Paclitaxel hypersensitivity reactions: assessment of the utility of a test-dose program

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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
Cancer patients prescribed paclitaxel were initially given a test dose before the first and second cycles of paclitaxel chemotherapy, to see whether they experienced hypersensitivity reactions (HSRs). The test dose consisted of a 12 mg dose prepared in 10 mL of normal saline and infused intravenously over 6 minutes. The patients were observed for 15 minutes after administration of the test dose. If the patient experienced an adverse reaction the paclitaxel infusion was immediately stopped and the patient was given an alternative chemotherapy. If there was no adverse reaction, a full paclitaxel dose (80 to 200 mg/m2) was given after a second short antihistamine pre-medication. A comparator group of patients was given the full dose of paclitaxel prescribed.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised cancer patients prescribed paclitaxel.

Setting
The setting was secondary care. The economic study was carried out in Lyon, France.

Dates to which data relate
The effectiveness and resource evidence dated from 1997 to 2003. No price year was given.

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

Link between effectiveness and cost data
The same patients provided both the cost data and the effectiveness data. Some of the costing was carried out retrospectively; it was not clear whether all of it was.

Study sample
Power calculations were mentioned at the end of the paper. It was stated that the power of the test was 40% and that 397 patients would have been needed to obtain a statistical power of 80%. The study sample was chosen from a retrospective analysis of patient records from one hospital where patients received one or two courses of chemotherapy containing paclitaxel, and from patients attending the same hospital at a later time period who received a test dose of
paclitaxel chemotherapy. There were 130 patients in the intervention group and 162 patients in the comparator group.

**Study design**
This was a single-centre, non-randomised trial with historical controls. The patients were not followed up after their chemotherapy treatment. No loss to follow-up was reported.

**Analysis of effectiveness**
The analysis was conducted on an intention to treat basis. The primary health outcome was the incidence of HSRs. No information on the comparability of the patient groups was given.

**Effectiveness results**
The incidence of HSRs was 6.2% before the test dose programme was introduced and 2.3% with the test dose programme, (p<0.20).

Before the test programme was introduced, 4 patients experienced an HSR during the first course of chemotherapy and 6 patients during the second course of chemotherapy.

After the introduction of the test programme, 1 patient experienced an HSR after the test dose, 2 after the first or second course, and 1 after the third course.

**Clinical conclusions**
The incidence of HSRs was lower during chemotherapy with the test dose programme, but it was not zero. This shows that the test dose programme does not guarantee that patients will not suffer HSRs during their chemotherapy.

**Measure of benefits used in the economic analysis**
No summary measure of benefit was produced as the authors carried out a cost-consequences analysis.

**Direct costs**
Discounting was not carried out as the costs were incurred during less than 2 years. Some quantities and costs were analysed separately. The unit costs of specific components of the test dose programme (i.e. paclitaxel, syringe and pre-medication) were given. The costs of drug wastage and the cost of the test dose were calculated. The costs were derived using actual data from the hospital. No price year was given.

**Statistical analysis of costs**
No statistical analysis of the costs was carried out.

**Indirect Costs**
No indirect costs were estimated.

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analysis was carried out.
Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The wastage costs per patient, which included the cost of the test dose, were $116 before the introduction of the test dose programme and $163 after its introduction.

Synthesis of costs and benefits
The costs and benefits were not combined as the study was a cost-consequences analysis.

Authors’ conclusions
The test programme did not reduce costs but did decrease the incidence of hypersensitivity reactions (HSRs). The authors described this result as showing that the test dose programme was not cost-effective.

CRD COMMENTARY - Selection of comparators
The choice of the comparator was implicitly justified by it representing current practice in many settings. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were derived from a single study. The analysis was based on a non-randomised study with historical controls. The study sample appears to have been representative of the study population. The patient groups were not shown to be comparable at analysis, but it was not clear that any non-comparability would be related to the incidence of HSRs. The analysis of effectiveness was handled credibly in some respects. However, the incidence of HSRs was measured over a possible three treatment cycles under the test dose regimen (compared with two cycles before the test dose regimen) and, therefore, would be likely to pick up more cases of HSR. Another drawback of the study was that the number of patients in the two groups was not sufficiently large to assess whether the difference in HSRs was statistically significant. There were no other sources of effectiveness data.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit since they carried out a cost-consequences analysis.

Validity of estimate of costs
From the cost perspective adopted (i.e. that of the hospital), not all of the costs were included. For example, the costs of treating HSRs and the cost of nursing time were not included. The omission of the costs of treating HSRs made the extra cost of the test dose programme larger than it really would be. Although the authors implied that nursing time would be used to carry out the test dose programme without clinical benefit, nursing time would also be necessary for the chemotherapy wastage as a result of HSRs for which patients need to be switched to another drug. It is not clear what effect this omission would have on the difference in costs between the two patient groups. The costs and the quantities were reported separately for the drugs involved in the test dose programme. The quantities were taken from a single study, while the unit costs were taken from the authors’ setting. No statistical, sensitivity or any other kind of analysis of the quantities or prices was conducted. The price year was not reported, which will hinder any future inflation exercises. Discounting was appropriately not carried out as the time horizon of the model was less than 2 years.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. The issue of generalisability to other settings was addressed in that the authors discussed the possibility that their results were dependent on the intensification of pre-medication after the test dose and before the full paclitaxel dose. The authors did not present their
results selectively but their conclusions do not reflect the scope of the analysis. They used 'cost-effective' as a synonym for cost reducing and, therefore, concluded that the test-dose programme was not cost-effective.

A serious drawback of the study was that, as a result of taking the perspective of the hospital in their analysis, the authors did not put any weight on the patients’ benefit from suffering fewer HSRs. The authors noted several further limitations of their study: inadequate patient numbers to give the statistical power needed, and the use of an intensified pre-medication regimen in the test dose programme.

**Implications of the study**
The authors’ view was that their study implied that giving a test dose of paclitaxel increases costs. However, their cost analysis did not include all of the costs. Even if costs are increased by a test dose programme, this would need to be weighed against the benefits of the programme, that is, a reduction in HSRs.

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