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Oral glucose and breast milk as a strategy for pain reduction during the heel lance procedure in newborns

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Abstract

Introduction: **This paper presents the results of a study on pain reduction in newborns that undergo painful medical procedures. This research analyzed the reactions of babies before and after the heel lance procedure, a diagnostic test performed to detect phenylketonuria. This test involved the extraction of a capillary blood sample with a heel lance, a medical procedure that is painful for neonates.**

Objective: **The main objective of this research was to evaluate the effectiveness of a 24% oral glucose solution and breastfeeding during heal lance.**

Method: **An experimental study was thus conducted on a sample of 93 newborns in the San Cecilio University Hospital in Granada in 2010. The babies in the sample were divided into three groups, depending on what they ingested during the heal lance.**

Results: **The results obtained showed that there was an association between the difference in HR and the time before the newborn's HR returned to normal after the heel lance (r = 0.562; p = 0.000). Moreover, a positive relation was found between the absolute difference in HR and the difference in oxygen saturation (OS) (r = 0.538; p = 0.000).**

Conclusion: **The OS was found to be greater in the group of newborns that received breast milk.**

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Key words: *Oral glucose. Phenylketonuria. Breastfeeding. Pain. Newborn.*

GLUCOSA ORAL Y LECHE MATERNA COMO ESTRATEGIA PARA REDUCCIÓN DEL DOLOR DURANTE EL PROCEDIMIENTO DE PUNCIÓN DEL TALÓN EN RECIÉN NACIDOS

Resumen

Introducción: **Para la detección de la fenilcetonuria, se realiza la prueba diagnóstica que consiste en la extracción de una muestra de sangre capilar, mediante la punción del talón al recién nacido. Este proceder es muy doloroso para el neonato.**

Objetivo: **Valorar la efectividad de la administración de glucosa oral al 24 % y lactancia materna durante la punción del talón en el recién nacido.**

Método: **Se realizó un estudio experimental en una muestra de 93 recién nacidos del Hospital Clínico "San Cecilio" de Granada durante el año 2010. La muestra se distribuyó en tres grupos en función del tipo de ingesta administrada en la realización de la prueba del talón.**

Resultados: **El estudio pone de manifiesto que existe asociación en la diferencia de la FC con el tiempo transcurrido hasta alcanzar la normalidad después de la punción (r = 0,562; p = 0,000). También se halló una relación positiva entre la diferencia absoluta en la FC y la diferencia en la Saturación de Oxígeno (SO) (r = 0,538; p = 0,000).**

Conclusión: **La SO es mayor en el grupo de lactancia materna que en el resto; así como en el de glucosa oral 24% que en el de control.**

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Palabras clave: *Glucosa oral. Fenilcetonuria. Lactancia materna. Dolor. Recién nacido.*

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Introduction

Pain is the most frequent cause of suffering in small children. Throughout history, infant pain has not been properly treated. The lack of suitable treatment has been justified by assuming that the immaturity of the central nervous system made newborns less capable of perceiving, transmitting, or interpreting pain.[1] In fact, it was previously believed that neonates were insensitive to pain. However, research on foetal development and behaviour in newborns has shown that neonates suffer pain and respond to the stimuli that cause it[2].

Infant pain is a great challenge to health professionals as well as to parents. Newborns, particularly preterm newborns, are especially vulnerable to pain. In fact, at this age, babies are less able to control pain than at any other time of life. Fortunately, in the last ten years, there has been a growing interest in alleviating pain in neonates. The number of research studies in high-impact medical journals has soared. Furthermore, such pain is now the focus of important research projects and relevant studies are included in medical databases. However, despite important advances in the understanding of this phenomenon, a truly effective instrument still needs to be found for evaluating and treating pain in small children[3, 4].

According to the North American Nursing Diagnosis Association (NANDA), acute pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage (International Association for the Study on Pain). Such pain can vary in intensity. Although its onset can be gradual or sudden, its duration is generally shorter than six months[5]. Since 1960, all newborns have undergone early screening for phenylketonuria. This test is given to all babies after they are five days old and 48 hours after they have begun oral feeding. Phenylketonuria is diagnosed by means of a blood test, and the blood is obtained by pricking or lancing the newborn's heel. This procedure is extremely painful for the baby[6].

