EFFECT OF ENTERAL BOVINE LACTOFERRIN ON NEUROBEHAVIORAL PERFORMANCE OF PRETERM INFANTS

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ABSTRACT:

Background: *Preterm neonates benefit from the anti-infective properties and the ability to enhance cognitive development of breast milk. Breast milk contains a glycoprotein called lactoferrin which possesses antibacterial, anti-inflammatory, and immunomodulatory properties. Lactoferrin contains two molecules of sialic acid and iron, which are essential for the infant's early neurodevelopment and cognitive function.*

Aim of the work: *To study the effect of enteral administration of bovine lactoferrin on the neurobehavioral performance of preterm neonates at 36 weeks corrected gestational age.*

Patients and methods: *This double-blinded randomized controlled study was conducted on 80 preterm neonates admitted to NICUs, Ain Shams University hospitals, over a period of 6 months. On starting trophic feeding, neonates were randomized, to either receive enteral bovine lactoferrin (Lactoferrin group) or placebo (Control group), for a minimum of 2 weeks or till 36 weeks corrected gestational age whatever comes later. Neonatal Intensive Care Unit Network Neurobehavioral Scale (NNNS) was conducted at 36 weeks corrected gestational age,*

Results: *At 36 weeks of corrected gestational age, there was no statistically significant difference in the neurobehavioral performance between lactoferrin group and control group. Lactoferrin group had significantly shorter duration of respiratory support than control group (mean ± SD 4.70 ± 1.80 vs. 7.10 ± 2.13 days respectively), shorter duration to reach full volume of enteral feeding (mean ±SD: 7.15 ± 1.88 versus 8.38 ± 1.66 days respectively, P:0.003) and shorter duration of septic episode (mean±SD 4.50 ± 0.97 versus6.62 ± 1.19 days respectively, P<0.001).*

Conclusion*: Bovine lactoferrin did not affect the neurobehavioral performance of preterm neonates at 36 weeks corrected gestational age. Intake for longer duration, follow up for longer time should be furtherly studied.*

Keywords: *Bovine Lactoferrin; Neurobehavioral Performance; Preterm Neonates.*

INTRODUCTION:

Over 15 million infants are born preterm with gestational age less than 37 weeks worldwide. Special consideration to their neurodevelopment is being sought nowadays [(1)]

Lactoferrin is one of the members of the transferrin class of glycoproteins and has 703

amino acid residues that bind iron at the amino acid level. It is more than 60% similar to transferrin at the amino acid level, and there is 77% similarity between the human and bovine species [(2)].

In human milk, the most prevalent glycoprotein is called lactoferrin. At the terminal position of N-linked glycan chains, it has one to four sialic acid residues for every lactoferrin molecule [(3)]. Because polysialic acid modulates the sticky capacity of neuronal molecule adhesion, it plays an essential part in neural development and is consequently associated with a variety of morphogenic events, such as cell migration, neuronal outgrowth, pathfinding, sprouting, regeneration, synaptic plasticity, and serving a "reservoir function" for neurotrophic factors. Sialic acid is a key monomeric building block of poly Sialic acid, which plays crucial roles in cell-to-cell interactions, neuronal outgrowth, modifying synaptic connectivity, and memory formation [(4)].

Bovine Lactoferrin has a strong affinity to binding iron, which is a crucial aspect of its functionality [(5)]. Bovine Lactoferrin controls the body's ability to absorb iron from food, which is necessary for healthy brain growth and development. The three processes that iron deficiency impacts the most throughout early neurodevelopment of the brain are: myelination, neurotransmitter function, and neuronal metabolism [(6)].

The incidence of preterm births has increased in most nations and due to an improved survival rate of children born preterm, these preterm infants are susceptible to infections, inflammation, and oxidative stress, and this may lead to life-threatening illnesses including sepsis, periventricular leukomalacia, premature encephalopathy, bronchopulmonary dysplasia, or necrotizing enterocolitis. Additionally, these disorders increase the chance of developing neurodevelopmental problems later on [(7)].

