Treatment, outcome, and cost of care in children with idiopathic thrombocytopenic purpura

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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
Four different treatments for children with idiopathic thrombocytopenic purpura (ITP) were investigated. The interventions were anti-D immune globulin (IG), intravenous immune globulin (IVIG), steroids and observation.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised children with ITP who were less than 18 years of age. Children with thrombocytopenia from other causes (i.e. congenital, bone marrow failure, or systemic diseases) were excluded from the analysis.

Setting
The study 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 derived from medical records of children seen between January 1997 and April 2001. The price year was not reported.

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

Link between effectiveness and cost data
The costing was undertaken retrospectively on 102 patients from the patient sample used in the effectiveness study.

Study sample
No sample size was determined in the planning phase of the study. In addition, no power calculations were performed retrospectively. Two hundred and forty-seven consecutive patients were identified from the hospital billing service (via the ICD-9 code for ITP) and from the records of the haematology clinic. From these, 201 medical records were available for review, but 15 patients were excluded because of thrombocytopenia from other causes. Hence, 186 medical records (95 male records, and 91 female records) were reviewed. Of these, 60 (32.2%) patients were treated with anti-D IG, 42 (22.6%) with IVIG, 42 (22.6%) with steroids, and a further 27 (14.5%) were observed. The authors did not report the mean age and gender distribution for each of the four groups.
Study design
The study was based on a retrospective cohort study of patients treated at a single institution. It would appear that the patients were followed up for less than one year. There was no loss to follow-up since this was a retrospective study. No blinded assessment was reported.

Analysis of effectiveness
All the patients included in the study were accounted for in the analysis. The primary health outcomes used were:

- the time to reach platelet counts of $20 \times 10^9$/L or more;
- the proportion of patients achieving platelet counts of $20 \times 10^9$/L or more by day 7;
- the proportion of patients being re-treated; and
- the side effects from treatment.

The patient groups were not comparable at analysis. Patients who received IVIG had more bleeding, including serious bleeds at diagnosis, ($p=0.014$). The median platelet count ($x \times 10^9$/L) at presentation was 5, 6 and 11 for patients treated with anti-D IG, IVIG and steroids, respectively. The children that were observed had a median platelet count of 47 $x10^9$/L at diagnosis.

Effectiveness results
The median number of days to reach platelet counts of $20 \times 10^9$/L or more was 4 (range: 1 - 19) for patients in the anti-D IG group, 3 (range: 1 - 200) for patients in the IVIG group, and 6 (range: 2 - 34) for patients in the steroids group. There was no difference in time to reach platelet counts of 20,000, 50,000 or 150,000, ($p=0.327$, $p=0.802$ and $p=0.772$, respectively). The authors did not report the results for the observation group as most of the patients had platelet counts in excess of $20 \times 10^9$/L at diagnosis.

The proportion of patients achieving platelet counts of $20 \times 10^9$/L or more by day 7 was 88% in the anti-D IG group, 78% in the IVIG group and 93% in the steroids group. The authors did not report the results for the observation group as most of the patients had platelet counts in excess of $20 \times 10^9$/L at diagnosis.

Platelet recovery during the first week did not differ, except that IVIG raised the platelet counts significantly higher than anti-D IG on day 1, ($p=0.018$).

The proportion of patients requiring re-treatment was 36.6% in the anti-D IG group, 59% in the IVIG group, 50% in the steroids group and 33% in the observation group. The IVIG group had a higher incidence of re-treatment in comparison with the anti-D IG group, ($p=0.0137$) and observation group, ($p=0.0192$).

Side effects from treatment were reported in 21.6% of the patients and were most commonly observed in patients receiving steroids. Sixty-two per cent of patients receiving steroids reported side effects, compared with 31% receiving IVIG and 11.6% receiving anti-D IG. Most side effects were mild and included gastritis, weight gain, sleep disturbances, moodiness, and fatigue in those receiving steroids.

Clinical conclusions
The authors concluded that there were no significant differences in time to reach platelet counts of $20 \times 10^9$/L or more across the different treatment groups.

Measure of benefits used in the economic analysis
As the outcome results suggested that the treatments were similar, the analysis should be considered a cost-minimisation analysis.
Direct costs
The direct costs included in the analysis were those to the patients or their families. Such costs were in the form of physician and hospital charges. Charges generated for each patient from their first clinic encounter or hospitalisation were obtained from the physician and hospital billing services. Charges were available for 102 of the 186 patients included in the effectiveness study. Charges for drugs administered as treatment for ITP were included in the hospital charges. The authors had to predict charges for laboratory tests done on the first visit, as the pathology billing service was unable to provide such information. In the same way, charges were calculated for the first re-treatment in those patients where available. In this case, of the 44 patients receiving a second course of therapy, charges were available for only 25 patients. It would appear that the costs were incurred during less than one year, although this was not explicitly reported. Therefore, discounting would not appear to be necessary. The price year was not reported. The median costs for each treatment group were reported.