Various studies have shown that before performing the heel lance procedure, babies suffer less if they receive non-pharmacologic therapies to reduce the pain. The administration of oral glucose or sucrose shows statistically significant differences in comparison to the administration of pharmacologic therapies[7, 8].

There have been relatively few studies on the long-term secondary effects of sucrose ingestion in newborn babies. Studies in Madrid (Spain) show that adverse reactions were investigated in six research studies. Only 3% of the newborns suffered minor adverse reactions (choking or oxygen desaturation episodes with spontaneous recovery). There are no clinical studies on the effects of the repeated use of sucrose[9]. Without a doubt, these results support the use of this substance as an effective alternative for pain relief in newborns who must undergo mildly or moderately painful medical procedures.

Research has found that subjecting newborn babies to such procedures alters their heart rate, breathing rate, and oxygen saturation. However, newborn babies that receive non-pharmacologic treatment before a heel lance recover their vital signs (i.e. baseline) in a shorter time than babies that do not receive such therapy[10, 11].

Other studies have found that painful procedures cause children to suffer multisystemic disorders such as a collapsed lung (atelectasis), build-up of secretions, and hypoxaemia. At the vascular level, such procedures can alter heart and regional flow rates as well as increase oxygen consumption and vasoconstriction. Intracranial pressure can also increase in the brain, which can cause haemorrhages. After painful procedures, some newborns have even suffered muscle spasms and urinary and gastrointestinal alterations[12].

Gallegos and Salazar (2009) highlight the fact that babies who had invasive procedures suffered behaviour alterations. Generally speaking, they showed a greater tendency to cry, but were otherwise passive and disconnected from their surroundings. Symptoms also included a lack of facial expression without smiling, motility and sleep disorders, and even psychological and developmental regression. These babies also had little appetite and were prone to vomiting or spitting up food, which potentially slowed their growth and development because of malnutrition[13, 14].

Objective

Based on these research findings, we decided to conduct a study to evaluate the effectiveness of the administration of a 24% oral glucose solution and breast milk during the heel lance procedure for the diagnosis of phenylketonuria.

Materials and Method

This experimental study was carried out in 2010 in the neonatal care unit at the San Cecilio University Hospital in Granada. A random sample of n=93 newborns were taken from all the babies in this unit, who were required to undergo the heel lance procedure. The population sample for the study was randomly divided into three groups, depending on whether the infant ingested oral glucose or breast milk during the heal lance. Accordingly, the first group of newborns received breast milk; the second group was given a 24% oral glucose solution; and the third group, which was the control group, received nothing at all. The variables analysed were recovery to baseline values as reflected in crying and the normalisation of vital signs, number of heel punctures, oxygen saturation, heart rate, and blood pressure. All of these variables were analyzed before (baseline values) and after the heel lance procedure (post-lance values), as specified in the protocol.

Before performing the experiment, the parents of the babies were asked to give their informed consent to their children's participation in the study. The pain assessment scale in term and preterm newborns (Aguilar 2011) can be found in table I. The items of the questionnaire were considered appropriate, based on the criteria of 30 informants or judges. The degree of adequacy of each item corresponded to the percentage of informants that evaluated the item as appropriate. Afterwards, all of the percentages were added up, and then divided by the highest value if all of the informants considered that all of the items were valid. The value obtained was 0.775, which confirms the validity of the assessment scale. Consequently, this pain assessment scale was considered to be a reliable instrument for our study. The results were processed by using the chi-square test and Student's *t*-test in which the value p>0.05 was regarded as significant.

Results

Table II gives the linear association between quantitative variables. These variables include days in hospital, weight (gr), gestational age, recovery to baseline after the heel lance, difference in heart rate, and difference in oxygen saturation. A negative association was observed between days in the hospital and wei-

Table I

Scale VADONE. Pain assessment scale in the term and preterm newborn during painful procedures. Aguilar MJ. 2012.

