HOME UTERINE ACTIVITY MONITORING FOR SECONDARY AND TERTIARY PREVENTION OF PRETERM BIRTH

ISSUE

Blue Shield continues to receive requests for coverage of home uterine activity monitoring (HUAM) for prevention of preterm birth. These requests include HUAM for both secondary and tertiary prevention of preterm birth. Secondary prevention of preterm birth refers to high-risk patients who have not experienced preterm labor in the current pregnancy. Tertiary prevention of preterm birth refers to patients who have experienced, and being treated successfully for, preterm labor in the current pregnancy. The Medical Policy Committee on Quality and Technology is asked to review the published data regarding the efficacy and safety of this technology in clinical practice.

CURRENT BLUE SHIELD POLICY

Ambulatory monitoring of uterine activity was reviewed by the Medical Policy Committee on Quality and Technology in March, 1986, October, 1990, and February, 1997 (see previous BSC Technology Assessment, 1997). At all three meetings, the committee concluded that HUAM was investigational.

BACKGROUND

Preterm birth is associated with significant neonatal mortality and morbidity nationwide (Kalchbrenner, 2001). Preterm labor is variously defined as increased frequency of uterine contractions; documented changes in the cervix, such as dilatation or effacement; premature rupture of the membranes; and gestational age under 37 weeks. The national rate of prematurity from preterm birth approaches 11%. Despite widespread use of tocolytic agents, the preterm birth rate has actually increased over the past 30 years in the U.S. (Mauldin et al 2001).

Yet, up to 50% of patients with suspected preterm labor eventually deliver at or near term (after 37 weeks). Primary prevention of preterm delivery involves obstetrical care to reduce risk factors known to be associated with preterm birth, including smoking, alcohol and illicit drug use, depression and stress, poor nutrition, and lack of prenatal care.
BACKGROUND, continued

Secondary prevention involves identifying groups at high risk for preterm delivery and attempting early diagnosis and early treatment of preterm labor. High-risk groups include women with a history of preterm labor or preterm birth in a previous pregnancy; twin or multiple gestations; uterine anomalies; history of abortions; and exposure to diethylstilbestrol (DES). Tertiary prevention involves attempting to prolong pregnancy in women who have already experienced preterm labor in the current pregnancy. The main treatments aimed at prolonging pregnancy in those experiencing preterm labor are bed rest and medications to inhibit uterine contractions (tocolytic agents). Bedrest (usually at home) is widely recommended, though there are no studies of its efficacy in reducing adverse neonatal outcomes. Tocolytic medications include beta-mimetic agents (e.g., terbutaline) and magnesium sulfate.

Home Uterine Activity Monitoring

Assessment of the frequency of uterine contractions has been proposed as a screening method to identify pregnant women at increased risk of preterm (<35 weeks gestation) delivery, and as a diagnostic test to detect preterm labor in its earliest stages (Iams et al 2002). HUAM is intended to detect preterm labor at an early stage. The monitoring device combines a tocodynamometer (worn with the belt around the abdomen), a data recorder and a data transmitter. The patient is usually instructed to use the device daily for two one-hour periods. More than 4-6 uterine contractions per hour may signal the onset of preterm labor.

TA Criterion 1: The technology must have final approval from the appropriate government regulatory bodies.

Two HUAM devices have received FDA 510k approval. The Genesis device was approved in September, 1990, and the Healthdyne System 37, in September, 1995. Both were approved as an aid in the early detection of preterm labor among women with a history of a previous preterm birth. No HUAM devices have been approved for indications other than a history of previous preterm birth (e.g., multiple gestations).

TA criterion 1 is met.
TA Criterion 2:  The scientific evidence must permit conclusions concerning the effectiveness of the technology regarding health outcomes.


Since the last BSC review of this topic, 2 retrospective case series (Kempe et al 1997; Morrison et al 2001), 2 randomized controlled trials comparing outcomes with conventional therapies (Dyson et al 1998; Brown et al 1999) and 1 large scale observational study (Iams et al 2002) have been published.  Each of these is described below.

Outcomes assessed in the various clinical trials of HUAM have varied, but have most often included the following measures: 1) frequency of preterm birth; 2) frequency of cervical dilatation 2 cms. or less at diagnosis of preterm labor; 3) neonatal morbidity, usually expressed as frequency of admissions to neonatal intensive care unit (NICU); and 4) mean birth weight.  The health outcomes of greatest importance are neonatal morbidity and mortality.  Unfortunately, direct health outcomes related to neonatal morbidity (e.g., respiratory distress or neurological complications) or neonatal mortality have rarely been reported in published trials.  Instead, frequency of referrals to a NICU is the most pertinent measure reported; low birth weight is also considered a reliable indicator, since it correlates highly with neonatal morbidity in prior research studies.  Other outcomes (frequencies of cervical dilatation) are considered less reliable intermediate outcomes with uncertain linkage to improved neonatal outcomes.

