J. Perinat. Med. 6 (1978) 149 **A comparison of two controlled trials concerning the efficacy of fetal intensive care**

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1 Introduction

In a recent journal of Perinatal Medicine, HOCHULI et al, [2] state that there is no doubt that intranatal monitoring is ineffective and that the reduction of perinatal mortality amply demonstrates this. The authors quote 14 articles to support this statement. None of the series quoted give more than circumstantial evidence based upon the coincidence of a reduction of mortality with the introduction of intranatal monitoring and this does not exclude the possibility of other factors contributing partially or wholly to the decline in perinatal mortality. The following may influence perinatal mortality: Social characteristics of the population, general health of the obstetric population, clinical expertise of staff and organisation of obstetrics services. The authors of the papers concerned with intranatal monitoring were unable to exclude the possibility of one or more of these factors causing the decline of perinatal mortality. Only properly controlled prospective trials can test the efficacy of newly introduced techniques. Two randomised controlled trials testing the efficacy of intranatal monitoring have been completed; unfortunately, the results differed [2, 3]. Therefore the value of fetal monitoring is not as clear cut as HOCHULI and other authors claim. The purpose of the present article is to compare the two controlled trials and to determine, if possible, why the results differed.

2 Material and Methods

The two control trials are compared in Tab. I. In both studies, care was taken to ensure that the

Curriculum Vitae

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patients in monitored and control groups were similar. However, the systems used for matching patients were different. The clinical condition of fetuses in the monitored and control groups may have been different. In the American trial there was an adverse loading in the monitored group early in labour, as judged by abnormalities of fetal heart rate recordings. In the Australian trial, the fetuses could not be compared as the control group was not monitored.

The problem of whether there were differences of obstetric care during labour were discussed in the reports of both studies. In the American study, nursing care was increased in the control group and this was thought to be due to a compensatory reaction of the nursing staff, trying to improve care in the control group. In the Australian study, observations by those not involved in the trial suggested that the quality of medical and nursing care was similar in the control and monitored

Tab. I. Comparison of two controlled trials using fetal intensive care

American Study HAVERKAMP <i>et al</i> , 483 cases		Australian Study RENOU <i>et al</i> , 350 cases
	<i>Criteria for-</i>	
Matched high risk point system	Comparability of patients in monitor	18 obstetric variables
Adverse loading in monitor group	Comparability of fetuses in monitor & control groups	Unknown
Increased nursing care in control	Comparability of care in labour	Uncertain, probably similar
FHR abnormality-classification of HON and KUBLI	Criteria for intervention	FHR abnormality and fetal scalp pH
Higher in monitored group	Incidence of Caesarean section	No difference
No difference	Perinatal morbidity	Higher in control group
No difference	Cord pH	Higher in monitor group
No difference	Neonatal Intensive Care	Higher in control group

groups; both the medical and nursing staff were interested in the outcome of the trial and were asked to avoid bias towards one or other group.

The criteria for intervention was different in the two studies. In the American study, HON and KUBLI's fetal heart rate classification was used and action taken according to the abnormalities defined by this classification. In the Australian study, fetal heart rate abnormality was defined by

a simpler fetal heart rate classification and when abnormalities were present, fetal scalp pH was carried out. Action taken in both studies differed. In the American study, the incidence of Caesarean section was higher in the monitored group, whereas in the Australian study this was not so.

In the American Study, perinatal morbidity, cord pH and neonatal intensive care were similar in the control and monitored group, whereas in the Australian study, perinatal morbidity and the incidence of neonatal intensive care were higher in the control group, and the cord pH was higher in the monitored group. These differences were statistically significant.

Indices of neonatal condition have been rearranged in order to compare the outcome of the studies Tab. II. Comparison of the two trials show differences. The monitored group in the Australian study had less neonatal complications than any of the other three groups. However, the control group of HAVERKAMP *et al*. [1], fared better than the control group of the Australian study. There were four infants in the Australian study control group who were suffering from brain damage 6 months after birth.

3 Discussion

A number of reasons may explain the differences in the results of the two trials.