FIRST ASSESSMENT **Days of Life** __ Aterm __ Preterm ___			SECOND ASSESSMENT **Days of Life** __ Aterm __ Preterm ___			THIRD ASSESSMENT **Days of Life** __ Aterm __ Preterm ___		
Blood Collection **Number of Punctures. 1___ 2___ 3___ Site of Puncture** _____			Peripheral IV Placement **Number of Punctures. 1___ 2___ 3___ Site of Puncture** _____			Heel Puncture **Number of Punctures. 1___ 2___ 3___ Site of Puncture** _____		
	B Sec.	PP Sec.		B Sec.	PP Sec.		B Sec.	PP Sec.
Observation of the Newborn Time in Seconds Heart Rate (FC)			**Observation of the Newborn Time in Seconds Heart Rate (FC)**			**Observation of the Newborn Time in Seconds Heart Rate (FC)**		
Observation of the Newborn Time in Seconds Respiratory Rate (FR)			**Observation of the Newborn Time in Seconds Respiratory Rate (FR)**			**Observation of the Newborn Time in Seconds Respiratory Rate (FR)**		
Blood Pressure (TA)			**Blood Pressure (TA)**			**Blood Pressure (TA)**		
SO2 Saturation			**SO2 Saturation**			**SO2 Saturation**		
Frowning Time in Seconds			**Frowning Time in Seconds**			**Frowning Time in Seconds**		
Tightly Closed Eyes. Time in Seconds			**Tightly Closed Eyes. Time in Seconds**			**Tightly Closed Eyes. Time in Seconds**		
Philtrum. Time in Seconds			**Philtrum. Time in Seconds**			**Philtrum. Time in Seconds**		
Uncoordinated Movements 15 sec YES or NO			**Uncoordinated Movements 15 sec YES or NO**			**Uncoordinated Movements 15 sec YES or NO**		
Audible Crying YES or NO			**Audible Crying YES or NO**			**Audible Crying YES or NO**		
Perspiration YES or NO			**Perspiration YES or NO**			**Perspiration YES or NO**		

The questionnaire was evaluated, based on the criteria of 30 informants or judges, who assessed each item as appropriate or inappropriate for the scale. In order to find the level of adequacy of the scale items we calculated the percentage of judges that assessed each item as appropriate. Subsequently, the percentages obtained were added up and divided by the highest value if all items that were considered valid by all judges. The value obtained was 0.775, which indicates the high validity of the scale. Consequently, this scale was considered to be a reliable instrument of evaluation.

B. **Basal** PP. **Post punture** Sec. **Secons**

ght (r = -0.243; p = 0.019), whereas there was a positive association between weight and gestational age (r = 0.723; p = 0.000). There was also a positive association between weight and difference in heart rate (r = -0.227; p = 0.029). Consequently, the absolute difference in the heart rate before and after the heel lance procedure decreased as the weight of the newborns increased. Absolute difference in heart rate was negative associated with gestational age (r = -0.234; p = 0.024). Accordingly, as the gestational age increased, the difference in heart rate became lower.

The association of the difference in heart rate with recovery to baseline was positive (r = 0.562; p = 0.000). This signified that an increase in the absolute difference in heart rate was associated with an increase in recovery to baseline after the heel lance. Similarly, a positive relation was found between absolute difference in the heart rate and difference in oxygen saturation (r = 0.538; p = 0.000).

Table III gives the means and typical deviations of the quantitative variables of the study for the complete sample as well as for each group. It also shows the F-test of the equality of variance to verify the equality of means, depending on the group. The results obtained show differences between the three groups in the heart rate after the heel lance (2;90) = 9.830; p = 0.000). Tukey's t-test showed that the mean heart rate of the newborns that ingested breast milk was lower than that of the control group and of the oral glucose group.

Table II
Linear association between variables

		Weight (g)	*Gestational age*	*Recovery to baseline*	*HR diff.*	*OS diff.*
Days in hospital	R		-0.127	-0.016	0.130	0.022
	p	0.019	0.224	0.876	0.215	0.836
Weight (gr)	R		0.723	0.020	-0.227	0.001
	p		0.000**	0.848	0.029*	0.990
Gestational age	R			-0.201	-0.234	-0.175
	p			0.053	0.024*	0.093
Recovery to baseline	R				0.562	0.775
	p				0.000**	0.000**
FC diff.	R					0.538
	p					0.000**

* p < 0.05; ** p < 0.01.

