Teicoplanin or vancomycin in febrile neutropenic children with cancer: a randomized study on cost effectiveness

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
Antibiotic regimens containing either teicoplanin or vancomycin were compared for children with cancer who were experiencing febrile neutropenia after conventional chemotherapy. The antibiotic regimen comprised ceftazidime (90 mg/kg/day, three times) with either teicoplanin (10 mg/kg) or vancomycin (10 mg/kg). Teicoplanin was administered every 12 hours for the first three injections, then every 24 hours either intravenously or by catheterisation. Vancomycin was administered every 6 hours by perfusions of at least 30 minutes (i.e. 40 mg/kg/day).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised children under 18 years of age with a solid tumour cancer, who were hospitalised in the paediatric oncology department (Gustave Roussy Institute) for febrile neutropenia. Febrile neutropenia was defined as a temperature of greater than 38 degrees C for at least 6 hours, with a polynuclear neutrophil count of less than 500/mm3. The children had also undergone conventional chemotherapy in the month preceding the study. The exclusion criteria for the study were a known allergy or hypersensitivity to teicoplanin or vancomycin, diabetes, human immunodeficiency virus, asthma, chronic kidney failure, or a previous inclusion in the trial.

Setting
The setting was secondary care. The economic evaluation was carried out at the paediatric oncology department of the Gustave Roussy Institute, France.

Dates to which data relate
The effectiveness and resource use data were collected between January 1995 and May 1996. The price year was 1995.

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

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.
Power calculations were not performed in the planning phase of the study to determine the sample size. However, the authors reported that this was due to there being insufficient data in the literature on the costs and the outcomes related to the study. The sample was selected from the study population using the inclusion and exclusion criteria. There were initially 33 patients in the teicoplanin group and 34 in the vancomycin group. Two patients (one from each group) were excluded from the study because they were transferred out of the department on the first (teicoplanin group) and second (vancomycin) day of the study. No patients were reported to have refused to participate.

In the teicoplanin group, 63% of the patients were male. Nine per cent were less than one year old, 31% were between 2 and 5 years old, 22% were between 6 and 10 years old, and 38% were between 11 and 18 years old. Six per cent weighed between 6 and 10 kg, 37.5% weighed between 11 and 20 kg, 19% weighed between 21 and 30 kg, and 37.5% weighed more than 31 kg but less than 89 kg. Of the patients, 16% had lymphoma, 44% had a nervous system tumour, 22% had a bone or soft tissue tumour, 6% had a kidney tumour, and 12% had another type of tumour. In addition, 41% were receiving a preventive treatment of G-CSF (blood growth factor) initiated with the chemotherapy.

In the vancomycin group, 64% of the patients were male. Three per cent were less than a year old, 27% were between 2 and 5 years old, 30% were between 6 and 10 years old, and 40% were between 11 and 18 years old. Three per cent weighed between 6 and 10 kg, 37% weighed between 11 and 20 kg, 27% weighed between 21 and 30 kg, and 33% weighed more than 31 kg but less than 89 kg. Of the patients, 18% had lymphoma, 37% had a nervous system tumour, 27% had a bone or soft tissue tumour, 12% had a kidney tumour, and 6% had another type of tumour. In addition, 36% were receiving a preventive treatment of G-CSF initiated with the chemotherapy.

The initial sample appears to have been appropriate for the clinical study question.

**Study design**
The study was a randomised controlled trial conducted at a single centre. The patients were randomised by drawing lots. Randomisation was stratified according to whether or not the patient was receiving G-CSF as a preventive treatment. The duration of follow-up was initiated when the antibiotic treatment regimen was begun. It was ended either by the transfer of the patient out of the paediatric oncology ward, or with the resumption of chemotherapy. The average duration of the follow-up was 7.5 days. There were no losses to follow-up. No blinding methods were reported.

**Analysis of effectiveness**
The effectiveness was analysed on an intention to treat basis. The primary health outcome used in the analysis was the average number of hours of sleep per night. A nurse assessed sleep, every hour for twelve hours for every night spent in the ward. The groups were shown to be comparable at analysis with respect to gender, weight, age, cancer diagnosis and preventive G-CSF treatment.

**Effectiveness results**
The mean number of hours of sleep ranged from 4.8 to 9.3 hours (median: 7 hours) in the teicoplanin group, and from 5.4 to 9.3 hours (median: 7.2 hours) in the vancomycin group. The difference was not statistically significant, (p=0.84).

