Health related quality of life using serum testosterone as the trigger to re-dose long acting depot luteinizing hormone-releasing hormone agonists in patients with prostate cancer

Oefelein M G

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 long-acting luteinising-hormone releasing hormone (LH-RH) agonists as androgen suppression therapy for metastatic prostate cancer was examined. In addition, re-dosing LH-RH on the basis of serum testosterone was evaluated.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients who had a histological diagnosis of prostate cancer and elected androgen suppression therapy. Patients were not enrolled if they reported self-administering PC-SPES.

Setting
The setting was tertiary care. The economic analysis was conducted in the Department of Urology, University Hospital of Cleveland (OH), USA.

Dates to which data relate
The dates during which the effectiveness and resource data were collected were not reported. The price year was not stated.

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

Link between effectiveness and cost data
The costing was undertaken prospectively on the same group of patients as that used in the effectiveness study.

Study sample
Power calculations to determine the sample size were not reported. A total of 22 patients who approved the protocol were enrolled in the study. One patient withdrew within 3 months of the start date and subsequently died. Thus, only 21 patients were included in the analysis. The median age was 73 years (mean: 71, range: 51 - 82). The median pretreatment prostate specific antigen (PSA) level was 9.7 ng/dL (mean: 51, range: 0.7 - 626) and the median pretreatment testosterone level was 318 ng/dL (mean: 358, range: 100 - 742). The median body mass index was 25.
kg/m² (mean: 26, range: 19 - 39).

**Study design**
The study had a within-group comparison, crossover design and was conducted in a single centre. During a 3-month lead-in period, in which each patient served as a control, 10.8 mg goserelin were administered. Subsequent re-dosing was based on total serum testosterone, determined at monthly intervals beginning 90 days after the last injection. Once the testosterone had increased to the castrate level of 20 ng/dL, 10.8 mg goserelin were re-administered and the cycle was repeated. The duration of follow-up was 18 months. A washout period was not explicitly reported, although there is some delay between the two treatments.

**Analysis of effectiveness**
The analysis of the clinical study was conducted on the basis of treatment completers only. The primary health outcome used in the analysis was the health-related quality of life. This was assessed at enrolment and at each repeat injection of goserelin, using the Expanded Prostate Index Composite (EPIC) and the SF-36. Responses to the SF-36 were summarised into 2 scores combining the mental and physical component summaries. The EPIC scores at enrolment were unavailable for 5 patients, therefore, these patients were eliminated from the EPIC analysis. Patient-reported satisfaction was also assessed at enrolment and at each repeat injection of goserelin. The secondary health outcomes were the median duration of castrate testosterone and the level of PSA.

**Effectiveness results**
The mean physical component summary scores were 68.2 versus 73 for enrolment versus control, (p=0.12), 68.2 versus 77 for enrolment versus crossover, (p=0.01), and 68.2 versus 71 for enrolment versus completion, (p=0.18).

The mental component summary score of the SF-36 remained unchanged throughout the study duration.

The sexual function domain of the EPIC was worse when the baseline scores were compared with completion scores, (p=0.05). However, the patients reported no significant bother from this decrease in sexual function at enrolment (3.3) versus completion (3.2), (p=0.89).

The hormonal domain score was stable at enrolment (82.6) versus completion (79.5), (p=0.41).

A significant increase in patient satisfaction was reported at crossover and maintained throughout study completion, (p=0.03).

The median duration of castrate testosterone was 5.5 months (mean: 6, range: 3.5 - 10).

The forward stepwise regression showed that a longer duration of castrate testosterone was significantly correlated with lower pretreatment serum testosterone and smaller body mass index.

**Clinical conclusions**
Short-term overall health-related quality of life and patient satisfaction were significantly improved over baseline measurements.

**Measure of benefits used in the economic analysis**
The author did not develop a summary benefit measure. A cost-consequences analysis was therefore conducted.

