JoCASS
Çukurova Anestezi ve Cerrahi Bilimler Dergisi
2018 Adana

CHOCOLATE OR FETAL DOPPLER SONOGRAPHY FOR NON-REACTIVE NON-STRESS TEST PATTERNS: RANDOMIZED PROSPECTIVE CONTROLLED STUDY

FETAL NON-REAKTİF NON-STRESS TEST PATERNİ TAKİBİNDE FETAL DOPPLER ULTRASON VEYA ÇİKOLATANIN YERİ: PROSPEKTİF RANDOMİZE KONTROLLÜ ÇALIŞMA

Gokhan Karakoc[1], Serenat Eris Yalcin[2], Hasan Eroglu[3], Halime Şen Selim[1], Kutlu Kurt[1], Mustafa Şengül[1], Aykan Yucel[4]

1 Department of Obstetrics and Gynecology, İzmir Katip Çelebi University Atatürk Training and Research Hospital, İzmir, Turkey
2 Department of Obstetrics and Gynecology, Antalya Education and Research Hospital, Antalya, Turkey
3 Department of Obstetrics and Gynecology, Gaziantep Cengiz Gökçek Maternity and Child Diseases Hospital, Antep, Turkey
4 Department of Obstetrics and Gynecology, Etlik Zübeyde Hanım Gynecology Training and Research Hospital, Ankara, Turkey

Sorumlu Yazar/Corresponding Author: Halime Şen Selim E-mail: dr.halime.sen.selim@gmail.com
Geliş Tarihi/Received: 03.02.2022 Kabul Tarihi-Accepted: 28.05.2022 Available Online Date/Çevrimiçi Yayın Tarihi: 31.08.2022
Cite this article as: Karakoc G, Yalcin SE, Eroglu H, et al. Chocolate or fetal Doppler sonography for non-reactive non-stress test patterns: randomized prospective controlled study. J Cukurova Anesth Surg. 2022;5(2):85-91.
Doi: 10.36516/jocass.1058996

Abstract

Aim: The aim of this study is to compare the effect of 20-second MCA Doppler ultrasonography and bitter chocolate on non-stress test (NST) patterns, fetal movements felt by the mother and cesarean delivery rates.

Methods: Single pregnancies between 36-41 weeks with non-reactive NST pattern were included in the study and prospectively randomized to Doppler ultrasound, bitter chocolate, and non-intervention control groups. NSTs of the patients at the 5th and 30th minutes were examined.

Results: The rate of improvement in the fetal movements felt by the mother did not differ significantly among groups ($p > 0.05$). The 5th minute reactive NST ratio in the Doppler group was significantly higher ($p < 0.05$) than in the follow-up and chocolate group. In the chocolate and non-intervention control group, the 5th minute reactive NST ratio did not differ significantly ($p > 0.05$). In the 30th minute NST, patients with non-reactive results had significantly higher fetal distress rates in the Doppler group compared to the other groups ($p < 0.05$).

Conclusions: We think that with the application of Doppler, the length of hospital stay and accordingly patient's anxiety will reduce. In addition, the patient should be monitored more carefully in terms of fetal distress because it quickly corrects false non-reactivity.

Keywords: Chocolate, Doppler, non-stress test

Öz

Amaç: Bu çalışmanın amacı, 20 saniyelik MCA Doppler ultrasonografi ve bitter çikolatanın, non-stres test (NST) paternleri; anne tarafından hissedilen fetal hareketler ve sezaryen doğum oranlarına etkisini karşılaştırmaktır.

Yöntemler: 36-41 hafta arası reaktif olmayan NST paterni olan tekil gebelikler çalışmaya dahil edildi ve prospektif olarak Doppler ultrason, bitter çikolata ve müdahalesiz kontrol gruplarına randomize edildi. Hastaların 5. ve 30. dakikadaki NST'leri incelendi.

Bulgular: Anne tarafından hissedilen fetal hareketlerdeki iyileşme oranı gruplar arasında anlamlı farklılık göstermedi ($p > 0.05$). Doppler grubunda 5. dakika reaktif NST oranı, takip ve çikolata grubuna göre anlamlı olarak daha yüksekti ($p < 0.05$). Çikolatalı ve müdahalesiz kontrol grubunda 5. dakika reaktif NST oranı anlamlı farklılık göstermedi ($p > 0.05$). 30. dakika NST'de, reaktif olmayan sonuçları olan hastalarda, Doppler grubunda diğer gruplara göre anlamlı derecede daha yüksek fetal distres oranları vardı ($p < 0.05$).

