Original Article

OPEN ACCESS

Effect of Induction of Early Meconium Evacuation Using Glycerin Suppositories in Promoting Feeding Tolerance in Low Birth Weight Infants

Ambreen Fatima[1], Syeda Shireen Gul[2], Atiya Jogezai[3], Fasih Hashmi[4], Nadeem Ahmed[5]

[1]Postgraduate Resident, Neonatology Department PIMS Islamabad
[2]Assistant Professor Neonatology Department PIMS Islamabad
[3]Senior Registrar Paeds Department PIMS Islamabad, [4]Quality Enhancement cell AIOU Islamabad
[5]Neonatologist, Fauji foundation hospital Rawalpindi

Author`s Contribution

[1,2,3]Substantial contributions to the conception or design of the work; or the acquisition, Concept and design of the work, acquisition, Final approval of the study to be published, [4]Data Analysis, [5]Active participation in active methodology

Funding Source: None
Conflict of Interest: None

Received: Dec 13, 2022
Accepted: May 23, 2023

Address of Correspondent
Dr Ambreen Fatima
Postgraduate Resident,
Neonatology Department PIMS Islamabad
dr.ambreenfatima@gmail.com

ABSTRACT

Objective: To determine the effect of Induction of early meconium evacuation using glycerin suppository in promoting feeding tolerance in low birth weight infants.

Methodology: This quasi-experimental study was conducted in the Department of Neonatology at Pakistan Institute of Medical Sciences (PIMS) in Islamabad. A total of 120 neonates were included in both groups of the study. The control group received standard treatment, while the intervention group received standard treatment along with glycerin suppository. The data was analyzed using SPSS version 26. The independent sample t-test was used to compare the time to achieve full feed and the time to achieve complete evacuation of meconium between the two groups. A p-value of 0.05 was considered significant.

Results: The mean gestational age was 30.30±1.19 weeks. Out of 240, 127 (52.9%) neonates were male. All neonates included in the study have a very low birth weight range from 1 to 1.6 kg with a mean weight of 1.32±1.29 kg. The intervention group showed a significant low time to achieve full feed and low time to achieve complete evacuation of meconium 11.21±1.54 and 4.99±1.16 days as compared to the control group 12.73±1.46 and 5.97±1.1 days, with p value 0.000.

Conclusion: Glycerin suppository helps to reduce the time to achieve full evacuation of meconium.

Keywords: Full Enteral Feed (FEF), Glycerin Suppository, Meconium, Preterm Birth, Very Low Birth Weight (VLBW)

Cite this article as: Fatima A, Gul SS, Jogezai A, Hashmi F, Ahmed N Effect of Induction of Early Meconium Evacuation Using Glycerin Suppositories in Promoting Feeding Tolerance in Low Birth Weight Infants. Ann Pak Inst Med Sci. 2023; 19(2):135-140. doi. 10.48036/apims.v19i2.748

Introduction

Infants born with low birth weight are often susceptible to several diseases. They are at a higher risk of suffering from gastrointestinal (GI) problems, specifically Necrotizing Enterocolitis (NEC), Spontaneous Intestinal Perforation (SIP), Focal Intestinal Perforation (FIP), and Meconium-Related Ileus (MRI).[1]

Recently, the prevalence of surgical MRI has considerably increased. Contrast enema medication has been suggested as an efficient solution for MRI disease, but some research studies have reported that this treatment can lead to complications such as intestinal perforation, NEC, shock, and, occasionally, death of the infant.[2]

The pathogenesis of MRI involves immature or ineffective peristalsis of the fetal intestine, leading to excessive water absorption.[3] This results in difficulties passing meconium, causing feeding intolerance, bilious vomiting, and progressive abdominal distension. Delayed enteral nutrition can lead to intestinal membrane atrophy, reduced absorption rates, and compromised barrier function of the intestinal mucosa, hindering nutrient absorption.[4]

