Cardiotocography only versus cardiotocography plus ST analysis of fetal electrocardiogram for intrapartum fetal monitoring: a Swedish randomised controlled trial

Isis Amer-Wåhlin, Charlotte Hellsten, Håkan Norén, Henrik Hagberg, Andreas Herbst, Ingemar Kjellmer, Håkan Lilja, Claes Lindoff, Maivi Månsson, Laila Mårtensson, Per Olofsson, Anna-Karin Sundström, Karel Marsál

Summary

Background Previous studies indicate that analysis of the ST waveform of the fetal electrocardiogram provides information on the fetal response to hypoxia. We did a multicentre randomised controlled trial to test the hypothesis that intrapartum monitoring with cardiotocography combined with automatic ST-waveform analysis results in an improved perinatal outcome compared with cardiotocography alone.

Methods At three Swedish labour wards, 4966 women with term fetuses in the cephalic presentation entered the trial during labour after a clinical decision had been made to apply a fetal scalp electrode for internal cardiotocography. They were randomly assigned monitoring with cardiotocography plus ST analysis (CTG+ST group) or cardiotocography only (CTG group). The main outcome measure was rate of umbilical-artery metabolic acidosis (pH <7·05 and base deficit >12 mmol/L). Secondary outcomes included operative delivery for fetal distress. Results were first analysed according to intention to treat, and secondly after exclusion of cases with severe malformations or with inadequate monitoring.

Findings The CTG+ST group showed significantly lower rates of umbilical-artery metabolic acidosis than the cardiotocography group (15 of 2159 [0·7%] vs 31 of 2079 [2·%, relative risk 0.47 [95% CI 0.25–0.86], p=0.02) and of operative delivery for fetal distress (31 of 2079 [2%] vs 227 of 2447 [9%], 0.83 [95% CI 0·69–0·99], p=0·047) when all cases were included accounting for intention to treat, and secondly after exclusion of cases with severe malformations or with inadequate monitoring.

Interpretation Intrapartum monitoring with cardiotocography combined with automatic ST-waveform analysis increases the ability of obstetricians to identify fetal hypoxia and to intervene more appropriately, resulting in an improved perinatal outcome.

Lancet 2001; 358: 534–38

Introduction

Since the introduction of intrapartum electronic fetal monitoring, intrapartum death has become a rare event, and neonatal morbidity as manifested by neonatal seizures has been reduced. However, electronic fetal monitoring has had little effect on long-term outcome, and clinical management of labour on the basis of this technique still causes concern. Moreover, some have claimed that the method results in an unnecessarily high rate of caesarean deliveries. Although most cases of fetal asphyxia are preceded by abnormalities detected by electronic fetal monitoring, similar abnormalities are not uncommon in cases that have a normal outcome, and misinterpretation of traces is often a contributing factor in cases of asphyxia. Results of fetal blood sampling can aid the interpretation of the cardiotocogram, but blood sampling requires dexterity and expertise. Hence, there is interest in the development of new methods for intrapartum fetal surveillance.

Analysis of the ST waveform of the electrocardiogram provides valuable information on how the adult myocardium responds to an increased workload during exercise. In fetal lambs exposed to hypoxia, an increase in the ST segment and T wave, quantified by the ratio of T wave to QRS amplitude (T/QRS), has been associated with a catecholamine surge, activation of β adrenoceptors, myocardial glycogenolysis, and metabolic acidosis—ie, the physiological response expected in hypoxia. In growth-retarded animal fetuses, the most common change was instead an ST-segment depression, probably as a consequence of endocardial cell hypoxia and an insufficient ability to compensate for oxygen depletion by use of anaerobic metabolism. These experimental observations prompted the development of a cardiotocography plus ST-waveform analyser (STAN). In a randomised, controlled trial, intrapartum monitoring with cardiotocography alone was compared with cardiotocography in combination with ST-waveform analysis in 2400 cases. A 46% reduction in operative interventions for fetal distress occurred when ST analysis was applied. The study also highlighted the need for technical improvements to identify an ST-segment depression that could be overlooked if only the T/QRS ratio is calculated, and the importance of staff training.

A new cardiotocography plus ST-waveform recorder has been developed. This instrument uses digital signal-processing techniques and automatic assessment of ST changes by means of an “expert system”, and has been assessed in observational clinical studies. We aimed to test the hypothesis that, compared with cardiotocography alone, intrapartum monitoring of term fetuses with cardiotocography and automatic ST-waveform analysis results in reduced rates of operative deliveries for fetal distress and metabolic acidosis at birth.