Sonuç: Doppler uygulaması ile hastanede kalış süresinin ve buna bağlı olarak hastanın kaygısının azalacağını düşünüyoruz. Ayrıca yanlış tepkisizliği hızla düzelttiği için hasta fetal distres açısından daha dikkatli izlenmelidir.

Anahtar Kelimeler: Çikolata, Doppler ultrason, non-stres test

Introduction

It is absolutely necessary to evaluate fetal well-being in terms of health of the mother and fetus during pregnancy. The most used method for antepartum fetal evaluation is electronic fetal monitoring method. Non-stress test (NST) is one of the key indices that reflect the biophysical activities of the fetus[1]. NST is a test based on an increase in fetal heart rate in response to fetal movements and reveals two patterns; if it is reactive, it can be said that the fetus is in good condition. If it is non-reactive, it may be associated with poor fetal outcome. According to the NST results, in patients delivered as fetal distress, the specificity is not at the level we want, but then in nearly half of these patients, a poorly affected newborn is obtained[2]. However, the average relative percentage time spent in a silent state is about 26% for the fetus between 30 and 40 weeks[3]. Therefore, if NST monitoring is performed during the quiet period of the fetus, the false non-reactive incidence will be higher; this length varies from 20 to 75 minutes but may also be associated with fetal hypoxemia or acidosis. Other factors associated with non-reactive NST results are maternal race, fetal immaturity, sepsis, maternal cigarette-alcohol intake, and the use of some drugs that can suppress fetal cardiac and neurological activity[4-6].

Many studies have shown that there is a relationship between maternal glucose administration and increased fetal activity[7]. Continuous-wave Doppler ultrasonography close to the fetal ear, which was applied intermittently for a total of 60 seconds within 3 minutes, has been shown to increase fetal movements[8]. It is thought that Doppler ultrasonography does not increase the risk for the fetus, even in the first trimester, unless the duration of exposure is more than 5 minutes[9]. Furthermore, a study of fetuses exposed in utero to vibroacoustic stimulation[10] and a recent study of fetuses exposed to noise generated during an MR exam of the pregnant women[11] showed any deleterious effect on the fetal auditory system.

NST procedures can cause maternal anxiety regarding both the duration of the procedure and the probability of perceived abnormal results[12]. In NST, early reactivation is extremely important both for the patient and her psychology and for the decrease in the hospital stay, beside non-reactivation is very important for the fetus. Therefore, it seems necessary to use strategies to reduce false positive results to identify high-risk fetuses, patient waiting period, medical team and equipment time, and retrench diagnosis and treatment costs.

We aimed to investigate whether Doppler application will provide earlier reactivation in NST and increase fetal movements faster than in patients receiving bitter chocolate or non-intervention.

Materials and Methods

We selected our study group among the patients who came to the outpatient clinic for routine control at Ankara Etlik Zübeyde Hanım Training and Research Hospital and applied to NST between November 2018 and March 2019. The local institutional review board has approved the study (HEK 2018/46, 21/11/2018).

Single pregnancies between 36-41 weeks with non-reactive NST were included in the study. Patients with hypertension, intrauterine growth retardation, oligohydramnios, diabetes (gestational or pregestational), chocolate allergy, fetal anomaly and deceleration in NST were not included in the study.

Fetal heartbeat traces were interpreted by a single physician (HE). The physician (GK) who performed Doppler for all selected Non-reactive NST patients was the same. All traces were recorded by Philips Avalon

FM 30 fetal monitors. Reactive NST was defined as having 2 accelerations of 15 pulses or more, which lasted at least 15 seconds in a 20 minute NST. Patients with non-decelerated nonreactive NST were selected for the study, and consent was obtained as to whether patients would participate in the study.