- (1) The patients admitted into the two trials may have differed.

Tab. II. Neonatal indices modified in order to compare two studies

	american study control	(HAVERKAMP <i>et al</i>) monitor	australian study (RENOU <i>et al</i>) control	monitor
Number in group	241	242	175	175
Intensive care nursery	28	35	30	11
Convulsions	2	2	4	0
Twitching	9	11	9	2
Apgar Score ≤ 7	62	70		
< 7			19	24
Umbilical* Arterial pH	7.27	7.27	7.26	7.30
Umbilical Venous pH	7.35	7.35	7.31	7.35

* pH measurements are not necessarily comparable between hospitals because there are no primary standards.

- (2) There may have been differences in the number of sick fetuses in the control and monitored groups at the commencement of each trial. Because of the matching of so many variables in the Australian study this seems unlikely but the fact that in early labour the American study demonstrated a difference in the numbers of abnormal fetal heart rate recordings in the control and monitored groups suggests this possibility cannot be excluded.
- (3) Better clinical care of the control group was thought possible in the American study although it was unlikely to have influenced the Australian study.
- (4) Differences between the two studies existed in the criteria for judging abnormal fetal heart rate and the action taken subsequent to this. The Australian study had the advantage of scalp blood pH measurements.
- (5) The general health and/or obstetric care of the control group in the American study may have been better than that of the control group in the Australian study. Four infants suffered brain damage in the Australian control group. Nevertheless, using other neonatal indices, the number of unhealthy babies in both control groups were similar.

The limitations of each study have been discussed fully. Nevertheless, the studies still may indicate the conditions under which fetal intensive care is valuable.

When a controlled trial produces a positive result, it is important to know that the fetal condition of both control and monitored groups are comparable as judged by an equal incidence of fetal heart rate abnormalities. This information was not available in the Australian study as clinicians considered that the results of fetal heart rate recordings in the control group may be communicated to the doctor in charge of the patient's management by nurses or residents or technicians, either overtly or subconsciously. However, the American study overcame this problem by hiding the fetal heart rate recordings from all personnel; the exact mechanism by which this was achieved is not clear but this is an important consideration for any future study. If a controlled trial produces a negative result, there being no differences between

the monitored and control groups, then it is important to determine whether the condition of the fetuses in the two groups were comparable at the commencement of the trial (fetal heart rate, scalp pH), whether the diagnostic tests have been properly done and properly interpreted, and whether appropriate clinical action has been taken.

It is important for further control studies to be done to define the conditions under which fetal intensive care is effective. It seems feasible that in some population samples, where the general health of the patient is good, few obstetric complications occur, general obstetric clinical standards are high and the obstetric services are well organised, that a negative result may occur. However, it seems equally likely, that in the absence of any of these favourable circumstances, that a positive result may occur. In order to aid administrators of health care decide where to place fetal intensive care units and how to run obstetric services economically, the conditions under which monitoring is effective has to be determined in more detail. The different results of the two controlled trials suggest that the coincidence of reduction in perinatal mortality and the introduction of fetal monitoring is insufficient evidence to base the introduction of fetal monitoring to all patients.

Sometimes it is difficult to organise control trials. Obstetric personnel may consider trials are unnecessary as they already believe they know what is correct. It is difficult to argue the ethical merits of trials — one group may be convinced that to withhold a new test or treatment is unethical, while another group may be convinced that to try a new method is unethical. Another problem in the organisation of controlled trials is the difficulty in obtaining informed consent of the patient. Patients may defer from a trial because they prefer either traditional or new care. Because of such difficulties, the possibility of reaching conclusions from perinatal mortality statistics remains. The limitations of interpretation of perinatal mortality statistics have been mentioned. However, under specified circumstances this information may be helpful. In order to draw valid conclusions from mortality data the following criteria for judging a change in mortality to be causally related to some other event, such as monitoring, may be helpful. The