Table III
Descriptive statistics of quantitative variables and F-tests for the equality of means, depending on the group

	Mean (dt)					
	Total	*Breast milk*	*Control*	*24% oral glucose*	*F(gl)*	*p*
Days in hospital	6.8(1.8)	6.6(1.6)	6.4(2.0)	7.3(1.6)	2.660(2;90)	0.075
Weight (gr)	2767.3(359.2)	2738.1(463.1)	2781.6(298.9)	2782.3(300.7)	0.114(2;58.3)[1]	0.893
Gest. age (weeks)	37.1(1.4)	37.1(1.4)	36.9(1.2)	37.4(1.4)	1.309(2;90)	0.275
HR before	136.1(8.0)	133.6(8.0)	136.7(8.2)	138.0(7.2)	2.604(2;90)	0.080
HR after	142.8(9.0)	137.4(9.9)	145.3(7.4)	145.5(7.0)	9.830(2;90)	0.000*
OS before	96.8(1.4)	96.8(1.5)	97.2(1.4)	96.4(1.4)	2.295(2;90)	0.107
OS after	91.0(2.8)	93.6(1.7)	89.0(2.6)	90.4(1.6)	43.512(2;58.1)[1]	0.000*
Recovery to baseline (sec)	24.0(12.0)	11.9(2.0)	38.2(8.4)	21.9(2.0)	285.059(2;54.3)[1]	0.000*
HR difference	6.6(3.2)	3.8(3.5)	8.6(2.4)	7.5(1.0)	20.392(2;47.9)[1]	0.000*
OS difference	5.8(2.7)	3.3(1.0)	8.2(2.9)	6.0(1.0)	78.961(2;55.3)[1]	0.000*

[1]Robust tests of equality of means (Welch).
* p < 0.01

The F-test showed that the time lapsed until the recovery to baseline after the heel lance also depended on the substance ingested (F (2; 54.3) = 285.059; p = 0.000). The group of newborns that received breast milk recovered baseline values in a shorter time than the other two groups. In addition, the absolute difference in heart rate is in direct relation to the substance ingested (F (2;47.9) = 20.392; p = 0.000). The results obtained show that that this difference was again smaller than in the control group and the oral glucose group.

Finally, a dependence was observed between the difference in the OS and the substance ingested (F (2;55.3) = 78.961; p = 0.000). More specifically, the difference in OS was smaller in the breast milk group than in the other two. This difference was also smaller in the oral glucose group than in the control group.

Discussion

The results in Table 1 highlight the fact that there is an association between the HR and the recovery to baseline after the heel lance procedure. This is evidence that the pain caused by the heel prick modifies vital signs and also alters oxygen saturation.

Research carried out by Harrison (2009) verifies the effectiveness of oral glucose in the reduction of isolated episodes of severe pain caused by invasive procedures in newborn babies. This author studied the effectiveness of repeated doses of sucrose and concluded that the administration of this substance helped to alleviate pain in all of the procedures. Of course, the effectiveness of this measure depended on the seriousness of the baby's condition[7].

According to Saitua (2009), blood extraction during breastfeeding substantially reduced the time during which the baby cried as compared to other non-pharmacologic techniques[15]. Similarly, it has been shown that the analgesic effect of breastfeeding is more powerful than the effect of other methods such as the oral glucose, a pacifier, or restraint. All of the previously mentioned results appear to be related to the sweetness of breast milk, its high content in beta-endorphins, and/or the skin-to-skin contact between baby and mother that takes place during breastfeeding[16].

Brovedani (2007) suggests that breast milk complemented with sucrose ingestion could be even more effective than breast milk or sucrose by themselves to alleviate pain in newborns that must undergo invasive procedures. This study was also on neonates and the heel lance procedure[17]. Despite the fact that the Academy of Breastfeeding claims that the use of breastfeeding for pain reduction has not been fully investigated, it states that sucrose is an effective means of treating pain until the child is twelve months old[18].

There are various studies on the effect of sucrose in the nociceptive response of hospitalized newborn babies. The initial hypothesis is that breast milk is rich in endogenous opioids, which besides calming the nursing infant, act as immunomodulators. The ingestion of a sweet substance is effective when performing heel lances as well as for the removal of adhesive tape or any type of device that adheres directly to the skin. Oral sucrose given to low birthweight infants just before painful medical procedures seems to be a safe and effective way of alleviating pain, particularly when it is combined with sterilized water or the use of a pacifier[19].

