Impact of a selenium chemoprevention clinical trial on hospital admissions of HIV-infected participants


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
The use of selenium chemotherapy (200 microg/day) in human immunodeficiency virus (HIV)-positive individuals.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population included patients with past or present use of illegal drugs, who were aged 18 years or older, with a confirmed HIV-positive status and adequate selenium status (greater than 85 microg/L). Patients with selenium levels below 85 microg/L were excluded for both ethical and scientific reasons.

Setting
The setting was tertiary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were gathered from 1998 to 2000. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was performed both retrospectively (pre-intervention period) and prospectively (intervention period) on the same sample of patients as that used in the effectiveness study.

Study sample
Power calculations do not appear to have been performed. Of an initial sample of 259 individuals, data were evaluated for 186 participants. There were 89 patients in the selenium group and 97 in the placebo group. In the selenium group, 44% of the participants were women and 12% were older than 49 years. In the placebo group, 48% were women and 12% were older than 49 years. Those patients who were not participating in the study (73 cases) were excluded due to incomplete data. The method used to select the sample was unclear.
Study design
This was a randomised, double-blind, placebo-controlled clinical trial. The methods of randomisation and blinding were not reported. The sites where the study was conducted were not explicitly reported. The length of follow-up was 2 years, including the pre-intervention and the intervention periods. The patients were assessed at baseline, at 6 months, and at one year in the intervention period. Seventy-three patients were lost to follow-up and excluded from the initial study sample because their data were incomplete.

Analysis of effectiveness
The analysis of the clinical study was conducted on the basis of treatment completers only. The primary health outcomes used in the effectiveness study were:

- the proportion of patients with plasma selenium levels below 135 microg/L;
- the proportion of patients that showed a decline in CD4 cell counts of less than 50;
- the number of patients requiring hospitalisation;
- the total number of hospital admissions in the pre-intervention and intervention periods;
- the number of admissions in the selenium and placebo groups;
- the relative risk (RR) of hospitalisation;
- the length of stay;
- the proportion of patients hospitalised between one and four times; and
- hospitalisations among patients not using antiretroviral treatment.

A Poisson regression model was used to identify those factors that were significantly related to the number of hospital admissions. The study groups were comparable at baseline in terms of their demographics and clinical characteristics. However, fewer patients in the placebo group were using highly-active antiretroviral therapy (HAART).

Effectiveness results
The proportion of patients with plasma selenium levels below 135 microg/L was 47% in the selenium group and 89% in the placebo group, (p=0.001).

The proportion of patients that showed a decline in CD4 cell counts of less than 50 was 25% in the selenium group and 46% in the placebo group, (p=0.01).

Twenty-six patients in the selenium group required hospitalisation versus 32 in the placebo group.

There were 157 hospitalisations in total (0.84 hospitalisations/patient) in the pre-intervention period and 103 (0.55 hospitalisations/patient) in the intervention period.

The rate of admissions was 22% in the selenium group and 52% in the placebo group, (p=0.004).

The RR of hospitalisation in the placebo group relative to the selenium group was 2.12 (95% confidence interval: 1.18 - 3.80; p=0.008).

The length of stay was comparable in both groups.

The proportion of patients hospitalised between one and four times was 33% in the selenium group and 67% in the placebo group, (p=0.0004).
The rate of hospitalisations among patients not using antiretroviral treatment was 10% in the selenium group and 34% in the placebo group, (p=0.04).

The regression analysis confirmed that the use of selenium therapy reduced the risk of hospitalisation in comparison with placebo. In addition, both age and a viral load of greater than 10,000 at baseline were independently associated with hospitalisation.

**Clinical conclusions**
The effectiveness analysis showed that the use of selenium supplements was effective in reducing the risk of hospitalisation among HIV patients.

**Measure of benefits used in the economic analysis**
The health outcomes were left disaggregated and no summary benefit measure was used. The study has therefore been classified as a cost-consequences analysis.

**Direct costs**
Discounting was not relevant since the costs were incurred within 2 years. The unit costs were analysed separately from the quantities of resources used. The economic analysis included only the cost of hospitalisation, which was estimated from a community hospital in Florida. The cost inputs included in the hospital stay were not reported. The cost/resource boundary adopted in the study appears to have been that of the hospital. Resource use was estimated alongside the clinical trial, using data coming from the same patients as those involved in the effectiveness study. The price year was not reported.

**Statistical analysis of costs**
The Wilcoxon non-parametric test and Student's t-test were performed to compare the days and costs of hospitalisation.

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

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were not performed.

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

**Cost results**
In the pre-intervention period, the total hospital costs were $360,878 in the selenium group and $518,371 in the placebo group. The corresponding costs in the intervention period were $151,235 (selenium group) and $358,792 (placebo group), respectively.

The decrease in the cost of hospitalisation was 58% in the selenium group and 30% in the placebo group.
Synthesis of costs and benefits
Not relevant as a cost-consequences analysis was conducted.

Authors' conclusions
Selenium therapy was effective in reducing both the rate of hospitalisation and the cost of treatment in patients with human immunodeficiency virus (HIV).

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. Placebo was selected because the aim of the study was to evaluate the active value of selenium supplements among HIV patients. You should assess whether no selenium therapy represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used a randomised trial, which was appropriate for the study question. A double-blind assessment of the outcomes was performed, thus enhancing the internal validity of the analysis. The length of and loss to follow-up were reported. However, several drawbacks have to be mentioned. First, the methods of randomisation and sample selection were not described. Second, power calculations do not appear to have been performed and there was no evidence that the initial study sample was adequate for the study question. Third, the study sample was not representative of the overall study population of patients with HIV. Finally, the basis of the clinical study was treatment completers only, which does not appear to have been appropriate given the substantial loss to follow-up. These issues tend to limit the internal validity of the analysis.

Validity of estimate of measure of benefit
No summary benefit measure was used in the economic analysis, which was therefore categorised as a cost-consequences analysis.

Validity of estimate of costs
The perspective adopted in the study was not explicitly stated and only hospitalisation costs were included in the economic analysis. The unit cost of one hospital day was provided, but a breakdown of the cost items was not given. The source of the cost data was reported. However, the authors did not mention the price year, thus making reflation exercises in other settings difficult. Statistical tests were conducted on the costs and quantities, but the cost estimates were specific to the study setting because sensitivity analyses were not performed. The adoption of a wider perspective with the subsequent inclusion of more categories of costs would have been interesting. In addition, it would have enhanced the validity and generalisability of the cost results.

Other issues
The authors made some comparisons of their findings with those from other studies. In terms of the generalisability of the study results to other settings, the authors acknowledged that their conclusions might not be extrapolated to the HIV-infected population in general due to the strict inclusion criteria used in the present study.

Implications of the study
The study results suggested that selenium therapy might be beneficial and efficient for specific patients with HIV. The authors stressed that selenium supplements may be an important aspect of HIV treatment in countries where HAART therapy is not available to all patients. They also noted that further research should be performed to confirm the results of their study, which should be interpreted with caution.

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