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Modification of the fetal reactivity by an intravenous glucose load to the mother

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1 Introduction

Antepartum cardiotocography is widely accepted as a highly reliable method in the surveillance of the fetal condition [1, 6, 7, 9, 10].

In the non-stress test (NST), the spontaneous movements of the fetus felt by the mother, followed by a transient acceleration of the fetal heart rate (FHR) are usually looked upon as a sign of fetal well-being.

The association of the NST with a period of physiological absence of fetal somatic activity is frequent and when it occurs raises a problem of the immediate evaluation of the fetus. The test is then classified as "non-reactive", and is usually followed by a contraction stress test (CST) that, in the majority of the cases, will be read as "negative".

In the attempt to prevent this situation, several kinds of management have been proposed, all of them with the goal of stimulating the initiation of fetal somatic activity, either by fetal mechanical stimulation using manual palpation of the uterine fundus — not always effective and only instantaneous — or the test repetition after a meal or the ingestion of glucose by the mother [2], having in mind the known feature of the postprandial increase in fetal activity.

Glucose is the major source of fetal energy; fetal glucose levels are dependent on maternal supply and also on placental transfer capacity; at least in theory fetal muscular activity must be diminished when the availability of maternal glucose remains below optimal levels.

Curriculum vitae

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The present investigation was designed to check if iv glucose administration to the mother could be useful as a discriminative test for the non-reactive fetuses, in order to reduce the number of unnecessary CSTs, thus avoiding the time and the risks associated in this procedure.

2 Material and methods

During a 14 month period (from the 1st of September to the 31st of October 1980) 582 fetuses from pregnant patients referred to the High-Risk Obstetrical Unit of the Santa Maria University Hospital at Lisbon, were evaluated by the NST, performed between 8:00 and 11:00 a. m.

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In all cases the mothers had fasted for at least 6 hours; pre-test blood sugar levels and arterial pressure were determined and repeated at 10 minutes intervals.

All the pregnancies had a duration of at least 34 weeks, assessed either by the date of the last menstrual period or by ultrasound measurements of the biparietal diameter.

The reasons for the NST are listed in Tab. I.

Tab. I. NST – Non-reactive fetus
Intravenous glucose load test

Indications for the NST		
1	Poor dates	12
2	Previous infertility.	6
3	Pre-eclampsia.	6
4	Previous hypertension.	6
5	Fetal growth retardation without hypertension	5
6	Maternal heart disease.	3
7	Previous perinatal deaths	3
8	Gestational glycosuria.	2
9	Mild hydramnios.	1
10	Premature rupture of membranes	1
11	Maternal pulmonary tuberculosis	1
12	Sub-normal estriols	1
13	Bloody amniocentesis.	1

With the patients in the semi-FOWLER position, a continuous recording of the FHR (provided by an ultrasound transducer), and of the uterine activity, were accomplished by means of Corometrics Fetal Monitors, models 110 or 112.

Fetal movements (FM), when felt by the mother, were plotted on the uterine activity channel through a remote marker.

The patients selected for the study were those in which FM were not observed and, consequently, there was a lack of stimulus to the eventual reactivity of the fetal heart rate. These fetuses were classified as "hypo-active" and the NSTs as "non-reactive", because at least two FHR accelerations, with 15 seconds of duration and an amplitude of 15 b p m, were not registered during the first 20 minutes of the test.

A total of 48 fetuses underwent the test, three of them twice. The test was accomplished by the intravenous injection to the mother of 20 milliliters of a 30 per cent solution of glucose, during

one minute. Ten minutes later the maternal blood sugar level was determined. After the glucose load, fetal monitoring was maintained for 30 minutes.

Another group of 10 fetuses, matched as close as possible with the study group for age of gestation and associated pathology, was used as control; a 20 milliliter saline injection was performed instead of the glucose load. The cardiotocographic tracings were classified as soon as they were obtained, always by the first author (L M G).

In 26 patients (22 from the study group and 4 from the controls) the FHR variability was read as decreased (5 b p m or less), but this did not suffice as a criterion for selection.

The lag time between the test and the delivery varied between 0 and 35 days. The perinatal outcome will be presented in the next section.