time sequence between the change in mortality and the introduction and rate of use of monitoring must be correct; there must be a consistency of this association in different studies; the degree of change of mortality and the type of change in mortality should be consistent with that expected from monitoring; and there should be a coherent explanation of a causal nature in how the monitoring effected mortality. In our own hospital there was a decline in the intrapartum anoxic stillbirths of mature fetuses over a period of time. While this change may undoubtedly be due to factors such as improvement of the obstetric health of the population, the standard of clinical care and the organisation of the obstetric services, the possibility of a relationship with the introduction of fetal diagnostic tests is suggested by the finding that the major change in mortality occurred at the time of the introduction of the tests, and in mature fetuses dying of intrapartum anoxia (Fig. 1). Nevertheless, the randomised controlled

trial remains the best available method of testing the effect of new therapeutic regimes.

Summary

Two controlled trials testing the efficacy of fetal intensive care have been compared. The results of the two trials differed and the reasons for the different results have been evaluated; both studies had methodological limitations. Nevertheless the fallacies associated with sequential studies exceed that of controlled trials.

In one controlled trial neonatal condition was better in the monitored than the control group. This was thought to result from the more accurate diagnosis of fetal distress by means of fetal heart rate monitoring and fetal scalp blood pH measurement rather than other factors involved in the trial. In the other controlled trial no difference in the neonatal morbidity was found between the monitored and control group. This was thought to be due to the high standard of general obstetric care in the control group but other factors such as the absence of scalp sampling in the monitored group and compensatory care in the control

group (auscultation of FHR at very frequent intervals), could not be excluded. In the positive controlled trial, the neonatal morbidity of the monitored and control groups was higher and lower respectively, than either of the groups in the negative controlled study. This suggests that monitoring is effective but the benefits depend upon the general standard of obstetric care. When general health of the population is good, few obstetric complications occur and obstetric care is of a high standard then monitoring may not be beneficial. However, in the absence of any of these favourable circumstances, monitoring may be beneficial.

Further controlled trials need to be carried out taking into account the limitations of the current trials and the need to define more clearly which obstetric patients may benefit from monitoring.

Keywords: Controlled trials, fetal heart rate monitoring, fetal intensive care, fetal scalp sampling, intrapartum management, organisation of obstetric services, perinatal morbidity, perinatal mortality, sequential trials.

Zusammenfassung

Vergleich zweier kontrollierter Studien über die Wirksamkeit intensiver vorgeburtlicher Betreuung.

Mit dem Ziel, die Effizienz fetaler Intensivüberwachung zu überprüfen, kamen zwei Kontrollanordnungen zum Vergleich. Die Kontrollen ergaben unterschiedliche Ergebnisse und die Ursachen dieser Differenz wurden näher bestimmt; beide Untersuchungen hatten methodologische Einschränkungen. Bei weitergehender Betrachtung ergab

sich jedoch, daß darüberhinaus Fehlschlüsse möglich waren, die die Toleranzgrenze von Kontrollanordnungen überschritten.

Nach dem einen Kontrolltest war der neonatale Status in der intensiv überwachten Gruppe besser als in der O-Kontrolle. Eine mögliche Ursache dafür liegt in der genaueren Diagnose von fetalen Stress-Zuständen. Die kontinuierliche Aufzeichnung der fetalen Herzfrequenz sowie die

Kopf-pH-Messung sind hinsichtlich einer exakten Diagnose sicherlich entscheidender als andere Parameter, die von dem Kontrollverfahren erfaßt wurden. Nach der zweiten Kontrollanordnung wurde bezüglich der neonatalen Morbidität kein Unterschied zwischen der intensiv überwachten Gruppe und der O-Kontrolle gefunden. Wahrscheinlich ist dieses Ergebnis auf einen hohen Standard der generellen geburtshilflichen Überwachung zurückzuführen. Es konnte auf jeden Fall nicht ausgeschlossen werden, daß in der intensiv überwachten Gruppe auf eine Kopf-pH-Messung verzichtet wurde, und, auf der anderen Seite, in der Kontrollgruppe durch eine „kompensatorische“ Überwachung (z. B. Abhören der fetalen Herzfrequenz in sehr kurzen Zeitintervallen) das obige Ergebnis begünstigt wurde. Nach der Kontrollanordnung mit positivem Ergebnis war die neonatale Morbidität in der intensiv überwachten Gruppe sowie in der O-Kontrolle höher bzw. niedriger als die Morbiditätsziffern, die sich