Statistical analysis of costs
The authors reported the median charges, together with a range of charges. An analysis of variance was used to compare the charges in the four treatment groups.

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

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analyses were performed.

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

Cost results
The median charges were $3,918 (range: 833 - 8,389) for the anti-D IG group, $4,699 (range: 0 - 9,517) for the IVIG group, $4,268 (range: 362 - 3,995) for the steroids group and $1,815 (range: 367 - 7,639) for the observation group.

The authors reported that there were no statistically significant differences in hospital charges between patients treated with anti-D IG and IVIG for the first episode of treatment.

Charges for the IVIG group were significantly higher than those for the steroid and observation groups, while charges for the anti-D IG group were higher than those for the observation group, (p<0.005). After excluding the actual drug charges, the patients in the IVIG group had a statistically higher charge ($2,121) than patients in the anti-D IG group ($1,070), (p<0.005).

There were no significant difference between the anti-D IG, IVIG and steroid groups when the initial treatment and first re-treatment charges were combined. The observation group remained least expensive.

Synthesis of costs and benefits
Not relevant since a cost-minimisation analysis was conducted.

Authors' conclusions
The outcome in childhood idiopathic thrombocytopenic purpura (ITP) was similar, regardless of initial treatment (anti-D immune globulin, intravenous immune globulin, steroids, or observation). Observation was the least expensive strategy, but very few children with acute ITP were observed without treatment. There were no statistically significant differences in hospital charges between patients treated with anti-D immune globulin (IG) and intravenous immune globulin (IVIG).

CRD COMMENTARY - Selection of comparators
The authors compared four different treatment options for ITP, all of which were current practices in their own setting. You should decide if these treatment options for ITP are current practices in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a retrospective cohort study. This study design is useful in that it allowed the authors to more easily and quickly identify patients receiving each of the treatment options, and to assess the outcomes of these treatments. However, this type of study is prone to selection bias. Hence, the use of a randomised controlled trial or a prospective cohort study would have been better to determine the effectiveness of such treatment options. The study sample appears to have been representative of the study population. However, the patient groups were not shown to be comparable in factors such as the number of platelets at diagnosis, or patients suffering from bleeding at baseline. It was unclear if the authors used statistical techniques to account for these potential biases. Although the authors undertook statistical analyses to compare differences in outcome between the four treatment groups, these were not always presented. Hence, it was unclear if some differences were statistically significant or not. Further, the study sample was small, given that four groups were investigated, and it was unclear if the study was appropriately powered to detect any statistically significant differences.

Validity of estimate of measure of benefit
The authors did not derive a measure of health benefits. Since the outcome for children with ITP was similar regardless of initial treatment, the authors therefore conducted a cost-minimisation analysis.

Validity of estimate of costs
The authors analysed hospital and physician charges. Thus, the perspective adopted was that of the third-party payer (i.e. the patients' family). Charges appear to have been used to proxy hospital costs. No major costs appear to have been omitted from the analysis. The costs and the quantities were not reported separately, which will hamper the generalisability of the authors' results. Charges were derived from the authors' settings. However, for some categories, such as re-treatment and laboratory tests, these charges were predicted rather than observed. Statistical analyses of the charges were performed but, again, the results were only presented for some comparisons. The period in which the costs were incurred was not explicitly reported, but they seem to have been incurred during less than one year. If so, the costs were appropriately not discounted. The price year was not reported, which will hamper any future inflation exercises.

Other issues
The authors made appropriate comparisons of their findings with those from other small randomised and retrospective studies that also indicated that all three modalities (IVIG, anti-D IG and steroids) could increase platelet counts. The issue of generalisability to other settings was not fully addressed. However, the authors acknowledged that the study setting was tertiary care involving more complicated patients. Hence, the results may not be applicable to what is observed in the community. The authors appear to have presented their results selectively, and their conclusions did not reflect the scope of the analysis. The patient groups were not comparable at baseline, and it was unclear if statistical analyses were undertaken to control for these baseline differences. Statistical analyses for differences in outcomes were not presented for all comparisons, and it was unclear which outcome measure was the most important in the analysis.

The authors reported a number of further limitations to their study. First, the amount and severity of bleeding were difficult to quantify from the chart review. Two, several dosage regimens of steroids were used on the basis of
individual preferences. Third, follow-up platelet counts were not available in all patients at defined times. Finally, the side effects of the treatments used were not prospectively evaluated, and could have been underestimated.

**Implications of the study**
The authors reported that, as all treatments for ITP appeared effective, the data could influence management by physicians as they could choose the least expensive modality. In addition, they suggested that very large, prospective, randomised trials of observation and treatment are needed to address the role of treatment in the prevention of serious bleeding in the management of ITP.

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