3 Results

From the 51 tests performed, 44 (41 fetuses) or 86% were classified as positive (Tab. II); FM began after a mean time of 6 minutes and 4 seconds after the glucose load, either as an isolated, or in a multiple fashion (Figs. 1 and 2); in 38 instances the number of FM was over 5 in the 20 minutes following the first movement; the mean number of FHR accelerations in the same period was about 6. The mean arterial blood glucose rose from a pre-

Tab. II. NST – Non-reactive fetus
Intravenous glucose load test

Positive test	
1. Number of studied fetuses	41
Number of tests performed	44
2. Time glucose load-FHR reactivity. . .	6 m 04 s ± 2 m 45 s
Number of FM (20 minutes). . . 2–5:	6 times
	> 5: 38 times
Number of FHR accelerations (20 minutes):	5.9 ± 2.3
3. Newborn state:	
40 cases: APGAR scores ≥ 7	
1 case: Progressive deterioration of the NSTs; Positive CST 12 days after the test, depressed newborn.

Fig. 1. About 5 minutes after the 6 g glucose load to the mother (arrow), the beginning of FM (deflections on the UA channel) can be seen with accompanying FHR accelerations. Paper speed: 1 cm/min.

Fig. 2. Top: In spite of good basal FHR variability, the acceleration pattern concomitant with FM only appears 4 minutes after the glucose load (arrow).

Bottom: A smoothed FHR variability becomes an average pattern, with episodic accelerations associated to FM triggered by the glucose load, administered 7 minutes earlier (arrow). Paper speed: 1 cm/min.

test level of 3.3 mmol/l (65.5 mg/100 ml) to 4.8 mmol/l (96.4 mg/100 ml) ten minutes after the bolus.

In three cases, a new NST performed 5 to 7 days after the first one was once again "non-reactive", but the reactivity had been enhanced with a new glucose load.

Of the 41 fetuses studied who showed a positive response to the glucose, 40 were delivered in good health after a variable number of days (0–35) following the test. With the exception of the three above mentioned and the cases where the delivery took place before 5 to 7 days after the test, the subsequent NST were always "reactive". In the remaining case the subsequent NSTs showed the following evolution: at 34 weeks and 3 days – reactive; at 35 weeks – unsatisfactory; at 35 weeks and 3 days – nonreactive, unresponsive to the glucose load, followed by a positive CST; considering the poor obstetric history (essential hypertension, two previous perinatal deaths) a cesarean section (CS) was performed; a 2100 grams child was born, with Apgar scores of 2 and 8 at 1 and 5 minutes, requiring resuscitation; nevertheless, the neonatal course was normal.

In the 10 cases of the control group (Tab. III), four did not show any FM during the 20 minutes following the maternal intravenous saline injection. Six fetuses became "reactive" but only after a mean lag time of 12 minutes after the bolus. The difference between the two groups is significant (Chi square = 13.490, $p < 0.001$).

Tab. III. NST – Non-reactive fetus
Intravenous glucose load test

Control group	
1.	10 cases, 36–41 weeks, non-reactive fetus
2.	Maternal intravenous bolus of 20 ml NaCl 0.9% in one minute
3.	Results:
4.	cases: FM not observed in the 20 minutes after the IV saline injection;
6.	cases: FM and FHR reactivity appeared in a mean time of 11.7 ± 5.2 minutes after the saline injection to the mother.

The 7 cases with a negative glucose load test (i.e. no accelerations of the FHR with or without the appearance of FM) are presented individually in Tab. IV. Only in case 2 there was no association between the negative glucose load test, the following CST and the APGAR score of the newborn; the reason for the fetal non-reactivity after the 6 grams glucose injection to the mother may perhaps be found rather in the hemodynamic modifications induced by the intra-amniotic hemorrhage than in the eventual lack of energy substrate. In the remaining 6 cases, the correlation was good between the lack of enhancement of the fetal somatic activity, the CSTs (5 positive and 1 suspicious) and the APGAR scores; in case number 29 there was a fetal death in utero diagnosed 12 hours after the test; in two cases neonatal death occurred, but in one of them (case number 46) the death can be ascribed to the major malformations present (absence of the left hemi-diaphragm, left lung hypoplasia and dextrocardia).