Human milk contains significant levels of lactoferrin, and following oral administration of bovine lactoferrin, the level increases a lot. Its transit from blood to cerebral and peripheral tissue is tightly controlled by binding sites on brain endothelial cells. It also appears to have the ability to decrease inflammation in several illnesses. Consequently, bovine lactoferrin is probably going to have beneficial effects on the developing brain as well as following perinatal brain injury [(8&9)].

AIM OF THE WORK:

To study the effect of enteral administration of bovine lactoferrin on the neurobehavioral performance of preterm neonates at 36 weeks corrected gestational age.

PATIENTS AND METHODS

This double-blinded randomized controlled clinical trial was conducted in the Neonatal intensive care units (NICUs) of Ain Shams University hospitals over a period of six months starting at January 2021 till July 2021.

Sample size: Using pass11 program for sample size calculation, setting power at 80% and alpha error at 5%, results from relevant study (RA EL-Farrash et al, 2019) revealed that the least statistical significance difference between the intervention and control group regarding different NNNS score was the non-optimal reflex score as it was 2.6± 0.68 Vs 3.20± 0.62 in the intervention and the control group respectively. Based on these a sample size of 80 infants (40/group) is sufficient to achieve the study objectives.

This study included 80 stable preterm neonates less than 35 weeks gestational age, and less than 72 hours of age at randomization, who had started enteral feeding, and reached 12ml/kg/day, and were randomized to either of the two groups by

simple randomization using closed envelopes.

Neonates with a history of perinatal hypoxia, a family history of cow milk allergy, neonates with severe congenital abnormalities, neonates with chromosomal abnormalities, neonates with structural brain anomalies, or neonates with other predisposing conditions that profoundly affect growth and development were also excluded also as were neonates with evidence of feeding difficulties or formula intolerance, such as vomiting or poor intake.

The Lactoferrin group included 40 preterm neonates, who received enteral bovine lactoferrin with their daily feds. Feeding was increased according to the neonate's tolerance. *Pravotin sachet HYGINT Pharmaceutics* was used, which contains bovine lactoferrin 100mg per sachet, a daily dosage of 150 mg per day was administered orally or by nasogastric tube. After mixing 4 mL of sterile water with the contents of the sachet, daily dose was given for at least two weeks, or until the preterm achieved 36 weeks of corrected gestational age whatever came later.

Forty preterm newborns with gestational age, gender and weight matched to the first group, not receiving bovine lactoferrin were included in the **control group** and received equivalent amount of distilled water as placebo with their feds.

Neonates in both groups were fed according to NICU protocol to receive breast milk when available or preterm formula (with no lactoferrin fortification) guided by tolerance and volume of feds. Time taken to reach full feeding was recorded in both groups.

All included neonates were subjected to full history taking including gestational age birth weight, gender, mode of delivery, Apgar score, resuscitative data, need for mechanical ventilation, maternal diseases during pregnancy, and premature rupture of membranes. Thorough physical examination, anthropometric measurements, and laboratory investigations (Complete blood count, C-reactive protein). Transcranial ultrasound: on days 3, 7, and 28 of life, abdominal ultrasound and Doppler were performed.

Patients were followed up to record their respiratory condition and for any morbidities as neonatal sepsis, intraventricular hemorrhage, pneumothorax, feeding intolerance, necrotizing enterocolitis or complications from the drugs administered. Patient who developed CRP positive and positive blood culture during enrollment in the study were diagnosed to have neonatal sepsis. Appropriate treatment was given and total duration till CRP negative was achieved was recorded.

At 36 weeks of corrected gestational age, full physical examination was performed weight, length, and occipto-frontal circumference were measured for all included neonates plotted on growth percentiles. In addition, Neonatal Intensive Care Unit Network Neurobehavioral Scale (NNNS) was performed on all included neonates by the same person[2*](M S K). CBC was performed.

This study was approved and submitted to the clinicaltrials.gov registry with ID: NCT06015828.