nach dem Kontrollverfahren mit dem negativen Ergebnis für die beiden Gruppen errechnen ließen. Das läßt vermuten, daß das Intensiv-Care effektiv ist, aber sein Nutzen in starkem Maße vom generellen Standard der geburtshilflichen Überwachung abhängt. Ist der allgemeine Gesundheitszustand der Bevölkerung gut, d. h. sind wenige geburtshilfliche Komplikationen zu erwarten, so wird bei einer geburtshilflichen Überwachung mit hohem Standard das Intensiv-Care nicht unbedingt Vorteile bringen. Fehlen diese günstigen Voraussetzungen jedoch, so wird man von der Intensiv-Überwachung profitieren.

Es müssen weitere Kontrollverfahren durchgeführt werden, wobei die Einschränkungen der gegenwärtigen Kontrollanordnungen in Rechnung gestellt werden müssen sowie auf die Notwendigkeit eingegangen wird, klarer zu definieren, welche geburtshilflichen Patienten von der Intensiv-Überwachung profitieren.

Schlüsselworte: Folgeversuche, intensive vorgeburtliche Betreuung, intrauterine Mikroblutentnahme aus der Kopfschwarte, Leitung der Geburt, Organisation der Schwangerenvorsorge, Perinatale Morbidität, Perinatale Mortalität, Überwachung der fötalen Herzfrequenz.

Résumé

Comparaison de deux tests de contrôle sur l'efficacité des soins intensifs aux foetus

L'étude présente porte sur la comparaison de deux essais de contrôle relatifs à l'efficacité des soins intensifs aux foetus. Ces deux séries d'examen ont donné des résultats divergents qui ont été analysés; il importe de souligner que la méthode a comporté certaines restrictions dans les deux cas. Néanmoins, les erreurs liées aux études de séquence ont dépassé celles des essais de contrôle.

Dans un essai de contrôle, la condition natale était meilleure dans le groupe enregistré que dans celui de contrôle, ce qui est dû peut-être au diagnostic plus précis de distress foetal au moyen de l'enregistrement du rythme cardiaque foetal et de la mesure du pH du sang crânien foetal plutôt qu'à d'autres facteurs impliqués dans l'essai. Dans l'autre essai de contrôle, aucune différence n'a été observée dans la morbidité néonatale entre le groupe enregistré et celui de contrôle, ce qui est dû sans doute au niveau élevé des soins obstétriques généraux dans le groupe de contrôle, mais il n'est pas possible d'exclure d'autres facteurs tels que

l'absence de spécimens de sang crânien dans le groupe enregistré et les soins compensateurs dans le groupe de contrôle (auscultation de la fréquence cardiaque foetale à intervalles très fréquents). Dans l'essai de contrôle positif, la morbidité néonatale des groupes d'enregistrement et de contrôle a été respectivement plus élevée et plus basse que pour chacun des groupes de l'étude de contrôle négative. Ceci fait supposer que l'enregistrement est efficace, mais que les bénéfices acquis dépendent du niveau général des soins obstétriques. Quand l'état de santé général de la population est bon, qu'on observe peu de complications obstétriques et que les soins obstétriques sont d'un niveau élevé, alors l'enregistrement peut ne pas être bénéfique. Cependant, en l'absence de certaines de ces circonstances favorables, l'enregistrement peut se montrer bénéfique.

Il s'avère nécessaire d'effectuer d'autres essais de contrôle tenant compte des limites des essais courants et d'établir avec plus de précision quelles parturientes peuvent tirer profit de l'enregistrement.

Mots-clés: Maniement intrapartum, morbidité périnatale, mortalité périnatale, organisation des services d'obstétrique, prélèvement du sang capillaire du foetus, soins intensifs aux foetus, surveillance continue de la fréquence cardiaque foetale, tests de séquence.

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