**Direct costs**
Only the direct medical costs were included in the analysis. Discounting was not carried out since the costs were incurred in less than 2 years. The direct costs included the cost per assay for PSA and testosterone including the phlebotomy charge, and the patient charge for 10.8 mg goserelin. Resource data were recorded from the Ohio NHS EED.
Medicare/Center Medicare Services reimbursement for the cost of goserelin dose, and were derived from the fees charged by the laboratory foundation at the setting for the cost per assay. The costs and the quantities were not reported separately. The average calculated yearly costs per patient, for dosing according to the manufacturer's recommendations or the serum testosterone method, were reported. The price year was not reported, and nor were the dates to which the resource data related.

**Statistical analysis of costs**
A statistical analysis of the cost parameters was performed using the Kendall matched pair and 2-sample Student t-tests.

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

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analysis was carried out.

**Estimated benefits used in the economic analysis**
Not applicable.

**Cost results**
The average yearly cost per patient was $7,315.80 with the control strategy and $3,972.60 with the experimental strategy, (p<0.001).

**Synthesis of costs and benefits**
The author did not produce a summary measure that combined the costs and effectiveness.

**Authors' conclusions**
The health-related quality of life was improved in the short term when using testosterone as the trigger to re-dose goserelin (10.8 mg) in patients with prostate cancer on androgen suppression therapy. In addition, the cost of care was decreased with no loss in the quality of care or patient satisfaction.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparator, the same LH-RH dose given to all patients, was justified on the grounds that it represented the current method used for patients with prostate cancer on androgen suppression therapy in the author's setting. You should consider whether this is a widely used health technology in your own setting.

**Validity of estimate of measure of effectiveness**
The quality of life was assessed through two validated questionnaires and full details on the scoring method were reported. In addition, the questionnaires were administered by a third-party assistant, which may help limit the bias. However, bias will still be present due to the nature of the study. Power calculations were not reported and the small study sample increases the possibility that the results were obtained by chance. The crossover nature of the study could lead to problems when identifying the results of each separate treatment. In addition, no washout period was reported, although it was implied that there was a time lag between treatments.
Validity of estimate of measure of benefit
The author did not derive a summary measure of health benefit.

Validity of estimate of costs
The perspective adopted for the economic analysis was not specifically stated, although it is likely to have been that of the health care system. Hence, it is unclear whether any relevant costs were omitted from the analysis. The cost estimates were specific to the Ohio Medicare Services reimbursement or University hospital of Cleveland. Thus, the results provided in this article cannot easily be generalised to other settings or to other countries. The average unit costs were reported, but the resource quantities and price year were not. These facts will limit the generalisability of the results obtained. Given the fact that the costing analysis was so specific, some attempt to improve generalisability would have been useful. Sensitivity analyses of the quantities and prices were not conducted. Discounting was unnecessary since all the costs were incurred during 18 months.

Other issues
The author did not compare the findings with those from other studies. In addition, the generalisability of the results to other settings or countries was not discussed. The author did not appear to have presented the results selectively. The study enrolled patients with prostate cancer on androgen suppression therapy and this was reflected in the author’s conclusions. The author reported two further limitations of the study. First, the potential for androgen flair at re-dosing (referred to as the acute-on-chronic effect). Second, the small number of patients (n=21). Hence, the results in terms of the health-related quality of life of patients investigated at 3 months, at crossover and at 18 months, should be interpreted with caution.

Implications of the study
The findings of the study continue to validate depot LH-RH agonist dosing based on serum testosterone. The use of serum testosterone to guide re-dosing has additional advantages in monitoring the pituitary-gonadal response to LH-RH agonist therapy.

Source of funding
None stated.

Bibliographic details

PubMedID
12478147

DOI
10.1097/01.ju.0000041413.30355.47

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM
MeSH
Adult; Aged; Aged, 80 and over; Androgen Antagonists /administration & dosage /adverse effects; Antineoplastic Agents, Hormonal /administration & dosage /adverse effects; Cross-Over Studies; Delayed-Action Preparations; Gonadotropin-Releasing Hormone /agonists; Goserelin /administration & dosage /adverse effects; Health Status; Humans; Injections; Male; Middle Aged; Patient Satisfaction; Prospective Studies; Prostate-Specific Antigen /blood; Prostatic Neoplasms /blood /drug therapy; Quality of Life; Surveys and Questionnaires; Testosterone /blood

AccessionNumber
22003000129

Date bibliographic record published
31/12/2003

Date abstract record published
31/12/2003