In-time detection of risk factors can assist in early diagnosis and starting proper medication and treatment. This condition affect the small intestine of the patient. Some of these risk factors include extreme prematurity and low birth weight (less than 1500 g), as well as perinatal comorbidities such as gestational age, maternal high blood pressure, preeclampsia/eclampsia, maternal diabetes, delayed intrauterine growth, placental abruption, cesarean section, and prenatal magnesium sulfate, which can have depressive effects on intestinal smooth muscle cells.[5]

Typical clinical symptoms of the disorder, however, include swelling in the abdominal section of the patient's body with marked bowel loops, vomiting, and sometimes a yellowish-green fluid. Various examination tests have been used for the diagnosis of this disorder, such as plain X-rays, ultrasound scans of the abdominal section, and contrast medium enema. Moreover, blood tests are reported to be inefficient in diagnosing this disorder.[6]

No preventive type of treatment is used or suggested for this disorder in the literature. Glycerin suppositories, osmotic contrast and physiological enemas are used or recommended in clinical studies.[7] Some oral techniques i.e. administration of PEG and acetylcysteine is quite common. PEG is an osmotic laxative which is testified to be safe and extensively established over the period of time to treat the constipation problem in the infancy.[8] Apart from theses treatment techniques, physical treatment methods are also used. Among physical interventions, abdominal massage and rectal stimulation are reported to be the good methods for treating this problem.[9]

In many Neonatal Intensive Care Units (NICUs), spontaneous meconium passage in preterm infants is significantly delayed compared to term infants. As a result, treatment is typically initiated within the first three postnatal days and administered multiple times.[10]

The rationale of the study is to investigate the effect of inducing early meconium evacuation using glycerin suppositories in promoting feeding tolerance in low birth weight infants.

Methodology

This quasi-experimental study was planned in the Department of Neonatology at Pakistan Institute of Medical Sciences (PIMS) in Islamabad from August and November 2022.The selection of neonates was made after obtaining ethical approval for the study from the ethical approval board. Written informed consent was obtained from the parents/caregivers of the neonates.

The sample size of the study was calculated based on the statistics mentioned in the reference study by Khadr et al.[11] The results showed that the time to achieve full feed in the control group was 9±2.2 days, whereas in the second group, where neonates were treated with glycerin suppository, the time to achieve full feed was 7.4±6.6 days. With a confidence level of 95% and a power of test of 80%, a minimum sample size of 120 was taken in each group, resulting in a total sample size of 240 for this study.

Neonates who were born prematurely before 32 weeks (preterm) and had a very low birth weight of less than 1.5 kg were included in our study. Neonates with major congenital malformations, known cases of metabolic disease, hemodynamic instability with features of shock, and suspected/confirmed coagulopathy were excluded from this study.

Half of the neonates included in the study were treated with standard treatment, while the intervention group received a 500mg glycerin suppository in addition to standard care, administered by the head nursing staff. Express breast milk feeding was initiated for clinically stable neonates, while formula milk through an orogastric tube was started for clinically unstable neonates or in cases of unavailability/inadequate mother's milk. Initially, this feeding regimen started at 10ml/kg and was gradually increased to 20ml/kg with an interval of 2 hours. This feeding policy remained unchanged in both groups. Routine laboratory investigations were performed to prevent infections during the study in suspected cases.

A complete history of the neonate, including gestational age, mode of delivery, age of the neonate at the start of the study, neonate's sex, birth weight, and feeding type, was recorded. The data were analyzed using SPSS version 26. An independent sample t-test was used to compare the time to achieve full feed and the time to achieve complete evacuation of meconium between the two groups. Neonatal sex, mode of delivery, and feeding type were used for stratification. A p-value of 0.05 was considered significant.

Results

A total of 240 preterm neonates were evaluated and equally divided into two groups. The distribution of mode of delivery of neonates with their gestational age and gender is shown in figure 1 & 2.