The use of sucrose is the most widely studied non-pharmologic method. It was observed that it resulted in a lower score on the PIPP scale in comparison to the control group. It relieved pain through the liberation of endogenous opioids. The recommended dosage was between (24 weeks) and 2 ml (RNT) in 24-50% solutions to be administered orally (by syringe or sucking) or by a nasogastric tube two or three minutes before the procedure. Sucrose was found to be efficient in short painful medical procedures such as venipuncture, heal lance, and spinal tap. No adverse effects have been reported from the use of this substance[20].

The results of these studies coincide with our results, which reflect the effectiveness of the administration of oral glucose to alleviate pain in newborns during the heal lance procedure. Other references center their analyses on breast milk and its high endorphin content. Even though this study has not specified the beta-endorphin content of breast milk (since it was not the focus of our research), we would also like to mention that there is much research that highlights the analgesic properties of this substance.

Endorphins, which are the body's natural opiates, come in three types: alpha, beta, and gamma endorphins. They alleviate pain and produce a feeling of general well-being in the body. Their secretion is directly related to stimuli that have been crucial to the survival of the human race. During breastfeeding, the secretion of endorphins in the mother causes a dependence on these opioids, which is evidently a powerful stimulus to prolong breastfeeding. Furthermore, researchers have discovered the role of beta-casein in human breast milk, which is transformed into beta-casomorphin (of the endorphin family) in the intestine of the baby, and thus contributes to reinforce the bond between mother and child. It has also been found that caresses or skin-to-skin contact also liberate endorphins. This finding explains the use of skin-to-skin contact for infant pain relief during medical procedures[21].

The analysis of these references shows that direct skin contact, oral glucose administration, and breast milk all stimulate a cascade of neuro-hormonal-biochemical events that establish, consolidate, and perpetuate the affective bond between mother and child. Moreover, they also relieve pain in newborns that must undergo mildly or moderately painful medical procedures[22].

Conclusions

The results of the study described in this paper show that vital signs of newborns are significantly modified after the heel lance procedure and that the administration of breast milk helps to reduce pain and decrease the discomfort of the neonate. This is mostly due to the high content of beta-endorphins in breast milk. It has also been claimed that similar results are achieved when a 24% oral glucose solution is administered.

This article has shown that non-pharmacologic methods are the first therapeutic step in most mild or moderately painful procedures, and that these methods should thus be systematically used in healthcare practice. Our results on the analgesic properties of breast milk contribute to reinforcing the bond between mother and child and fomenting breastfeeding, not only because of the excellent nutritional properties of breast milk, but also because breastfeeding is an effective strategy for alleviating pain in newborn babies who must undergo painful medical procedures.