Participants and methods

Participants

The trial took place from Dec 1, 1998, to June 4, 2000, at three major labour wards in Sweden: University Hospital...
Lund (2829 deliveries, perinatal mortality 8-2 per 1000, caesarean section rate 12-5% [in 1999]), University Hospital Malmö (3220, 4-0 per 1000, 13-0%), and Sahlgrenska University Hospital, Gothenburg (4229, 6-5 per 1000, 14-7%).

Eligible participants were women in active labour at more than 36 completed gestational weeks, with singleton fetuses in the cephalic presentation, and about whom a clinical decision had been made to apply a fetal scalp electrode for continuous internal cardiotocography. At all three centres, internal monitoring was the preferred method of surveillance in high-risk pregnancies, women with suspicious or abnormal external cardiotocography, induced or oxytocin-augmented labour, meconium-stained amniotic fluid, or epidural analgesia.

Research ethics committees at the respective universities approved the trial, and all participating women gave their informed consent before entering the study.

Methods

Before the trial, labour-ward staff received training and 2 months' experience of using the STAN S21 fetal heart monitor (Neoventa Medical, Gothenburg, Sweden). The training consisted of lectures, written information, and multimedia-based teaching, including a simulator that displayed previously recorded cases with ST-analysis. At each centre, a research midwife was appointed to train and support staff during the trial, and to verify the data entered into a computer database. The usual labour-ward staff (more than 300 obstetricians and midwives in total) managed all women included in the trial.

The labour wards were equipped with prototypes of the STAN S21 fetal heart monitor. The instrument employs signal amplification and analogue-to-digital data conversion at 500 Hz; signal processing and data presentation are based on dedicated software that uses a real-time operating system (Phar Lap Software, Cambridge, MA, USA). Fetal heart rate, uterine activity (recorded as either external or internal tocograph), fetal electrocardiogram ST-waveform changes (T/QRS ratio and biphasic ST) are continuously displayed onscreen and printed out on paper (figure 1). Fetal electrocardiogram signals for identification of ST-waveform changes were sampled via a unipolar lead from a single spiral fetal scalp electrode. A skin electrode placed on the maternal thigh was used as reference.

Women were randomly assigned fetal monitoring by cardiotocography (CTG group) or cardiotocography with ST-waveform analysis (CTG+ST group). Randomisation was done as follows: when the STAN S21 software was started up, the first number available from a computer-generated table of random numbers was used to assign the woman being monitored to one group or the other according to whether the number was even or odd. Once a number had been used, it could not be reused. Once randomisation had taken place, the selection was fixed for 2 h in case the unit was restarted. Although no electrocardiographic information was available to delivery staff at the time of monitoring in the CTG group, fetal electrocardiogram signals were automatically stored for both groups for future analysis.

Clinical management in the CTG group was guided by cardiotocography interpretation according to guidelines produced by the International Federation of Gynecology and Obstetrics (FIGO),17 with the option of fetal blood sampling at the discretion of the obstetrician. In cases with consistently abnormal cardiotocograms, intervention was suggested. Dependent on the clinical circumstances, the intervention could be delivery, fetal blood sampling, or alleviation of a possible cause of fetal distress—eg, uterine hypertonus or maternal hypotension. In cases with scalp-blood pH lower than 7-20 or preterminal cardiotocograms, immediate delivery was always recommended.

In the CTG+ST group, clinical management was guided by cardiotocography interpretation and supported by computerised ST-waveform assessment (ST log) according to the trial protocol (table 1). The ST log automatically informed delivery staff if any of the ST events listed in the protocol occurred. Intervention, as described above for the CTG group, was indicated at the occurrence of preterminal cardiotocography, irrespective of ST change, or in instances of abnormal or intermediate cardiotocography patterns with ST events as listed in the protocol. No intervention was recommended if the cardiotocogram was normal, irrespective of the ST waveform. During the second stage of labour, immediate delivery was recommended if ST changes appeared. Fetal blood sampling was also optional in this group.