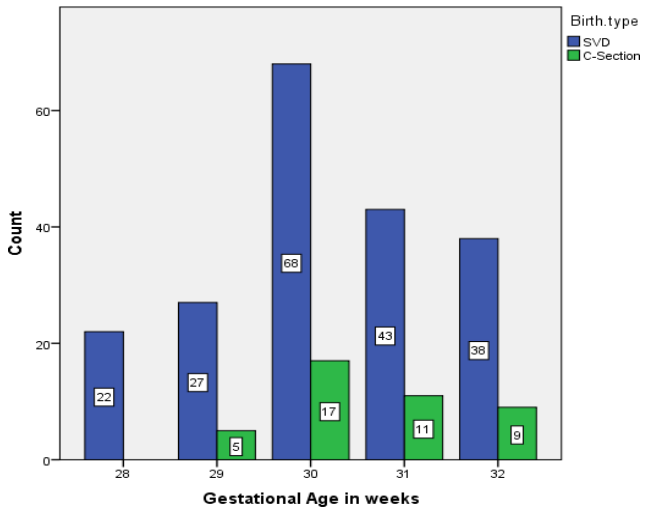

Figure 1. Relationship of gestational age of neonate with respect of birth type.

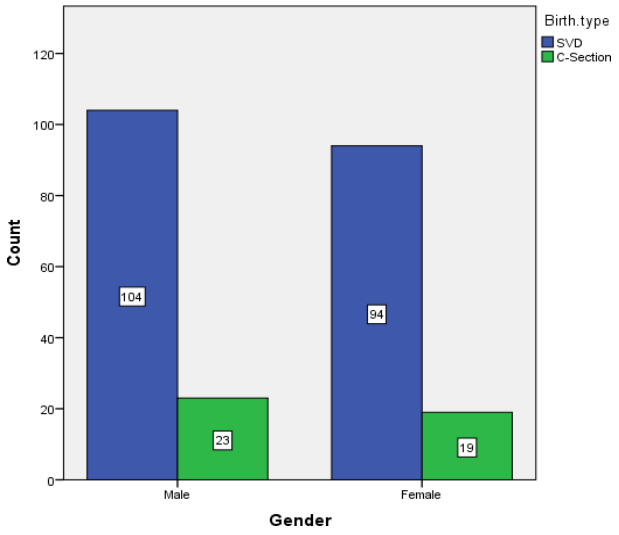

Figure 2. Relationship of neonate gender with birth type.

The proportions of neonates having the mode of delivery SVD and C-section were not statistically different between the two study groups (p-value = 0.497). Similarly, the percentage of male neonates was not significantly different between the two groups (54.2% vs. 51.7%, p-value = 0.698). The mean gestational age and birth weight were also not significantly different between the two study groups (p-value = 0.746 and 0.274, respectively). In the glycerin suppository group, 45.8% of neonates were exclusively on breast milk, while only 15% of neonates in the control group were on breast milk only. The proportion of neonates exclusively on breast milk was significantly different between the two groups (p-value = 0.000). Additionally, the mean age of neonates included in the glycerin suppository group was significantly lower compared to the mean age of neonates in the control group (p-value = 0.002). Both neonatal age and feed type were used as stratification factors to compare the actual effect of glycerin suppository (Table I).

The results showed that glycerin suppository significantly reduced the number of days to achieve full feed and complete evacuation of meconium compared to the control group (p-value = 0.000 for both). In the post-stratification analysis with respect to feed type, glycerin suppository showed significantly better results, with a significantly shorter time to achieve full feed and complete evacuation of meconium in neonates who were on formula milk + breast milk (p-value = 0.000 for both). In neonates exclusively on breast milk, glycerin suppository treatment resulted in a significantly shorter time to achieve full feed (p-value = 0.02), while the average time to achieve complete evacuation of meconium was slightly better but not significantly different compared to the control group (p-value = 0.249). The results showed that glycerin suppository treatment was equally effective for neonates on either breast milk alone or a combination of formula milk and breast milk (Table II).