References

1. Aguilar Cordero MJ, Batran Ahmed SM, Padilla López CA, Guisado Barrilao R, Gómez García C. Lactancia materna en bebés pretérminos; cuidados centrados en el desarrollo en el contexto palestino. *Nutr Hosp*. 2012; 27(6): 1940-1944.
2. Aguilar Cordero MJ , González Jiménez E, Álvarez Ferre J, Padilla López CA, Mur Villar N, García López PA, Valenza Peña MC. Lactancia materna: un método eficaz en la prevención del cáncer de mama. *Nutr Hosp*. 2010; 25(6): 954-958.
3. Aguilar Cordero MJ. Tratado de Enfermería del niño y el adolescente. Cuidados Pediátricos. Elsevier 2012. ISBN: 978-84-8086-862-4.
4. Aguilar Cordero MJ. Lactancia Materna. Elsevier 2005. ISBN: 84-8174-768-8.
5. Cortes Castell E, Rizo-Baeza MM, Aguilar Cordero MJ, Rizo-Baeza J, Gil Guillén V. Maternal age as risk factor of prematurity in Spain; Mediterranean area. *Nutr Hosp*. 2013; 28(5): 1536-1540.
6. Shah V. Ohlsson A. Venopunción versus punción del talón para tomar muestras de sangre en recién nacidos a término (Spanish translation). In: La Biblioteca Cochrane Plus. 2008 No.4. Oxford: Update Software Ltd. Available at: http://www.update-software.com.
7. Harrison D; Loughnan P; Manias E; Gordon I; Johnston L. Repeated doses of sucrose in infants continue to reduce procedural pain during prolonged hospitalizations. *NursingResearch* 58(6): 427-34. 2009 Nov-Dec.
8. Slater R. Cornelissen L. Fabrizi L. Patten D. Yoxen J. Worley A. Boyd S. Meek J. Fitzgerald M.. Oral sucrose as an analgesic drug for procedural pain in newborn infants: a randomised controlled trial. *Lancet* 2010 Oct 9; 376(9748): 1225-32.
9. Aguilar Cordero MJ, Sáez Martín I, Menor Rodríguez MJ, Mur Villar N, Expósito Ruiz M, Hervás Pérez A, González Mendoza JL. Valoración del nivel de satisfacción en un grupo de mujeres de Granada sobre atención al parto, acompañamiento y duración de la lactancia. *Nutr Hosp*. 2013; 28(3): 920-926.
10. Obeidat H. Kahalaf I. Callister LC. Froilicher ES. Use of facilitated tucking for nonpharmacological pain management in preterm infants: a systematic review. *Journal of Perinatal and Neonatal Nursing* 23(4): 372-7. 2009 Oct- Dec.
11. Rizo MM. Escolano A. Oliver A. Salazar M. Aguilar MJ. Cortés A. Dolor en la toma de muestra de sangre en el recién nacido mediante la punción en el talón. *Rev Paraninfo Digital* 2008; 4. Available at: <http:/www.index-f.com/para/n4/p040.php>
12. Cortés E, Rizo-Baeza MM, Aguilar MJ, Hidalgo MJ, Gil V. Relación entre los ácidos grasos en suero y en los fosfolípidos de membrana en niños sanos. *Nutr Hosp*. 2013; 28(5): 1541-1545.
13. Gallegos Martínez J. SalasarJúerez M. Dolor en el neonato: Humanización del cuidado neonatal. *EnfNeurol* (Mex) Vol. 9 No. 1: 26-31. 2010.
14. Narbona López E. Contreras Chovas F. García Iglesias F. Miras Baldo MJ. Manejo del dolor en el recién nacido. Asociación Española de Pediatría. Protocolos actualizados del 2008. Available at: http://www.aeped.es/sites/default/files/documentos/49.pdf.
15. Saitua Iturriaga. Aguirre Unceta-Barrenechea. Suárez Zárate K. Zabala Oleachea. Rodríguez Núñez A. Romera Rivero MM. Efecto analgésico de la lactancia materna en la toma sanguínea del talón en el recién nacido. *An Pediatr* (Barc). 2009; 71(4): 310-313.
16. Díaz Gómez M. Prevención del dolor en el recién nacido. Intervenciones no farmacológicas. *AnPadiatrContin*. 2010; 8(6): 318-321.
17. Brovedani P. Montico M. Shardlow A. Strajn T. Demarini S. Suckling and sugar for pain reduction in babies. 2007. Available at: http://download.thelancet.com/pdfs/journals/lancet/PIIS0140673607606667.pdf.
18. Maya Bunik MD. Chantry CJ. Howard CR. Lawrence RA. Marinelli KA. Noble L. Powers NG. Taylor JS. ABM Clínica Protocolo Nº 23: Non-pharmacologic management of procedure-related pain in the breastfeeding infant. Academy of Breastfeeding Medicine Protocol Committee. Breastfeeding Medicine. Volume 5. Number 6. 2010ª Mary Ann Liebert. Inc. DOI: 10.1089/bfm.2010.9978.
19. Pérez Villegas R, Villalobos Alarcón E, Aguayo García K. Valoración y estrategias no farmacológicas en el tratamiento del dolor neonatal. *Rev Cubana Pediatr* 2006; 78(3).
20. Aguilar Cordero MJ, Vieite Ravelo M, Padilla López CA, Mur Villar N, Rizo Baeza M, Gómez García CI. La estimulación prenatal. Resultados relevantes en el periparto. *Nutr Hosp*. 2012; 27(6): 2102-2110.
21. Zanardo V, Nicolussi S, Favaro F, Faggian D, Plebani M, Marzari F, Freato F. Effect of postpartum anxiety on the colostral milk beta-endorphin concentrations of breastfeeding mothers. *J Obstet Gynaecol*. 2001; 21(2): 130-4.
22. Cortés E, Aguilar MJ, Rizo MM, Gil V, Hidalgo MJ. Ácidos grasos trans en la nutrición de niños con trastornos neurológicos. *Nutr Hosp*. 2013; 28(3): 1140-1144.