TA criterion 2 is met.

Levels of Evidence: 1, 2,5
TA Criterion 3: The technology must improve the net health outcomes.

Early studies suggested a reduction in the incidence of preterm birth with HUAM (Morrison et al 1987; Iams et al 1987a and 1987b), but these trials were strongly criticized for their flawed design (Sachs et al 1991; Grimes et al 1992); some of these studies were identified as having biases and errors sufficient to warrant dismissing the results (Keirse et al 1993). Other trials of HUAM enrolled a limited number of patients, raising the possibility of a type II error (lack of sufficient subjects to find an effect).

The previous Blue Shield Technology Assessment (BSC, 1997) concluded that meta-analysis of 8 randomized, controlled trials of HUAM for secondary prevention, and review of 4 published studies of HUAM for tertiary prevention, of preterm birth failed to show a consistent benefit among all women/all pregnancies, singleton pregnancies or twin pregnancies. There was no consistent difference in the outcomes associated with HUAM in all pregnancies in studies that controlled for the amount of nursing contact versus studies than did not do so. Evidence that HUAM affected important health outcomes such as neonatal morbidity and mortality was considered to be lacking.

The first randomized controlled trial published since the Committee last reviewed this topic concerned secondary prevention of preterm labor.

Secondary Prevention

Dyson et al. (1998) randomly assigned 2422 pregnant women with known risk factors for preterm labor (including 844 women who were pregnant with twins) to receive education and one of the following: weekly contact with a nurse, daily contact with a nurse, or daily contact with a nurse and HUAM. End points included the incidence of preterm birth at <35 weeks' gestation, cervical status at the time of preterm labor, and birth weight. Results showed that there were no significant differences among the groups in the incidence of birth at <35 weeks (14% in the weekly-contact group, 13% in the daily-contact group, and 14% in the home-monitoring group), in the mean amount of cervical dilatation at the time preterm labor was diagnosed (1.8 cm, 1.5 cm, and 1.4 cm, respectively), or in neonatal outcomes such as birth weights of <1500 g or <2500 g. However, daily contact with a nurse increased the mean number of unscheduled visits to obstetricians (1.2 in the weekly-contact group, 1.8 in the daily-contact group, and 2.3 in the home-monitoring group) and the proportion of women who received prophylactic tocolytic drugs (12%, 14%, and 19%, respectively). The authors concluded that women who have daily contact with a nurse, with or without HUAM, have pregnancy outcomes no better than women who have weekly contact with a nurse.
TA Criterion 3 (Secondary Prevention), continued

The other randomized controlled trial published since 1997 concerned tertiary prevention of preterm labor.

Tertiary Prevention

Brown et al. (1999) reported results of a randomized comparison of HUAM in reducing the rate of preterm birth among 162 women who had been treated in the hospital with magnesium sulfate for preterm labor. Overall, 82 women were prospectively randomized to the monitored group and 80, to an unmonitored control group. Other than monitoring, all women received identical prenatal follow-up, including daily perinatal telephone contact and oral terbutaline therapy. Outcome comparisons included incidence of preterm birth at <35 weeks' gestation, readmissions for recurrent preterm labor, and observations lasting <24 hours. Results showed that gestational ages at delivery were similar in the monitored and control groups. There was no significant difference in the overall rate of preterm delivery at <35 weeks' gestation between the monitored group and the control group (10.9% vs. 15.0%, p=N.S.). There was no difference in the numbers of women with readmissions or hospital observation lasting <24 hours. Compliance with monitoring did not significantly differ for women who were delivered at <35 weeks' gestation. The authors concluded that there was no reduction in the likelihood of preterm delivery at <35 weeks' gestation from the addition of HUAM to the outpatient management regimens of women treated for preterm labor.

Finally, a recent observational study of HUAM may help to explain why the preponderance of evidence from the published randomized trials of HUAM indicates that it does not reduce the rate of prematurity.