To test the effect of neonatal age we used bivariate correlation between study outcome and neonatal age. The result showed that neonatal age was not correlated with the outcome “day to achieve full feed” with correlation coefficient 0.077 with p value 0.232. The result was not different when we observe the relation separately between two groups showed correlation -0.05 with p value 0.588 and 0.029 with p value 0.75 in glycerine suppository and in control group respectively. Similarly,

Table I: Comparison of groups with respect of demographic characteristics.

Characteristics	Categories	Glycerin Suppository	Control	P value
Mode of Delivery	Spontaneous Vaginal Delivery	97 (80.8)	101 (84.2)	0.497
	C-Section	23 (19.2)	19 (15.8)	
Gender	Male	65 (54.2)	62 (51.7)	0.698
	Female	55 (45.8)	58 (48.3)	
Feed	Formula milk + Breast milk	65 (54.2)	102 (85)	0.000
	Breast milk only	55 (45.8)	18 (15)	
Gestational age (mean± standard deviation)		30.28±1.19	30.33±1.20	0.746
Neonatal age (mean± standard deviation)		2.91±0.62	3.14±0.52	0.002
Birth weight (mean± standard deviation)		1.31±0.13	0.133±0.13	0.274

Table II: Comparison of study outcome between groups.

Feed type	Groups	Day to achieve full feed	Day to achieve complete evacuation of meconium
Formula milk + Breast milk	Glycerin Suppository	11.05±1.64	4.77±1.21
	Control	12.78±1.38	6.03±1.04
	p value	0.000	0.000
Breast milk only	Glycerin Suppository	11.40±1.41	5.25±1.04
	Control	12.39±1.88	5.61±1.38
	p value	0.02	0.249
Overall	Glycerin Suppository	11.21±1.54	4.99±1.16
	Control	12.73±1.46	5.97±1.1
	p value	0.000	0.000

the result showed that neonatal age was not correlated with the outcome "day to achieve complete evacuation of meconium" with correlation coefficient 0.047 with p value 0.465. The result was not different when we observe the relation separately between two groups showed correlation -0.06 with p value 0.518 and -0.006 with p value 0.945 in glycerine suppository and in control group respectively. These non-significant correlations indicate that the results of both groups were not influenced by neonatal age, which was significantly different between them.

Discussion

The administration of orally applied contrast agents was observed to be the second most commonly used method for treating the meconium obstruction problem. However, it is often applied when a single, rarely repeated, therapeutic or diagnostic procedure is needed, especially when all other treatment techniques to mobilize meconium have failed.[12]

High osmolar contrast agents are provided to the infant if the problem persists beyond the first 24 hours of neonatal life. However, no significant difference in the prevalence rate of NEC was observed between the users of high vs. low osmolar contrast agents.[13]

In more than 90 percent cases, meconium is passed by newborns easily within 24 to 48 hours. Passage of meconium is usually observed to be delayed in case of preterm infants. However, in case of very low birth weight infants, this phenomenon is more prevalent.[14] In our study the mean age of infants admitted in NICU was 3.02±0.59 days which strengthen the above phenomenon. Enema solutions include saline, glycerin, mixtures thereof, and contrast agents areused against this disorder.[15]

In a 7-year cohort analysis conducted in the Neonatal Intensive Care Unit (NICU) of Tubingen University Children's Hospital, the researchers compared 141 neonates treated with enema to 55 neonates treated without enema. The results showed a significant difference in the average day of life of the first meconium, average day of life of the first transition stool, average day of life of the first normal stool, and average day of life to achieve full enteral feed (p-value = 0.001 for all outcomes).[16]

In a small clinical trial of 30 neonates, the result showed a very satisfactory results with respect of full enteral feed. Out of 30, 26 (86.67%) neonates reached full enteral feed without any adverse event. Out of remaining 4 (13.33%) neonates, 3 (10%) were affected from rectal bleeding and one neonate assigned to active treatment developed necrotizing enterocolitis.[17]

