Economic analyses of toxicity secondary to anthracycline-based breast cancer chemotherapy

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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
Using equidoses of either doxorubicin (FAC) or epirubicin (FEC) in the treatment of breast cancer.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients diagnosed with breast cancer who had at least one course of chemotherapy with either FAC or FEC exclusively.

Setting
Hospital. The economic study was carried out in Ontario, Canada.

Dates to which data relate
Effectiveness and resource data were collected over the period 1985 to 1994. June 1995 prices were used.

Source of effectiveness data
The evidence for the final outcomes was derived from a single retrospective study.

Link between effectiveness and cost data
The costing was undertaken retrospectively on the same patient sample as that used in the effectiveness study.

Study sample
Power calculations were used to determine the sample size. Each group of the study contained the medical charts of 100 patients. The one-hundred medical charts for patients undergoing FAC chemotherapy were randomly chosen from the charts of 536 patients receiving FAC, and similarly the one-hundred medical charts for patients undergoing FEC chemotherapy were randomly picked from the charts of 389 patients receiving FEC.

Study design
The study was a retrospective case series carried out in a single centre. The median duration of treatment for each group was 4 months with a range of 1 to 12 months for the FAC group versus 1 to 24 months for the FEC group.
Analysis of effectiveness
The analysis of the study was based on intention to treat. The health measures consisted of:

number of cases of cardiotoxicity (including cases of abnormal electrocardiogram (ECG) changes),

number of cases of congestive heart failure (CHF),

number of cases of abnormal left ventricular ejection fraction (LVEF),

the rate of anthracycline-induced hospitalisation,

the median length of anthracycline-induced hospitalisation,

number of cases of myelosuppression (including cases of therapy delay and the percentage of therapeutic delay which occurred below the 400 mg/m-square cumulative dosage, cases of dose reduction and the percentage of dose reduction occurring below the 400 mg/m-square cumulative dosage),

the rate of FN-induced hospitalisation and the the median length of hospitalisation in those cases,

the number of cases of septic death,

the overall trend of FN incidence.

The groups were shown to be comparable with respect to physical characteristics, diagnoses and metastatic sites.

Effectiveness results
Results for FAC and FEC groups respectively:

Abnormal electrocardiogram (ECG) changes: 28 (FAC) vs. 22 (FEC)

Cases of congestive heart failure (CHF): 2 (FAC) vs. 1 (FEC)

Cases of abnormal left ventricular ejection fraction (LVEF): 3 (FAC) vs. 1 (FEC)

Rate of anthracycline-induced hospitalisation: 5% (FAC) vs. 2% (FEC) (odds ratio: 2.6 for FAC).

Median length of anthracycline-induced hospitalisation: 7 days (FAC) vs. 3 days (FEC)

Cases of myelosuppression-induced therapeutic delay: 40 (FAC) vs. 42 (FEC)

Percentage of therapeutic delay below the 400 mg/m-square cumulative dosage: 85% (FAC) vs. 50% (FEC)

Cases of myelosuppression-induced dose reduction: 43 (FAC) vs. 38 (FEC)

Percentage of dose reduction below the 400 mg/m-square cumulative dosage: 100% (FAC) vs. 45% (FEC)

Rate of FN-induced hospitalisation: 25% (FAC) vs. 14% (FEC) (odds ratio: 0-0.14 of 2.0 for FAC)

Median length of hospitalisation in FN-induced cases for both groups were 7 days.

Cases of septic death: 5 (FAC) vs. 1 (FEC)

The overall trend of FN incidence was higher in the FAC group (P= 0.074).

Clinical conclusions
The study revealed that "unlike the doxorubicin protocol, dosage reduction and delays secondary to epirubicin myelosuppression are less prevalent at the lower dosage ranges”. Overall, FEC had a better performance than FAC in the management of CT and FN secondary to breast cancer chemotherapy.

**Measure of benefits used in the economic analysis**
The main measures of benefits used in the economic study were the rate of anthracycline-induced hospitalisation and the rate of FN-induced hospitalisation.

**Direct costs**
Resource quantities were not reported separately. Cost items were reported separately. The total cost of cardiotoxicity per case, and the total cost of febrile neutropenia per case and per course of chemotherapy were calculated. The cost components consisted of the cost of hospitalisation, supportive medications (including pharmacy preparation and nursing administration costs), drug therapy, laboratory tests for patient monitoring and specialist consultation. The cost analysis was conducted from the point of view of a hospital. The sources of the cost data were local or regional health organisations. 1995 price data were used. The acquisition costs of FAC and FEC were omitted from the cost analysis since they were cost equivalent in the study site.

**Statistical analysis of costs**
Statistical tests were carried out using non-parametric Mann-Whitney U-test to compare the groups in terms of the total cost of toxicity per course of chemotherapy.

**Indirect Costs**
Not calculated.

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
A one-way sensitivity analysis was performed using the 95% confidence interval (CI) for the difference in the incidence rates.

**Estimated benefits used in the economic analysis**
The rate of anthracycline-induced hospitalisation for the FAC group was 5% versus 2% for the FEC group (with the an odds ratio of 2.6 for FAC). The rate of FN-induced hospitalisation for the FAC group was 25% versus 14% for the FEC group [with an odds ratio of (0-0.14) of 2.0 for FAC].

**Cost results**
The total cost of CT per case (range) in the FAC group was Can$4,268.08 (1,240 - 8,251) versus Can$2,447.28 (2,445 - 2,450) in the FEC group. The total cost of FN per case in the FAC group was Can$5,418.62 (1,235 - 1,6463) versus Can$5,193.83 (2,041 - 11,028) in the FEC group.

**Synthesis of costs and benefits**
The total cost of cardiotoxicity and FN per course of chemotherapy were calculated. The total cost of CT per course of chemotherapy in the FAC group was Can$80.77 (range: 0 - 8251) versus Can$51.9 (range: 0 - 2450) in the FEC group (P=0.64. The total cost of FN per course of chemotherapy in the FAC group was Can$268.20 (range: 0 - 16,463) versus Can$145.72 (range: 0 - 11,028) in the FEC group (P= 0.058).
Authors' conclusions
The results of the study support the substitution of equidose epirubicin for doxorubicin in women undergoing treatment for malignancies of the breast. Such a policy may result in reduced toxicity-related management costs.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator is clear as it was considered "to be the most active single agent in the treatment of advanced breast cancer". You should consider whether this is a widely used health technology in your own setting.

Validity of estimate of measure of benefit
Lack of randomisation is likely to make the study susceptible to potential biases.

Validity of estimate of costs
Resource quantities were not reported separately from the costs. It would seem relevant, in studies which mainly focus on the side effects of alternative health technologies, to include indirect costs to patients and others. However, this study did not consider these costs.

Other issues
The issue of generalisability was discussed.

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