Optimization of peripheral blood stem cell collection by leukopheresis: interaction between economic and clinical assessment of an innovation


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
Collecting peripheral blood stem cells (PBSC) using central venous access through a catheter (CVA) or peripheral venous catheter access (PVA) for autologous transplantation in cancer patients with nonleukemic malignant diseases.

Type of intervention
Treatment and supportive care.

Economic study type
Cost-effectiveness analysis.

Study population
Cancer patients with non-leukemic malignant diseases, who were to undergo autologous transplantation.

Setting
Hospital. The economic study was carried out in France.

Dates to which data relate
Effectiveness and resource use data were collected between January 1992 and April 1994. The price year was 1995.

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

Link between effectiveness and cost data
Costing was prospectively performed on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not used to determine the sample size. The study sample consisted of 149 patients undergoing bone marrow harvest (n=79) with a median age of 44 years (range: 16 - 64) or PBSC collection (n=70) with a median age of 44 years (range: 16 - 64). The PBSC collection with CVA was performed in 10% of patients.

Study design
This was a prospective cohort study, carried out in a single centre. The duration of the follow-up was until discharge. No loss to follow-up was reported. The bone marrow harvest involved 4 hours under general anaesthesia and 2 days of hospitalisation, while the PBSC collection protocol required three leukophereses (about 4 hours each) and three
consecutive days with either CVA or PVA procedures.

**Analysis of effectiveness**
The principle used in the analysis of effectiveness (intention to treat or treatment completers only) was not explicitly specified. The clinical outcome reported in the paper was the proportion of patients not reaching the target of the cell product collected (in terms of mononuclear cells ($2 \times 10^8$/kg) for bone marrow harvest and CD34+ cells ($3 \times 10^8$/kg) for PBSC collection) and undergoing a second procedure. The patient groups were found to be comparable in terms of diagnosis, age, sex, and time between diagnosis and collection.

**Effectiveness results**
33% of patients in the bone-marrow harvest group did not reach the target of $2 \times 10^8$/kg mononuclear cells and underwent a second procedure. 42% of the PBSC group (undergoing three leukophereses) failed to reach the target of $3 \times 10^8$/kg CD34+ and underwent a second collection cycle. According to an iterative PBSC procedure performed, two leukophereses would have been enough for 36% of patients who underwent three leukophereses to reach the $3 \times 10^8$/kg CD34+ threshold. In this iterative procedure the collection of CD34+ cells was not conducted according to a predetermined number of leukopheresis sessions, instead the sessions were continued until an a priori number of CD34+ had been collected.

**Clinical conclusions**
Aside from improving supportive care, no demonstration yet exists that the use of PBSC improves the overall outcome and survival of cancer patients. Although the substitution was already effective, neither the optimal cell dose to collect for PBSC transplantation nor the PBSC collection technology itself has been standardised, and as a result, a lot of variation in procedure has existed from centre to centre.

**Measure of benefits used in the economic analysis**
No summary benefit measure was identified in the economic analysis. The authors undertook a form of cost-minimisation analysis but the criterion of equivalent effectiveness was not easy to demonstrate due to the different methods of determining effectiveness for the intervention and comparator.

**Direct costs**
Costs were not required to be discounted due to the short time frame of the study. Quantities of resource use were not reported separately from the costs. Cost items were reported separately. The cost analysis covered the costs of hospitalisation, equipment (with an 8% depreciation rate), consumable supplies, laboratory tests, staff, cell treatment, and G-CSF stimulation. The perspective adopted in the cost analysis was that of the hospital. Resource use data was mainly obtained from detailed economic observations in the study institution. True costs were estimated instead of hospital charges. 1995 price data were used.

**Statistical analysis of costs**
The least-square method was employed to estimate polynomial fit of the iterative PBSC collection cost.

**Indirect Costs**
Not considered.

**Currency**
French francs (Ffr). A conversion to US dollars ($) was carried out.
Sensitivity analysis
One-way sensitivity analysis was conducted on the unit cost of stem cell collection (involving the quantity of blood products consumed, the operating room length of stay, and the recovery room length of stay) and the percentage of patients requiring a CVA. The threshold values in terms of CD34+ cells were detected for the iterative procedure to become less costly than bone marrow harvest.

Estimated benefits used in the economic analysis
Not applicable. The reader is referred to the effectiveness results reported above.

Cost results
The total unit costs of stem cell collection procedures were $2,542 for two leukophereses with PVA, $3,483 for two leukophereses with CVA, $3,464 for three leukophereses with PVA, $4,803 for two leukophereses with CVA, and $3,118 for the bone marrow harvest. The bone-marrow harvest group had a mean cost of $4,146 including the cost of harvest failures versus $5,113 for the three systematic leukophereses collection. It was further shown in an iterative simulation that the cost of PBSC collection was mainly affected by the CD34+ threshold.

Synthesis of costs and benefits
Costs and benefits were not explicitly combined, but the threshold values in terms of CD34+ cells were detected for the iterative procedure to become less costly than bone marrow harvest. The threshold value for the percentage of patients requiring a CVA having a value of 0% was 2 x 10^8/kg CD34+ and 30% was 1.5 x 10^8/kg CD34+.

Authors' conclusions
One consequence of the study was to demonstrate that an iterative collection protocol (stopping leukophereses sessions as soon as the threshold was reached) was an efficient way of minimising cost. The case of PBSC suggests that ongoing economic evaluation should start as early as possible. Throughout the research and development process, economic evaluations can contribute to innovation development, can help predict subsequent diffusion of the technology over time, and can participate in the evolution of clinical utilisation and costs.

CRD COMMENTARY - Selection of comparators
A justification was given for the choice of the comparator. It was the routine procedure in the context in question in the study institution at the time of the study. You, as a database user, should consider whether this is a widely health technology in your own setting.

Validity of estimate of measure of benefit
The internal validity of the effectiveness results cannot be guaranteed due to the inherent limitations of the study design. The study was put forward as a cost-minimisation analysis but the necessary criterion of equal effectiveness was not clearly demonstrated. The authors pointed to the difficulties of making comparisons between the two techniques given that the technical criterion for assessing the quality of cell product was not the same.

Validity of estimate of costs
Quantities were not reported separately from the costs. Adequate details of the methods of cost estimation were given.

Other issues
The authors' conclusions appear to be justified given the uncertainties tackled in the sensitivity analyses. The issue of generalisability to other settings was not fully addressed although appropriate comparisons were made with other studies. It should be noted that the use of PSBC collection has been shown to generate less pain and anxiety for patients, a fact which might have been captured by means of a cost-utility analysis.
Implications of the study
The iterative protocol has ultimately been adopted in most French cell therapy units. Additional studies about the impact of alternative priming protocols on PBSC collection cost are required.

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