In another study, the researchers compared the outcome of two groups G1: Treated with glycerin suppository and G2: Treated with standard protocol (control). The study group showed a better result with respect of time to pass first meconium with an average of 1.4 days versus 3.7 days with p value 0.001 and time to achieve full enteral feeding with a hazard ratio of 2.9. The stratification of the result with respect of infant birth weight was more significantly differentagainst the infants <1000 gm with a hazard ratio of 4.6.[18]

In our study, the neonates treated with glycerin suppository showed a better response and the time to achieve full feedand time to achieve complete evacuation of meconium was significantly less as compared to the control group with pvalue 0.000.

Contrary to this, in a specific to the very low birth weight infant meta-analysis, the researcher included only 3 studiesspecific to the very low birth weight of infant. The researcher concluded that glycerin suppository is not helpful to reduce the time to achieve full enteral feed in very low birth weight infants.[19]

In an open-label pilot study, the researchers compared the outcome of rectal washout and glycerin suppository to reachfull enteral feed in preterm, low birth weight infants. The results showed that the infants treated with rectal washout have a significant shorter median time to reach full enteral feed 11 days as compared to the infants treated with glycerinsuppository 15.6 days, with p value 0.027. They

also stratified the results with respect of birth weight and found that both treatments were equally effective for neonates having very low birth weight 10.2 vs. 10.1 days with p value 0.304.[20]

In a meta-analysis, the researchers found that different clinical trials showed either way results of efficacy of glycerin suppository. Earlier initiation of stooling was significantly earlier in neonates treated with a glycerin suppository, with p value 0.02. Another trial included in the meta-analysis showed that the average of earlier evacuation of meconium was not significantly improve with a glycerin suppository, with a p value 0.11. Similarly, the meta-analysis concluded that the intervention is not very effective for the transition to enteral feeding, which is on average just 0.7 days faster than the control group with a p value 0.43.[21]

In an Indian study, conducted in an arm forces hospital in Delhi, the researchers included 50 preterm very low birth weight neonates and divided in two groups treated with glycerine suppository and a control group. The result showedthat the mean duration of full enteral feed was 11.1±1.31 days in intervention group as compared to the control group11.9±2.8 days with p value 0.2.[22] The same result showed in another Indian trial that the mean time to achieve full enteral feed with intervention group 11.9±3.1 days which was not statistically significant with control group 11.33±3.57 days with p value 0.58.[23]

A meta-analysis consisting of 12 clinical trials with 1879 infants was conducted in 2019. The results showed that formula-fed infants exhibited better growth in terms of weight gain, linear growth, and head growth compared to infants on donor breast milk.[24]

In our study, the results changed after stratifying the sample based on feed type. The intervention of glycerin suppository was significantly effective for the complete evacuation of meconium in neonates who were on a combination of formula feed and breastfeed (p-value = 0.000). However, the intervention was not significantly effective for neonates who were exclusively breastfed (p-value = 0.249).

In a detail analysis included 13 NICU consisting 2947 infants of very low birth weight the time to reach full enteral feed was varied between 8-33 days which was due to spread of the samples containing 5 continents. The result showedthat the average time to achieve full enteral feed was comparatively high in units from China 26 days as compared tothe other infants 11days.[25]

Recently, researchers plan with a larger sample to study the merits and demerits of early achieve of full enteral feed versus progressive approach for enteral feed in preterm low birth weight infants. They also plan to stratify their findings with respect of type of feed and compare the main outcome between infants on formula feed and on human milk.[26]

Conclusion

Our study demonstrates that the use of glycerin suppositories is effective in reducing the time to achieve full enteral feed and promoting early evacuation of meconium in low birth weight infants.

Limitations of Study: The limitation of the study is that it is a single center study.

