors’ conclusions. The authors acknowledged that results should not be extrapolated to infants on longer courses of antibiotics or to older infants.

**Implications of the study**
The authors recommended a change to once daily administration rather than twice.

**Source of funding**
Supported by National Institutes of Health Grants HD01061 and 5-MOI-RR00069.

**Bibliographic details**

**PubMedID**
10049962

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Cost-Benefit Analysis; Costs and Cost Analysis; Gentamicins /administration & dosage /blood /economics; Humans; Infant, Newborn; Prospective Studies; Sepsis /drug therapy /economics

AccessionNumber
21999000485

Date bibliographic record published
30/04/2001

Date abstract record published
30/04/2001