The main outcome variable was metabolic acidosis at...
birth, which was defined as a cord-artery blood pH of less than 7·05, and a base deficit in the extracellular fluid compartment (BD$_{ECF}$) of more than 12·0 mmol/L, as measured by the Sigggaard-Andersen acid base chart algorithm. The secondary outcome variable was the rate of operative deliveries (caesarean sections, or forceps or ventouse deliveries) for fetal distress. Additionally, neonatal morbidity was assessed in terms of Apgar scores at 1 and 5 min, and admissions to the neonatal intensive-care unit.

A paediatrician, who was unaware of which study group the neonate belonged to, assessed all paediatric files for babies admitted to the neonatal intensive-care unit, and judged whether there had been any signs of neonatal encephalopathy.

**Statistical analysis**

The primary analysis of outcome was done according to intention-to-treat—ie, without any exclusions. However, according to the protocol, a secondary analysis was made with the exclusion of neonates with severe malformations and inadequately monitored cases (those monitored for less than 20 min and those for whom monitoring was interrupted more than 20 min before delivery). This secondary analysis was done to assess the potential of the monitoring method. The monitor needed at least 20 min to establish a baseline T/QRS-ratio, and we judged that cases with severe malformations and those without monitoring during the last period before delivery might obscure possible associations between monitoring and outcome.

On the basis of data from the CTG group of the Plymouth trial, a power analysis indicated a requirement of 3200 cases to show a 70% reduction in the number of neonates with cord-artery metabolic acidosis, assuming a rate of 1·3%, β=0·20 and α=0·05. The trial protocol included an interim analysis after enrolment of 1600 cases, to assess the true rate of cord-artery metabolic acidosis. Because a lower rate than expected was found, a second power analysis was done to calculate the number of additional cases needed. According to the previous recruitment rate, the deadline for the study was decided. The interim analysis also revealed protocol violations, in which the recommendations to intervene were disregarded and babies with cord-artery metabolic acidosis were born. Therefore, retraining took place and these and other cases from the trial were discussed.

The results were analysed with Medcalc statistical software (version 5, Mariakerke, Belgium). χ$^2$ or Fisher’s exact tests were used for discrete variables, and the relative risk with 95% CI was calculated.

**Results**

4966 women entered the trial, of whom 2447 were assigned to the CTG only group and 2519 to CTG+ST (figure 2). Background obstetric characteristics were similar in the two groups (table 2). 1465 (36% of all women delivered during the study period), 1514 (31%), and 1987 (33%) women were enrolled in Lund, Malmö, and Gothenburg, respectively.

The main outcome, analysed according to intention to treat, is shown in table 3. The rate of metabolic acidosis at birth was significantly lower in the CTG+ST group than in the CTG group. The number of operative deliveries for fetal distress was also significantly lower in the CTG+ST group. The rates of operative deliveries for other indications (in most cases failure to progress) did not differ significantly between the two groups. No significant differences between the groups were found regarding Apgar scores, admissions to neonatal intensive care, or neonatal encephalopathy.

There were five perinatal deaths, two caused by malformations (combined congenital heart malformation and pulmonary hypoplasia), and three related to intrapartum events. Of the three cases with metabolic acidosis at birth, two occurred in the CTG+ST group. In the first, maternal fever occurred during labour, and the CTG showed a preterminal pattern without ST-waveform changes. Caesarean section was done after an undue delay, and the baby died 36 h after birth with clinical signs of neonatal encephalopathy and sepsis. In the second case, second-stage CTG and ST changes were not recognised; the scalp electrode was disconnected during ventouse extraction for failure to progress, and a severely asphyxiated baby was delivered. In both cases, a delay of more than 20 min occurred between the end of recording and delivery. The third case occurred in the CTG group with the recorder disconnected for unknown reasons 2 h and 11 min before an operative vaginal delivery for non-reassuring fetal heart rate. The baby was severely asphyxiated at birth, and...
severe intrapartum hypoxia, and the number of operative delivery was capable of reducing the risk of babies being exposed to perinatal outcome. The new fetal monitoring procedure ST waveform leads to a significant improvement in our results show that monitoring of term fetuses with transcutaneous nerve stimulation for pain relief [70], or signal quality [182], technical failure [48], use of electrical min before delivery (because of poor electrocardiogram (215 cases), or monitoring was interrupted more than 20 events, including biphasic ST changes. Another difference was that our protocol stated that intervention should take place in cases with a non-reassuring or abnormal interpretation of ST changes, which highlighted significant differences between the two groups and unspecific reasons [59]). Among the excluded cases, there were no significant differences between the two groups with unspecified reasons [59]). Among the excluded cases, there were no significant differences between the two groups with unspecified reasons [59]).