Iams et al. (2002) assessed the frequency of uterine contractions as a predictor of the risk of spontaneous preterm (<35 weeks gestation) delivery. Enrolled women had singleton pregnancies of 22-24 weeks gestation and either a history of spontaneous preterm delivery or bleeding in the second trimester of the current pregnancy, both risk factors for preterm delivery. Enrollees were give a uterine contraction monitor to use at home to record contraction frequency twice daily on 2 or more days per week from study enrollment to delivery or 37 weeks of gestation.
TA Criterion 3 (Tertiary Prevention), continued

The investigators obtained 34,908 hours of successful monitoring recordings from 306 women. Although more contractions were recorded from women who delivered at <35 weeks than from women who delivered at ≥35 weeks, the authors could identify no threshold frequency that effectively identified women who delivered preterm infants. At 22-24 weeks gestation, the sensitivity of a maximal frequency of evening contractions of ≥4 per hour was only 9% and the positive predictive value, only 25%. At 27-28 weeks, the sensitivity and PPV were only 28% and 23%, respectively. Although the likelihood of preterm delivery rose with an increased frequency of uterine contractions, this measurement had low sensitivity and low predictive value for impending preterm delivery in women at increased risk for preterm delivery. There was only a small difference in the frequency of contractions between women who subsequently delivered a preterm infant and those who gave birth at term. The authors concluded that ambulatory monitoring of uterine contractions was not a clinically useful predictor of preterm delivery and thus explained the failure of this method to reduce the risk of prematurity in clinical practice.

TA Criterion 4: The technology must be as beneficial as any established alternatives.

The available alternatives to HUAM for monitoring of women who are at high-risk for preterm labor or women who have previously experienced preterm labor during the current pregnancy are intensive (daily) or less intensive (weekly) nursing contact and standard high-risk obstetrical care. Recent published evidence suggests that women who have daily contact with a nurse, with or without HUAM, have no better pregnancy outcomes than women who have weekly contact with a nurse (Dyson et al 1998).

Measures undertaken to stop preterm labor once it has started have included bed rest, intravenous hydration, and tocolytic agents such as terbutaline and magnesium sulfate. Current evidence does not support improved pregnancy outcomes with these therapies (Maxwell, 2001). The U.S. Preventive Services Task Force report (1993) concluded that the use of tocolytic agents to reduce uterine contractions produced only a slight (1–2 day) prolongation of pregnancy. Long-term tocolysis, usually with oral agents, has not been shown to prolong pregnancy or improve perinatal outcomes (Lockwood, 2002). Lockwood concludes, “Our limited ability to stop preterm labor once it has started is even more disheartening than our frustrated efforts to predict it.”
**TA Criterion 5:** The improvement must be attainable outside the investigational setting.

HUAM has been studied in multiple centers. Whether HUAM improves health outcomes for secondary or tertiary prevention of preterm birth has not been unequivocally demonstrated in the investigational setting. Whether HUAM will improve health outcomes in the community setting under conditions of usual medical practice remains to be demonstrated.

**RECOMMENDATIONS OF OTHERS**

**Blue Cross Blue Shield Association (BCBSA)**

The BCBSA last reviewed this topic in October, 1996 and concluded that HUAM did not meet BCBSA TEC criteria.

**American College of Obstetricians-Gynecologists (ACOG)**

In October 2001, ACOG published a position statement which reads as follows:

“At least 13 randomized controlled trials examining the efficacy of HUAM have published results. The studies vary in design, criteria for inclusion of patients, and measurements of endpoints and outcomes. These differences make comparisons difficult. Furthermore, many of these studies had limitations with their research design, including sample size (power) or numbers of patients, that preclude reaching conclusions about the usefulness of HUAM. Results vary, with some trials reporting no difference and some reporting a difference in outcome in monitored and unmonitored women. The largest study involved 2422 women at risk and showed no improvement in outcome.

Earlier studies that showed a reduction in the incidence of preterm birth with HUAM have been criticized for their flawed design; some studies have been identified as having biases and errors sufficient to warrant dismissing the results. The U.S. Preventive Services Task Force performed an independent review and concluded the device was not effective. Although the U.S. Food and Drug Administration has approved a HUAM device for women with a prior preterm birth, there is no demonstrated role for HUAM in the prevention of preterm birth. Data are insufficient to support a benefit from HUAM in preventing preterm birth; therefore this system of care is not recommended.” (ACOG, 2001).
U.S. Preventive Services Task Force

The U.S. Preventive Services Task Force reviewed the literature regarding HUAM in 1993 and concluded in a policy statement that there was insufficient evidence to recommend for or against the use of HUAM.

CONCLUSION

Although ambulatory monitoring of uterine contractions continues to be employed by some practitioners, measurement of the frequency of uterine contractions has not proven useful in either secondary or tertiary prevention of preterm delivery in multiple randomized clinical trials. Home uterine activity monitoring has also not been shown to significantly decrease neonatal complications. Recent data suggest that measurement of the frequency of uterine contractions has low sensitivity and low predictive value for impending preterm delivery, even in women at increased risk for preterm delivery.

TA criteria 3-5 are not met.

RECOMMENDATION

It is recommended that home uterine activity monitoring does not meet Blue Shield TA criteria.

Committee approval as recommended.

June 12, 2002
REFERENCES


REFERENCES, continued


REFERENCES, continued