Recommendations: There should be plan a relatively massive study included different centers from differentprovinces of the country so that analyze the data to decide the effect of intervention and stratified the results with confounders.

References

1. Okuyama H, Ohfuji S, Hayakawa M, Urushihara N, Yokoi A, Take H, et al. Risk factors for surgical intestinal disorders in VLBW infants: case-control study. Pediatr Int. 2016; 58(1):34-9. https://doi.org/10.1111/ped.12815
2. Hasan MS, Mitul AR, Karim S, Ferdous KM, Islam MK. Comparison of t tube ileostomy and bishop koop ileostomy for the management of uncomplicated meconium ileus. J Neonatal Surg. 2017; 6(3):56. https://doi.org/10.21699/jns.v6i3.617
3. Byun J, Han JW, Youn JK, Yang HB, Shin SH, Kim EK, et al. Risk factors of meconium-related ileus in very low birth weight infants: patients-control study. Scien Rep. 2020; 10(1):1-6. https://doi.org/10.1038/s41598-020-60016-3
4. Song WS, Yoon HS, Kim SY. Clinical and growth outcomes after meconium-related ileus improved with Gastrografin enema in very low birth weight infants. PloS one. 2022; 17(8):e0272915. https://doi.org/10.1371/journal.pone.0272915
5. Kwon HS, Jung JM, Lim YJ, Nam SH, Lim G, Chung ML. Impact of meconium obstruction-related risk factors on surgical intervention in very low birth weight infants. Neonatal Med. 2015; 22(2):84-91. https://doi.org/10.5385/nm.2015.22.2.84
6. Solaz-García AJ, Segovia-Navarro L, de Dios-Benlloch JR, Benavent-Taengua L, Castilla-Rodríguez DY, Company-Morenza MA. Prevention of meconium obstruction in very low birth weight preterm infants. Enfermería Intensiva (English ed.). 2019; 30(2):72-7. https://doi.org/10.1016/j.enfie.2019.04.003