Using the newborns' APGAR scores (greater than or equal to 7 and less than 7) a significant difference was noted between the groups of positive and negative responses to the glucose load test (Chi square = 32.371, $p < 0.001$), as is shown in Tab. V.

Tab. V. Differences between the APGAR scores in the Positive and Negative responsive groups

Test \ APGAR	Positive	Negative	Σ
< 7	1	6	7
> 7	40	1	41
Σ	41	7	48

4 Comment

Intrauterine fetal movements are the expression of fetal well-being, which is confirmed by the observation of associated transitory FHR accelerations [9]. The decrease or absence of fetal somatic activity can be conditioned either by a stressing pathological situation, as described by SADOVSKY et al. [11, 12, 13] or by the fetal physiological

Tab. IV. NST – Non-reactive fetus
Intravenous glucose load test
Negative test

Case number	Parity	Weeks	Diagnosis	Minutes of fetal hypo-activity	Time load-1st FM (min-utes)	Nr. FM after glucose load (20 min)	Nr. of FHR accéléra-tions (20 min)	Following CST	Perinatal data (AS = APGAR scores)
2	2-1	37	Bloody amniocentesis	24	—	0	0	Negative	Vaginal delivery, 2800 g, male, AS: 7-10, anemic
19	1-0	37	IUGR**	20	10	5	0	Positive	CS, 1850 g, male, AS: 3-6, death at 3rd day
28	2-1	36	Previous death inutero	20	—	0	0	Positive	Vag. delivery, 3650 g, female, AS: 3-6, survived
29	1-0	35	Essential hypertension	30	—	0	0	Positive	Fetal death during the next 12 hours
34	3-1	38	Renal hypertension	24	—	0	0	Positive	CS, 2040 g, female, AS: 3-7, survived
46	2-1	≥ 38	Poor dates (Bip = 9 cm)	24	—	0	0	Suspicious basal FHR 105 bpm.	Vag. delivery, AS: 2-2, major malformations, neonatal death
48	3-1	35	Severe preeclampsia	23	—	0	0	Positive	CS, 1860 g, male, AS: 2-2-8, survived

* All the deliveries performed during the 24 hours following the test.

** Intra Uterine Growth Retardation

resting state, coinciding in general with a marked decrease of the respiratory movements [3].

On the other hand, to undertake the fetal muscular activity, the availability of maternal glucose must be maintained at acceptable levels since fetal glucose, main source of fetal energy [15], is dependent on maternal supply [5, 14]; therefore, one can accept the hypothesis that one of the fetal defense mechanisms to insufficient glucose transfer would be the cessation of somatic movements. Furthermore, hypoxemic fetuses do not show any significant increase in glucose uptake even with increasing materno-fetal glucose gradients [4].

Adopting the proposal of ALADJEM et al. [2] it can be thought that the administration of an intra-

venous glucose load to the mother may release the somatic activity of the non-hypoxemic fetus; therefore, it is possible to make a quick differentiation between the cases in which the fetus does not show movements and FHR accelerations by a lack of energy supply, from the cases of fetal hypoactivity and non-reactivity caused by hypoxemia.

The present results are confirmative of this hypothesis, for in 44 instances, the non-reactive pattern could be changed to a reassuring activity and reactive FHR pattern after a lag time of about 6 minutes; these results agree with the works of SPELLACY and GELMAN [8, 16] as far as fetal somatic activity is concerned, but a substantial difference

is patent in the shorter load – response intervals than we found.

The fetal well-being was confirmed by subsequent reactive NSTs and by APGAR scores at birth, with the exception of one case in which the cardiotocographic tests performed during the following days showed a progressive deterioration of the fetal state that culminated in a positive CST.

Perhaps the most important finding in the present work were the negative tests: in 6 of 7 instances a positive CST and/or low APGAR scores were anticipated.

Summary

The effect of an intravenous maternal glucose load upon fetal activity and FHR was studied 51 times in 48 pregnancies at 34 or more weeks, in which the fetuses were classified as non-reactive during the NST.

The initiation of fetal muscular activity was observed in 44 instances (41 fetuses) approximately 6 minutes after a 6 grams glucose load to the mother, which lead to the diagnosis of a state of fetal well-being without the need of a CST.