Eight neonates had malformations not identified before birth. In 574 cases excluded after the primary analysis (figure 2), the duration of the recording was insufficient (215 cases), or monitoring was interrupted more than 20 min before delivery (because of poor electrocardiogram signal quality [182], technical failure [48], use of electrical transcutaneous nerve stimulation for pain relief [70], or unspecific reasons [59]). Among the excluded cases, there were no significant differences between the two groups and regard to the number of cases, operative delivery rates, cord-artery blood acid-base data, and Apgar scores.

After these exclusions, there were significantly fewer cases of metabolic acidosis in the CTG+ST group than in the CTG group, and significantly fewer operative deliveries for fetal distress, including a significantly lower rate of caesarean sections for fetal distress (table 4).

Discussion
Our results show that monitoring of term fetuses with cardiotocography and ST monitoring than with cardiotocography alone. In the Plymouth study, there was a difference that our protocol stated that intervention should take place in cases with a non-reassuring or abnormal interpretation of ST changes, which highlighted significant differences between the two groups and unspecific reasons [59]). Among the excluded cases, there were no significant differences between the two groups with unspecified reasons [59]). Among the excluded cases, there were no significant differences between the two groups and regard to the number of cases, operative delivery rates, cord-artery blood acid-base data, and Apgar scores.

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After these exclusions, there were significantly fewer cases of metabolic acidosis in the CTG+ST group than in the CTG group, and significantly fewer operative deliveries for fetal distress, including a significantly lower rate of caesarean sections for fetal distress (table 4).
towards fewer cases of low Apgar scores and neonatal encephalopathy in the CTG+ST group.

After exclusion of cases with inadequate monitoring, the differences between the study groups were more pronounced, supporting the assumption that the results were truly an effect of monitoring, and that the benefits with ST analysis might increase with further technical improvements and adequate application of the method. The successful clinical introduction of any new technology or method depends on its acceptance and appropriate application by the users.23,24 We are therefore not surprised that iterated training was necessary before the new method was fully accepted by the clinicians.

The STAN recorder analyses the fetal electrocardiogram automatically, but the method still requires interpretation of the cardiotocogram by the clinician. Naturally, intervention must be based on the results of electronic fetal monitoring in the context of the stage of labour and additional clinical information. More information is needed on fetal electrocardiogram changes in specific clinical groups—e.g., fetuses with intrauterine infection and preterm fetuses. However, for term pregnancies, our results indicate that use of cardiotocography combined with automatic ST-waveform analysis substantially increases our ability to detect fetal hypoxia, and more appropriately intervene in cases of life-threatening asphyxia.

Contributors
Karel Mars ál initiated and coordinated the study, and all investigators contributed to the design of the protocol. Isis Amer-Wåhlin, Charlotte Hellsten, Håkan Norén, Henrik Hagberg, Andreas Herbst, and Maivi Månsson contributed to the design of the protocol. Isis Amer-Wåhlin, Anna-Karin Sundström, Andreas Herbst, and Laila Mårtensson participated in the teaching of clinical staff and in data collection. Anna-Karin Sundström, Laila Mårtensson, and Maivi Månsson maintained the database and were responsible for the quality control of clinical data. Isis Amer-Wåhlin, Anna-Karin Sundström, Andreas Herbst, and Karel Mars ál did the interim and final statistical analyses. Ingemar Kjellmer analysed the neonatal data. All investigators participated in the interpretation of results and revision of the paper, which was drafted by Isis Amer-Wåhlin, Andreas Herbst, Per Olofsson, and Karel Mars ál.

Acknowledgements
We thank Ingemar Ingemarsson and Lars-Åke Mattsson for their valuable input during planning and execution of the study and their comments on the paper, and to Ulla-Stina Wilson for her participation in data collection. We also thank all midwives and obstetricians of the Departments of Obstetrics and Gynaecology in Lund, Malmö, and Gothenburg for their cooperation in the study. The loan of STAN equipment by Neoventa Medical, Gothenburg, Sweden, is gratefully acknowledged.

The study was supported by Neoventa Medical, Gothenburg, and the Knowledge Foundation, Stockholm, Sweden, and by grants to researchers in the public health service from the Swedish government.

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