Clinical and cost-effectiveness of continuous subcutaneous terbutaline versus oral tocolytics for treatment of recurrent preterm labor in twin gestations

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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
Two methods of treating recurrent preterm labour in twin gestations, continuous subcutaneous terbutaline (SQT) and oral tocolytics (PO), were examined.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The patient population comprised women with twin pregnancies who were hospitalised for recurrent preterm labour and who, following stabilisation of their acute condition, were treated as outpatients with either continuous SQT or PO.

Setting
The setting was secondary care (outpatients). The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data corresponded to women who had twin gestations between January 1992 and July 1998. The prices were standardised estimates.

Source of effectiveness data
The evidence for the final outcomes was derived from a single study.

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

Study sample
Power calculations to determine the sample size were not carried out. The study population was identified from women enrolled by their health care provider in a nationally available, outpatient, preterm labour identification programme. A total of 6,545 women with twin gestations were identified from this database. Of these, 1,208 women had experienced an initial episode of preterm labour that was treated with PO, were subsequently hospitalised for recurrence of preterm labour symptoms of less than 35 weeks' gestation, and were then stabilised and discharged to resume outpatient services. There women were either initiated on continuous SQT infusion (n=505) or they continued
on PO (n=703). Using a random number table, the two groups of patients (SQT and PO) were matched 1:1 by gestational age at hospitalisation for recurrent preterm labour. Those without a match were excluded. There were 353 patients in each arm of the trial. The inclusion criteria meant that a clearly defined group of patients participated in this study.

**Study design**
This was a retrospective matched cohort study. A random number table was used to match those who received continuous SQT with those who received continued PO by gestational age at hospitalisation for recurrent preterm labour. The authors did not explicitly state whether this study took place in a single centre or multiple centres. However, it can be assumed that it took place in a number of different centres since the patient distribution was nationwide. It would appear that the patients were followed up until the newborn left the newborn nursery. The loss to follow-up was not reported. The outcome assessment was not blinded.

**Analysis of effectiveness**
The authors did not state whether the basis of the analysis was intention to treat or treatment completers only. The primary health outcomes were:

- additional days of pregnancy gained,
- the gestational age at delivery,
- the weight at birth,
- the number of nursery days,
- the number of days spent in a neonatal intensive care unit (NICU) and
- perinatal losses.

The authors stated that, overall, women receiving continuous SQT were slightly older, more likely to be married, and experienced their first preterm labour episode 1.4 days earlier than their PO counterpart. The authors considered those receiving PO to be at a marginally increased risk due to a history of a prior preterm birth.

**Effectiveness results**
The SQT group had a higher gestational age at delivery (35.2 +/- 2.0 weeks) than the PO group (34.5 +/- 2.3 weeks), (p<0.001). The gestational age was less than 32 weeks for 6.2% in the SQT group versus 11.3% in the PO group, (p<0.001), and less than 35 weeks for 38.8% (SQT group) and 52.7% (PO group), respectively, (p<0.001).

A Caesarean delivery was had by 54.2% of the SQT group versus 50.1% in the PO group, (p=0.164).

The babies in the SQT group weighed more at birth (2,343 +/- 493 g) than those in the PO group (2,207 +/- 523 g, p<0.001). In addition, fewer babies in the SQT group weighed less than 2,500 g (61.6% versus 71.5%, p<0.001) or less than 1,500 g (4.1% versus 8.6%, p=0.001).

The total days spent in the nursery were less for babies in the SQT group (9.0 +/- 12.2) than for those in the PO group (12.9 +/-15.6), (p<0.001). The mean number of nursery days was 4 (range: 1 - 103) for the SQT group versus 7 (range: 1 - 100) for the PO group.

NICU admissions were experienced by 38.5% of the SQT group, compared with 55% of the PO group, (p<0.001). The number of days spent in the NICU was 17.3 (+/- 16.1) for the SQT group versus 20.8 (+/- 17.4) for the PO group, (p=0.009).
Clinical conclusions
The outcomes from the study showed that babies whose mothers received continuous SQT had a higher birth weight, spent fewer days in the nursery, had fewer admissions to the NICU and a shorter stay in the NICU, than babies whose mothers received PO for the treatment of recurrent preterm labour.