We divided the selected patients into three groups: Doppler, chocolate and non-intervention control group. 90 patients from each group were written in envelopes by GK, including 1: 1: 1 ratio in three groups. A sample size of 242 was calculated as sufficient for 0.05 error margin and 95% power with G power 3.1.9.2 program. These envelopes were mixed and sealed and delivered to the physician (HE) interpreting NST. The patient with nonreactive NST selected his envelope from HE and brought it to the physician (GK), who would do whatever it takes, without opening the envelope. GK applied the necessary procedure to the patient regardless of which group appeared in the envelope. MCA Doppler was performed by GK in the Doppler group for 20 seconds (Voluson 730 Expert 4D Ultrasound Machine). He gave 50 gr of bitter chocolate to the chocolate group and was allowed to eat next to him (1927 special series nestle bitter chocolate with 60% Cocoa). Nothing was done to the control group. Patients were told not to eat anything else. Then, the patients were connected to NST by HE and the traces were examined in the 5^{th} minute. The procedure was terminated at 20^{th} minute in patients with reactive NST. NST evaluation was repeated at 30^{th} minute in patients with non-reactive NST. Patients were asked whether fetal movements increased. During this process, HE certainly did not know in which group the patients were. NST results were recorded as reactive and non-reactive. The patients whom second NST was non-reactive were hospitalized in the hospital delivery room for a biophysical profile and close follow-up. It was followed whether the hospitalized patients were taken into cesarean section due to fetal distress.

- *Statistical Analysis*

Average, standard deviation, median lowest, highest, frequency and ratio values were used in the descriptive statistics of the data. The distribution of variables was measured by Kolmogorov Simirnov test. In the analysis of quantitative independent data, Kruskal-Wallis and Mann-Whitney U tests were used. Chi-square test was used in the analysis of qualitative independent data. SPSS 22.0 program was used in the analysis.

Results

During this period, a total of 270 patients were randomized and 257 were evaluated for the final analysis. The 5^{th} minute reactive NST rate in the Doppler group was significantly higher than the non-intervention control and chocolate group ($p < 0.05$). In the non-intervention control and chocolate group, the 5^{th} minute reactive NST ratio did not differ significantly ($p > 0.05$). Although fetal movements were improved in the control, chocolate and doppler groups, respectively, there was no statistically significant difference ($p = 0.066$). (Table 1)

In the Doppler group whose NSTs were non-reactive in 30^{th} minute, fetal distress rate was significantly higher compared to the chocolate group and non-intervention controls ($p < 0.05$). (Table 2)

Discussion

NST maintains its importance in fetal monitoring due to its ease of performance and cost effectiveness. Khooshideh et al. showed that the sensitivity and specificity of NST to predict fetal distress are 62 and 42%, respectively, and the negative predictive value is 94%[13]. One of the handicaps of NST application is that it cannot control the incidence of hypoxic-ischemic encephalopathy and increases the

Table 1. Data comparisons among groups

		Non-intervention control group			Bitter Chocolate group			MCA Doppler group			
		Mean±s.d./n-%		Med	Mean±s.d./n-%		Med	Mean±s.d./n-%		Med	p
Gestational age		37.6 ± 1.1		38.0	37.7 ± 1.1		38.0	37.2 ± 1.0		37.0	0.008[K]
NST at 5. min	Reactive	47	55.3%		54	62.8%		79	91.9%		0.000[x2]
	Non-reactive	38	44.7%		32	37.2%		7	8.1%		
	Not perform	47	55.3%		54	62.8%		79	91.9%		
NST at 30. min	Reactive	8	9.4%		7	8.1%		0	0%		0.000[x2]
	Non-reactive	30	35.3%		25	29.1%		7	8.1%		
	Fetal distress	6	7.1%		6	7%		5	5.8%		
Non-reactive	Normal pregnancy follow-up	79	92.9%		80	93%		81	94.2%		0.935[x2]
Improving of fetal moving	Yes	66	77.6%		71	82.6%		78	90.7%		0.066[x2]
	No	19	22.4%		15	17.4%		8	9.3%		

Kruskal-wallis (Mann-whitnes u test)/[x2] Ki-kare test
NST; non-stress test, MCA; middle cerebral artery

Table 2. Fetal distress rates in patients with non-reactive non-stress test in the 30th minute.

		Non-intervention control group		Bitter Chocolate group		MCA Doppler group		P value
		n	%	n	%	n	%	
Non-reactive	Fetal distress	5	16.7%	5	10%	5	71.4	0.008[x2]
	Normal pregnancy	25	83.3%	20	40%	2	28.6	

[x2] Ki-kare test

rate of cesarean section in case of false positivity. One of the most important causes of earlier hospitalization and over-intervention is that false non-reactive NST is very common, and it is very difficult to identify true and false non-reactive[1].