Three adverse reactions occurred. One patient treated with teicoplanin suffered from moderate kidney failure, and skin reactions occurred in two patients during the first injection of vancomycin. One of the patients with a skin reaction was switched to teicoplanin, whilst the other received cefotaxim and amikacin instead.

**Clinical conclusions**
There was no difference in the number of hours of sleep per night in patients receiving vancomycin (4 injections per 24 hours) and those receiving teicoplanin (one injection per day).

**Measure of benefits used in the economic analysis**
The effectiveness analysis showed no difference in effectiveness between the two interventions. Thus, the economic
analysis was based on the cost-differences only (cost-minimisation).

**Direct costs**
Discounting was not carried out as the study duration was less than two years. The quantities and the costs were not reported separately. The quantity/cost boundary adopted was that of the hospital. The direct costs were for the antibiotic regimen, any other treatments received for febrile neutropenia (anti-infection agents, allergy treatments, anticonvulsants and antipyretics), G-CSF, solutions, electrolytes, and any other biological and/or radiological examinations that were required.

The costing also included the costs of preparing and administering the treatments, and conducting blood, urine, faeces or skin tests. The costs included the products and materials used, and the time spent by the nurses in preparing and administering the treatments and testing the patients.

The resource use data were obtained for each individual patient. Material use and nurse time was estimated by a physician, using a sample of three to five injections performed by the nurse. The unit cost data were obtained from actual data, which were derived from the cost to the hospital of materials and nursing salaries. The cost of the radiological and biological tests was obtained from official publications. The price year was 1995.

**Statistical analysis of costs**
The costs were compared using the Kruskall-Wallis non-parametric test.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
French francs (Ffr).

**Sensitivity analysis**
A one-way sensitivity analysis was performed on the cost of teicoplanin.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The median total cost per patient was 8,071 Ffr (range: 3,079 - 23,309) in the teicoplanin group and 6,144 Ffr (range: 1,732 - 29,616) in the vancomycin group. The difference was 1,927 Ffr, (p=0.18). The duration of the intervention was 7.5 days on average. The costs of adverse effects were included in the analysis.

**Synthesis of costs and benefits**
Not applicable.

**Authors' conclusions**
The two antibiotic regimens assessed were comparable in terms of sleep. However, the cost analysis, in terms of the cost of the treatment regimen alone, showed that the vancomycin regimen was preferable to its teicoplanin counterpart.
CRD COMMENTARY - Selection of comparators
The choice of the comparators was justified as both of the treatment regimens were used in the authors’ settings to treat febrile neutropenia. You should decided if these are widely used health technologies in your own setting.

Validity of estimate of measure of effectiveness
In general, the analysis of effectiveness was well reported and well conducted. The validity of the estimate of effectiveness is likely to be high, because the evidence was derived from a randomised controlled trial. This study design was appropriate for the study question under consideration. The study sample was representative of the study population, children with cancer suffering from febrile neutropenia. The patient groups were shown to be comparable at analysis. The analysis of effectiveness was well reported in terms of how the authors conducted the intention to treat analysis. In addition, potential confounding factors, such as the use of preventive growth factor treatments, were accounted for using stratified randomisation. The study could have been improved by reporting whether the nurses were blinded to the treatment regimen when they assessed sleep.

Validity of estimate of measure of benefit
The analysis of the benefits was based upon the therapeutic equivalence of the treatment alternatives, which was appropriate. The economic analysis, therefore, only included the costs.

Validity of estimate of costs
In general, the costing was well conducted and well reported. From the cost perspective adopted, namely that of the hospital, all the categories of relevant costs appear to have been included in the analysis. In addition, all the relevant costs within each category were included. The source of the resource use data and the unit costs was well reported. A sensitivity analysis was conducted on the price of one of the treatments. Discounting was not conducted, which was appropriate. The price year was reported. The validity of the cost estimates could have been improved by reporting the quantities and the costs separately. Also, by conducting statistical analyses on the quantities.

Other issues
The authors did not compare their findings with those from other studies. The issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively. However, they concluded that vancomycin should be recommended because its cost was cheaper than teicoplanin, although in terms of the total costs, there was no significant difference between either regimen. The authors did not report any further limitations of their study.

Implications of the study
The findings suggest that vancomycin offers an advantage (economic) over teicoplanin. The authors suggest that this study could be extended to include patients who are not hospitalised and who receive outpatient treatment.

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