7. Deshmukh M, Balasubramanian H, Patole S. Meconium evacuation for facilitating feed tolerance in preterm neonates: a systematic review and meta-analysis. Neonatology. 2016; 110(1):55-65. https://doi.org/10.1159/000444075
8. Leung AK, Hon KL. Paediatrics: how to manage functional constipation. Drugs in Context. 2021;10. https://doi.org/10.7573/dic.2020-11-2
9. Yarkin Y, Maas C, Franz AR, Kirschner HJ, Poets CF. Epidemiological study on intestinal volvulus without malrotation in VLBW infants. Arch Dis Childhood-Fetal Neonatal Ed. 2019; 104(4):F415-8. https://doi.org/10.1136/archdischild-2018-315282
10. Bekkali N, Hamers SL, Schipperus MR, Reitsma JB, Valerio PG, Van Toledo L, Benninga MA. Duration of meconium passage in preterm and term infants. Arch Dis Childhood-Fetal Neonatal Ed. 2008; 93(5):F376-9. https://doi.org/10.1136/adc.2008.138024
11. Khadr SN, Ibhanesebhor SE, Rennix C, Fisher HE, Manjunatha CM, Young D, et al: Randomized controlled trial: impact of glycerin suppositories on time to full feeds in preterm infants. Neonatology 2011; 100: 169-176. https://doi.org/10.1159/000323964
12. Mitani Y, Kubota A, Goda T, Kato H, Watanabe T, Riko M, Tsuno Y, Kumagai T, Yamaue H. Optimum therapeutic strategy for meconium-related ileus in very-low-birth-weight infants. J Ped Surg. 2021; 56(7):1117- 20. https://doi.org/10.1016/j.jpedsurg.2021.03.029
13. Gross M, Hummler H, Haase B, Quante M, Wiechers C, Poets CF. Interventions for Promoting Meconium Passage in Very Preterm Infants-A Survey of Current Practice at Tertiary Neonatal Centers in Germany. Children. 2022; 9(8):1122. https://doi.org/10.3390/children9081122
14. Lange M, Figura Y, Böhne C, Beske F, Bohnhorst B, Heep A. Management of prolonged meconium evacuation in preterm infants: A survey-based analysis in German Neonatal Intensive Care Units. Acta Paediatr. 2022 Nov;111(11):2082-2089. doi: 10.1111/apa.16528
15. Burchard PR, Lay R, Ruffolo LI, Ramazani SN, Walton JM, Livingston MH. Glycerin Suppositories and Enemas in Premature Infants: A Meta-analysis. Pediatrics. 2022; 149(4): e2021053413 https://doi.org/10.1542/peds.2021-053413
16. Gross M, Poets FC. Lipid enemas for meconium evacuation in preterm infants - a retrospective cohort study. BMC Pediatr. 2021; 21: 454. https://doi.org/10.1186/s12887-021-02905-8
17. Livingstone MH, Elliott T, Williams C, Jones SA, Rosenbaum PL, Walton JM. Glycerine suppositories used prophylactically in premature infants (supp): A pilot randomized control trial. J Neonatal Perinatal Med. 2020; 13(4): 495-505. https://doi.org/10.3233/NPM-190310
18. Shim SY, Kim HS, Kim DH, Kim EK, Son DW, Kim BI, et al. Induction of early meconium evacuation promotes feeding tolerance in very low birth weight infants. Neonatol. 2007; 92(1): 67-72. https://doi.org/10.1159/000100804
19. Anabrees J, Shah VS, AlOsaimi A, AlFaleh K. Glycerin lexatives for prevention or treatment of feeding intolerance in very low birth weight infants. Cochrane Database Syst Rev. 2015; 9: CD010464. https://doi.org/10.1002/14651858.CD010464.pub2
20. Ibrahim T, Wei CL, Bautista D, Sriram B, Fay LX, Rajadurai VS. Saline enemas versus Glycerin suppositories to promote enteral feeding in premature infants: A pilot randomized controlled trial. Neonatol. 2017; 112(4): 347- 53. https://doi.org/10.1159/000477999
21. Livingston MH, Shawyer AC, Rosenbaum PL, Williams C, Jones SA, Walton JM. Glycerin enemas and suppositories in premature infants: a meta-analysis. Pediatr. 2015; 135(6): 1093-106. https://doi.org/10.1542/peds.2015-0143
22. Gupta AK, Tomar RPS, Surendran S. Effect of glycerine suppository in achieving early full feeds in premature infants: A randomized controlled trial. Ind J Neonat Med Res. 2019; 7(4): 6-10. https://doi.org/10.7860/IJNMR/2019/43478.2260
23. Shinde S, Kabra NS, Sharma SR, Avashti BS, Ahmed J. Glycerine Suppository for promoting feeding tolerance in preterm very low birth weight neonates: A randomized controlled trial. Ind Pediatr. 2014; 51: 367-70. https://doi.org/10.1007/s13312-014-0418-8
24. Quigley M, Embleton ND, McGuire W. Formula versus donor breast milk for feeding preterm or low birth weight infants. Cochrane Database Syst Rev. 2019; 7: CD002971. https://doi.org/10.1002/14651858.CD002971.pub5
25. De-Waard M, Li Y, Zhu Y, Ayede AI, Berrington J, Bloomfield FH, et al. Time to full enteral feeding for very low-birth-weight infants varies markedly among hospitals worldwide but may not be associated with incidence of necrotizing enterocolitis: The NEOMUNE-Neo-NutriNet cohort study. J Parenter Enteral Nutr. 2019; 43(5): 658-67. https://doi.org/10.1002/jpen.1466
26. Walsh V, Brown JVE, Copperthwaite BR, Oddie SJ, McGuire W. Early full enteral feeding for preterm or low birth weight infants. Cochrane Database Syst Rev. 2020; 3: CD013542. https://doi.org/10.1002/14651858.CD013542