In the 7 cases which were not responsive to the load, CSTs were performed; of these, 5 were positive, 1 negative and 1 suspicious. These pregnancies resulted in one fetal death during the 12 hours following CST and 5 newborns showed an APGAR Score less than 4 at one minute,

Keywords: Cardiotocography, fetal activity, fetal reactivity, glucose.

Zusammenfassung

Änderung der fetalen Reaktivität durch intravenöse Glukosegabe an die Mutter

Bei 48 Schwangerschaften, bei denen die Feten als nicht-reaktiv im Non-Stress-Test eingestuft wurden, wurden fetale Reaktivität und Herzfrequenz durch intravenöse Glukosegabe an die Mutter untersucht. 44mal (41 Feten) wurde sechs Minuten nach der Infusion von 6 g Glukose eine beginnende fetale Muskelaktivität festgestellt und ließ damit auf einen gesunden Zustand des Feten schließen, ohne daß ein Oxytocin-Belastungstest (OBT) notwendig gewesen wäre.

In 7 Fällen, bei denen auf die Glukosegabe keine Reaktion folgte, wurde der OBT durchgeführt (fünfmal mit positivem, einmal mit negativem und einmal mit zweifelhaftem Befund). Eine dieser Schwangerschaften endete mit einer Totgeburt 12 Stunden nach dem OBT. Fünf

Schlüsselwörter: Fetale Aktivität, fetale Reaktion, Glukose, Kardiotokographie.

Résumé

La réaction foetale suite à une administration intraveineuse de glucose chez la mère

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An extension of the present investigation, comparing one group undertaking the test with another not submitted to it, could confirm the idea that the "intravenous maternal glucose load test" would become a discriminative method to distinguish between the hypo-reactive fetuses metabolically compensated, from the genuinely hypoxemic ones, providing a way to diminish the number of unnecessary CSTs and clearing the need for the indispensable ones.

with 2 neo-natal deaths. The reason for the negative glucose load test with a negative CST was probably related to hemodynamic changes induced by intra-amniotic bleeding following a bloody amniocentesis, and not to the lack of fetal energy substrate.

The proposed method may constitute a screening possibility for the clinical management and prognosis of the hypoactive fetus, because the glucose load to the mother may release the somatic activity of the non-hypoxemic fetus. A fetus unable to show any significant increase in glucose uptake, even with increasing maternal-fetal gradients, could be identified by the negative response to the test.

Neugeborene hatten einen Einminuten-Apgarwert von 4, zwei dieser Kinder starben neonatal. In einem Fall mit negativem Glukosebelastungstest, negativem Oxytocin-Belastungstest und guten Apgarzahlen beruhte die fehlende Reaktivität wahrscheinlich weniger auf einem fetalen Energiesubstratmangel, sondern auf hämodynamischen Veränderungen im Zusammenhang mit einer intraamniotischen Blutung nach Amniozentese.

Die vorgestellte Methode könnte ein Screening-Verfahren für die klinische Überwachung von hypoaktiven Feten darstellen, da die Glukosebelastung der Mutter eine höhere Reaktivität des nicht hypoxischen Feten bewirken kann. Ein Fet, der trotz steigendem materno-fetalen Gradienten keinen signifikanten Anstieg der Glukoseaufnahme zeigt, könnte durch die negative Reaktion auf den Glukosebelastungstest identifiziert werden.

L'effet d'une administration i.v. de glucose chez la mère sur l'activité foetale et la fréquence cardiaque foetale a été

étudié 51 fois dans 48 cas de grossesse > 34 semaines, lesquels ne réagissaient pas durant le non-stressed-test (N.S.T.). Le début d'une activité musculaire foetale a été observé dans 44 cas (41 foetus) approximativement 6 minutes après l'administration de 6 g de glucose chez la mère, d'où le diagnostic de vitalité foetal qui ne nécessite pas le contraction-stressed-test (C.S.T.). Dans 7 cas où il n'y avait pas de réponse à l'administration de glucose, le CST a été effectué. 5 réactions étaient positives, une négative et une douteuse. Une de ces grossesses s'est terminée par un mort-né 12 heures après un CST. 5 nouveau-nés avaient après une minute un score de moins de quatre dans l'échelle d'APGAR parmi lesquels deux sont morts dans la période neonatale.

Mots-clés: Activité foetale, cardiotocographie, glucose, réactivité foetale.

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