Selective high dose gamma-globulin treatment in Kawasaki disease: assessment of clinical aspects and cost effectiveness.

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 health technology studied was selective high-dose intravenous gamma-globulin plus aspirin treatment. The comparator was no high-dose intravenous gamma-globulin treatment.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with acute Kawasaki disease (KD) who had no coronary artery complications on admission.

Setting
The setting was hospital. The economic analysis was carried out in Japan.

Dates to which data relate
Effectiveness, resource use, and cost data were collected between January 1991 and December 1995. The price year was not reported.

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

Link between effectiveness and cost data
The costing was carried out prospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Patients were assigned to the 2g group (n=72), the 400mg group (n=73), or no IVGG treatment (n=58). The patients were selected when they were admitted to the hospital. The age of patients in months was 23.9 in the 2g group, 22.0 in the 400mg group, and 26.1 in the no IVGG group. The number of days of illness was 6.1 in the 2g group and 6.0 in the 400mg group before start of IVGG treatment. No power calculations were reported.

Study design
This was a prospective randomised controlled trial and cohort study carried out in a single centre. Patients were randomly assigned to one of the two IVGG groups by means of randomisation stratified according to age, gender, and illness days. Patients who scored three or less on Harada’s score received no IVGG treatment. Patients were followed up until discharge. No patient was lost to follow-up.

Analysis of effectiveness
The analysis of the clinical study was based on intention to treat. The primary health outcomes used were: development of coronary artery aneurysms (CAAs), duration of fever, occurrence of chills with fever, hypotension, nausea, urticaria and pruritus. Significant differences were found between the IVGG group and the non-IVGG group in terms of age at onset of KD, white blood cell count, platelet count, C-reactive protein, haematocrit and albumin levels.

Effectiveness results
The effectiveness results were as follows:

The rate of CAAs in the 2g group (1.39%) was lower than in the 400mg group (9.59%; p=0.03).

The duration of high fever, bilateral injected conjunctiva, changes in the oral cavity, cervical lymphadenitis and changes in the extremities after IVGG treatment in the 2g group were shorter than in the 400mg group, (p<0.05).

The total duration of fever was shorter in the non-IVGG group (6.7 days) than in the IVGG groups (2g group, 7.5 days, p<0.05; 400mg group, 9.2 days, p<0.001). Both the total duration of fever and the fever duration after IVGG treatment in the 2g group were shorter than in the 400mg group (p<0.01).

The number of hospital days for the non-IVGG group (11 days) was less than for the 2g group (13.1 days, p<0.05) and the 400mg group (15.9 days, p<0.001). The number of hospital days for the 2g group was less than that for the 400mg group (p<0.05).

The onset of desquamation after IVGG treatment in the 2g group (4.6 days of illness) was earlier than in the 400mg group (5.5 days; p=0.021).

Duration of positive C reactive protein in the 2g group (8.9 days) was shorter than in the 400mg group (11.2 days; p=0.045).

The maximum white blood cell count in the 2g group (11461) was lower than in the 400mg group (13141; p=0.007).

The minimum haematocrit in the 2g group (32.04) was higher than in the 400mg group (30.47; p=0.01).

The maximum platelet count in the 2g group (62.14) was lower than in the 400mg group (69.22; p=0.043).

Clinical conclusions
"The single 2g/kg treatment had a clear advantage over the 5-day 400mg/kg per day therapy with lower frequency of coronary artery complications and better clinical progress."

Measure of benefits used in the economic analysis
The authors did not report a summary health benefit and left clinical outcomes disaggregated. Hence, a cost-consequences analysis was conducted.

Direct costs
Direct costs were not discounted due to the short time horizon of the study (less than one year). Quantities and costs were not reported separately. Direct costs related to charges of hospitalisation, the cost of IVGG and aspirin, several laboratory examinations, chest X-ray, electrocardiogram and echocardiography, charges for catheterisation and
selective coronary angiograms as required. The quantity/cost boundary adopted was that of the hospital. The source of the cost data was not reported. The price year was not reported.

Statistical analysis of costs
The student's t-test was used to compare costs between treatment groups.

Indirect Costs
Indirect costs were not included.

Currency
Japanese Yen (¥) and US dollars ($).

Sensitivity analysis
No sensitivity analyses were reported.

Estimated benefits used in the economic analysis
See effectiveness results above.

Cost results
Total costs for the non-IVGG group (¥238,000 or $1,904) were less than those for the 2g group (¥631,000 or $5,048; p<0.001) or those for the 400mg group (¥696,000 or $5,568; p<0.001).

Synthesis of costs and benefits
The authors did not combine cost and health benefit measures into a cost-effectiveness ratio as they conducted a cost-consequences study.

Authors' conclusions
The authors argued that the single 2g/kg treatment had a clear advantage over the 5-day 400mg/kg per day therapy with lower frequency of coronary artery complications, better clinical progress, and lower medical costs.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used, namely differing dosage levels for those meeting the Harada selection threshold adopted. You, as a user of the database, should decide if these health technologies are relevant to your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a prospective randomised controlled trial, which was appropriate for the study question and which should have high validity. The authors did not show whether or not the study sample was representative of the study population, although they did report some demographic characteristics which assists in determining this. The groups were shown not to be comparable at analysis and the authors did not account for this in the analysis.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. The analysis was therefore a cost-consequences study.
Validity of estimate of costs
Good features of the cost analysis were that all relevant direct cost categories were included and statistical analyses were conducted. However, the price year was not reported, which makes it difficult to replicate the cost results in other settings. The authors did not conduct sensitivity analyses on quantities or costs, which may limit the generalisability of the results. Some of the cost data were based on charges.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, and addressed the issue of generalisability to other settings by discussing the impact of variations in the cost of IVGG on choice of treatment. The authors did not seem to present their results selectively. The study considered patients with acute KD and this was reflected in the authors’ conclusions. The authors did not choose a summary measure of health benefit, which makes it difficult to compare the results with those of similar health technologies.

Implications of the study
The authors argued that this study provides evidence that Harada’s score is reliable for selecting which patients should be treated with IVGG. However, in a country where the high dose of IVGG is not so expensive, to apply this method to all patients may not be effective for the earlier improvement from acute symptoms. The authors also stated that it is effective to use a single 2g/kg gamma-globulin dose on the first day in combination with daily ASA for acute KD if Harada’s score is four or more.

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