There are many factors that affect reactivity in NST. The most common of these is fetal sleep period. However, fetal distress causes, such as fetal hypoxia, may also cause non-reactive NST in the early period. In this sense, if non-reactive NST is caused by a cause such as fetal hypoxia, it is of great importance to detect it as early as possible. Methods such as maternal glucose intake or mother's change of position are used in clinical practice for many years to increase the activity of the baby[6-7]. Orange juice and chocolate intake is often recommended for maternal glucose uptake[14]. Maternal serum glucose levels have been shown to be associated with NST patterns[15]. Another study showed that high cocoa (70% cocoa) in chocolate provides increased fetal movements and FHR reactivity[16]. McShea and his colleagues have shown that bitter chocolate improves cerebral blood flow[17]. However, there are publications stating that

maternal glucose concentration is not related to fetal activity and FHR patterns[15]. Esin and his colleagues found that orange juice provides more NST reactivation than chocolate[14].

Hasanpour and his colleagues found that acoustic stimulation, another factor other than glucose uptake, improved NST nonreactivity. Based on their findings, it can be concluded that with the feeding of mothers, more NST false cases can be identified than acoustic stimuli. However, when evaluated in terms of time, acoustic stimuli can be a better approach in most false positive cases and can determine test results within a minimum of time[18].

Kisilevsky and his colleagues showed that the maturation of the human fetal response to vibroacoustic stimulation started at the age of about 26 weeks of gestation[19]. In the study of Xi and his colleagues, when NST is applied to pregnant women without stimulation, 29.5% of NST is not reactive; however, when women were given advanced acoustic stimulation with flapping, 92.3% NST were observed to become reactive[1].

In a previous study, listening to music during the NST procedure increased the number of fetal movements, basal heart rate, and large accelerations, but decreased processing time and did not affect the suspected NST number[12].

Fetal ultrasonography has been shown to increase fetal movements[8]. Troyano et al. researched a method for the qualitative and quantitative evaluation of fetal reflex reactivity to external stimuli via the Doppler device. They suggested using this technique as a complementary in determining the moderate response of fetus to hypoxia[20]. Although there is a prominent increase in fetal mobility via Doppler stimuli, there are no prospective studies on the effectiveness of NST in this regard.

In current study, it was observed that Doppler exposure corrected the FHR pattern faster than chocolate. There was no difference between chocolate and non-intervention control groups. As a result, we found that Doppler application corrected the false positive Non-reactive NST of the fetus much more quickly. In addition, the rates of going to cesarean section due to fetal distress were strongly observed in the Doppler group in patients with non-reactivity at 30th minutes NST. Although an increase in fetal movements was observed in Doppler, chocolate and control groups, respectively, this increase did not show a statistically significant difference ($p = 0.066$). This may be secondary to inappropriate reporting of fetal movements due to the mother's lack of information for the concept of fetal movement.

The advantages of this study are its relatively large sample size, prospective and randomized nature. The most important limitation of the study is performing Doppler with a device, even if it is 20 seconds. With the recommendation of the FDA[21], health practitioners should always apply the “reasonably low enough” concept and minimize Doppler ultrasound use during pregnancy while maintaining diagnostic quality. Repetitive vibroacoustic stimulation applications in non-reactive NST cases may pose a risk for fetal safety. In addition, there is a cost created by this application and extra time allocated to the patient by the expert. Future researches’ with more cases with similar pregnancy risks by using more practical Doppler device (such as hand Doppler devices) will yield more practical and better results.

Conclusion

As a result, 20 second Doppler application corrects NST patterns much faster than bitter chocolate and non-intervention control group in the presence of a non-reactive NST. In addition, in patients who underwent Doppler, non-reactive NST ongoing cases are much more likely to go to cesarean section due to fetal distress than bitter chocolate and control group. With this result, we think that with the application of Doppler, the length of hospital stay and accordingly patient’s anxiety will reduce. In

addition, the patient should be monitored more carefully in terms of fetal distress because it quickly corrects false non-reactivity.

Author contributions

All authors contributed to the study conception and design. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

Funding

Authors declared no financial support.

Ethical approval

This study, in which patients participated on a voluntary basis, was conducted in accordance with all ethical procedures /standards and the Declaration of Helsinki.
The study was approved by the Ankara Etlik Zübeyde Hanım Training and Research Hospital Ethics Committee (HEK 2018/46, 21/11/2018).