Modelling
The authors stated that, to evaluate the cost-effectiveness of each treatment, a model was applied in which the charges incurred for antepartum hospitalisation, outpatient services and nursery days during the study period were standardised. The type of model was not specified.

Measure of benefits used in the economic analysis
No summary measure of benefit was used. The study was therefore a cost-consequences analysis.

Direct costs
A model was applied in which the charges incurred during the study period were standardised. The analysis included antepartum hospitalisation, outpatient services, nursery days and stay in the NICU. The estimated daily cost for hospital care combined the accommodation and ancillary charges, but did not take the indirect costs into account. Physician charges and increased first-year and lifetime medical costs were not considered in the model. The amount of each resource used came from the electronic database used in the preterm labour identification programme, and from the patients' health care provider. The data were collected over six years (1992 - 1998).

Statistical analysis of costs
Not applicable.

Indirect Costs
The indirect costs were not reported.

Currency
US dollars ($).

Sensitivity analysis
Not applicable.

Estimated benefits used in the economic analysis
Not reported.

Cost results
Both the estimated mean and median total cost for a twin pregnancy experiencing recurrent preterm labour were higher in the PO group. The mean total cost was $38,152 (+/- 50,822) for the SQT group and $55,261 (+/- 60,932) for the PO group, (p<0.001). The median total cost was $17,950 (range: 3,000 - 392,500) for the SQT group and $34,470 (range: 2,810 - 404,120) for the PO group.

The nursery costs were the single largest contributor to the total pregnancy costs for both groups. The mean nursery cost was $28,296 (+/- 50,570) for the SQT group versus $45,880 (+/- 61,450) for the PO group, (p<0.001)

The second largest cost contributors were outpatient nursing for the SQT group and antepartum hospitalisation for the
PO group. The costs of outpatient nursing were $6,197 (+/- 4,172) in the SQT group versus $1,257 (+/- 1,236) in the PO group, (p<0.001). The costs of antepartum hospitalisation were $8,127 (+/- 9,039) in the PO group versus $3,660 (+/- 5,953) in the SQT group, (p<0.001).

Synthesis of costs and benefits
Not relevant.

Authors’ conclusions
The authors concluded that the improved clinical outcomes and decreased nursery utilisation suggested that outpatient continuous subcutaneous terbutaline (SQT) was cost-effective, compared with oral tocolytics (PO), for the treatment of recurrent preterm labour.

CRD COMMENTARY - Selection of comparators
The authors did not provide an explicit justification for their choice of comparator. However, it would appear that others (eight references quoted) have carried out research comparing the same two drugs. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The authors acknowledged that the retrospective, non-randomised design of this analysis, and the lack of a placebo control group, limits what may be concluded from the observations. The individuals included in the study complied with clearly defined selection criteria. However, there were some differences in the baseline maternal and obstetric characteristics. The outcomes were analysed for all women taking part in the study.

Validity of estimate of measure of benefit
The study may be regarded as a cost-consequences analysis given the lack of an explicit summary benefit measure.

Validity of estimate of costs
Physician charges and increased first-year and lifetime medical costs were not considered in the cost model. In determining antepartum charges, the authors did not include charges for hospital observation admissions of less than 24 hours. They stated that this omission may have decreased the overall estimated charges for inpatient care. Neonatal deaths were calculated at zero cost since the length of nursery stay prior to death was not consistently documented. The authors stated that, had this cost been included, it would have increased the costs, particularly in the PO group. The costs and the quantities were not reported separately. The quantities of resources used were not detailed.

The costs used in this study were estimates, but details of how these estimates were derived were not reported. A sensitivity analysis of the costs was not conducted. When costs in the model were compared with other sources, the authors concluded that their model was conservative in terms of the costs of antepartum hospitalisation, neonatal intensive care and newborn nursery. The authors recognised the additional emotional and financial burden of family separation, but no attempt was made to quantify these factors.

Other issues
The authors compared their findings with those from published studies. Their results were reported selectively. The issue of generalisability was addressed. This study examined a cohort of women with twin pregnancies hospitalised for recurrent preterm labour and this was reflected in the authors’ conclusions. The authors reported that their study was further limited by its design (retrospective, non-randomised design) and the lack of a placebo group.

Implications of the study
Not reported.

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None stated.

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