References

1. Xi Q, Du J, Liu X, et al. Clinical study on detecting false non-reactive of non-stress test by improved acoustic stimulation. Arch Gynecol Obstet. 2011; 284 (2): 271-4. doi: 10.1007/s00404-010-1621-z
2. Black RS, Campbell S. Cardiotocography versus Doppler. Ultrasound Obstet Gynecol. 1997; 9 (3):148–51. doi: 10.1046/j.1469-0705.1997.09030148.x.
3. Suwanrath C, Suntharasaj T. Sleep-wake cycles in normal fetuses. Arch Gynecol Obstet. 2010; 281 (3): 449–54. doi: 10.1007/s00404-009-1111-3.
4. Paine LL, Strobino DM, Witter FR, et al. Population differences affect nonstress test reactivity. J Perinatol. 1991; 11 (1): 41–5.
5. Johnson MJ, Paine LL, Mulder HH, et al. Population differences of fetal biophysical and behavioral characteristics. Am J Obstet Gynecol. 1992; 166 (1): 138–42. doi: 10.1016/0002-9378(92)91847-4.
6. Esin S. Factors that increase reactivity during fetal nonstress testing. Curr Opin Obstet Gynecol. 2014; 26 (2): 61-6. doi: 10.1097/GCO.0000000000000050.
7. Miller FC, Skiba H, Klapholz H. The effect of maternal blood sugar levels on fetal activity. Obstet Gynecol. 1978; 52 (6):662–5.
8. Fatemi M, Ogburn PL Jr, Greenleaf JF. Fetal stimulation by pulsed diagnostic ultrasound. J Ultrasound Med. 2001; 20 (8): 883-9. doi: 10.7863/jum.2001.20.8.883.
9. Miller DL, Quddus J. Diagnostic ultrasound activation of contrast agent gas bodies induces capillary rupture in mice. Proc Natl Acad Sci. 2000; 97 (18): 10179-84. doi: 10.1073/pnas.180294397.
10. Nyman M, Barr M, Westgren M. A four-Year follow-up of hearing and develop-ment in children exposed in utero to vibroacoustic stimulation. Br J Obstet Gynaecol. 1992; 99 (8): 685-8. doi: 10.1111/j.1471-0528.1992.tb13856.x.
11. Reeves MJ, Brandreth M, Whitby EH, et al. Neonatal cochlear function: measurement after exposure to acoustic noise during in utero MR imaging. Radiology 2010; 257 (3): 802-9. doi: 10.1148/radiol.10092366.
12. Kafali H, Derbent A, Keskin E, et al. Effect of maternal anxiety and music on fetal movements and fetal heart rate patterns. J Matern Fetal Neonatal Med. 2011; 24 (3): 461-4. doi: 10.3109/14767058.2010.501122.
13. Khooshideh M, Izadi S, Shahriari A, et al. The predictive value of ultrasound assessment of amniotic fluid index, biophysical profile score, nonstress test and foetal movement chart for meconium- stained amniotic fluid in prolonged pregnancies. J Pak Med Assoc. 2009; 59 (7): 471–4.
14. Esin S, Baser E, Cakir C, et al. Chocolate or orange juice for non-reactive non-stress test (NST) patterns: a randomized prospective controlled study. J Matern Fetal Neonatal Med. 2013; 26 (9): 915-9. doi: 10.3109/14767058.2013.766698.
15. Phelan JP, Kester R, Labudovich ML. Nonstress test and maternal serum glucose determinations. Obstet Gynecol. 1982; 60 (4): 437–9.
16. Buscicchio G, Piemontese M, Gentilucci L, et al. The effects of maternal caffeine and chocolate intake on fetal heart rate. J Matern Fetal Neonatal Med. 2012; 25 (5): 528–30. doi: 10.3109/14767058.2011.636104.
17. McShea A, Ramiro-Puig E, Munro SB, et al. Clinical benefit and preservation of flavonols in dark chocolate manufacturing. Nutr Rev. 2008; 66 (11): 630–41. doi: 10.1111/j.1753-4887.2008.00114.x.
18. Hasanpour S, Raouf S, Shamsalizadeh N, et al. Evaluation of the effects of acoustic stimulation and feeding mother stimulation on non-reactive non-stress test: a randomized clinical trial. Arch Gynecol Obstet. 2013; 287 (6): 1105-10. doi: 10.1007/s00404-012-2695-6.
19. Kisilevsky BS, Muir DW, Low JA. Maturation of human fetal responses to vibroacoustic stimulation. Child Dev. 1992; 63 (6): 1497–508.
20. Troyano Luque JM, Maeda K, Kurjak A, et al. Fetal extremity kinetics quantified with Doppler ultrasonography. J Perinat Med. 2008; 36 (1): 82-6.

doi: 10.1515/JPM.2008.008.
21. U.S. Food and Drug Administration (FDA). Information for manufacturers seeking marketing clearance of diagnostic ultrasound systems and transducers. Rockville, MD: FDA; Sept 30, 1997.