Statistical Analysis:

The data was collected, edited, coded, and added to IBM SPSS, a package of statistics for social science subjects, version 23. Parametric data was expressed as mean ±standard deviation, and range while non-parametric, they were expressed as median and inter-quartile range (IQR). Numbers and percentages were used to display the qualitative data. Chi-square was used to compare groups based on qualitative data. The t-test was used to compare two distinct groups with quantitative data and parametric distribution; the Mann-Whitney test was used

for non-parametric distribution. The statistical Paired t-test was utilized for the comparison of both paired groups with quantitative data and a parametric distribution; a Wilcoxon Rank test was used for non-parametric data.

The allowable margin of error was set at 5%, while the confidence interval set at 95%. Thus, the following p-value was deemed significant at P<0.05, highly significant (HS) at P<0.01, and non-significant (NS) at P>0.05.

Ethical Considerations:

Research was started after approval of the Research Ethics Committee of Ain Shams University (FMASU MS 634/ 2020). An informed written consent was taken from the parents or the legal guardians before enrollment in the study. Data collected were strictly confidential and used for research purposes only.

RESULTS:

The study groups were comparable in terms of their basic demographic data and clinical characteristics (Table 1). Neonates with respiratory distress syndrome in both groups were managed with nasal CPAP. The duration of respiratory support used was significantly shorter in lactoferrin group than control group (Table 2 and figure 1). Full enteral feeding was achieved at an earlier age in lactoferrin group than the control group. The frequency of late-onset sepsis was equal in both groups. Sepsis was diagnosed at later age in the lactoferrin group than in the control group with shorter duration (table 2). In both groups, no morbidities were detected (no necrotizing enterocolitis, no hypoxic ischemic encephalopathy, no intraventricular hemorrhage, no bronchopulmonary dysplasia, no retinopathy of prematurity) with no mortality. No packed RBCS transfusion was given in both groups. No detected side effect from bovine lactoferrin was detected.

No statistically significant difference was found in the NNNS between both groups at 36 weeks corrected gestational age Table (3).

Laboratory investigations were comparable in both groups at time of enrolment. At 36 weeks corrected gestational lactoferrin group had significant increased hematocrit level than control group Table (4).

Table 1: Comparison between lactoferrin group and control group regarding demographic data and clinical characteristics of the studied neonates

		Lactoferrin group N = 40	Control group N = 40	Test value	P-value
Weight (gm) initial at recruitment	Mean ± SD. Range	1868.25±161.06 1540 – 2140	1981.50 ± 153.25 1600 – 2200	-3.222	**0.002**
Weight (gm) at 36weeks corrected gestational age	Mean ± SD. Range	2212.50±199.05 1750 – 2600	2315.25±175.40 1900 – 2600	-2.449	**0.017**
Gestational age (weeks)	Mean ± SD. Range	33.65 ± 0.48 33-34	33.55 ± 0.50 33-34	0.906•	0.368
Post-natal age at time of NNNS assessment (days)	Mean ± SD	16.45 ± 3.38	17.15 ± 3.53	-0.906•	0.368
	Range	14 – 21	14 – 21		
Gender	Male	23 (57.5%)	18 (45.0%)	1.251*	0.263
	Female	17 (42.5%)	22 (55.0%)		
Mode of delivery	NVD	2 (5.0%)	13 (32.5%)	9.928	**0.002**
	C.S.	38 (95.0%)	27 (67.5%)		
Maternal Risk factors	DM	2 (5.0%)	0 (0.0%)	2.051	0.152
	HTN	9 (22.5%)	4 (10.0%)	2.296	0.130

	UTI	1 (2.5%)	5 (12.5%)	2.883	0.090
	Hge	1 (2.5%)	1 (2.5%)	0.000	1.000
	PROM	8 (20.0%)	5 (12.5%)	0.827	0.363

*: Chi-square test; •: Independent t-test NVD: Normal Vaginal Delivery, CS: Cesearian Section, DM: Diabetes Mellitus, HTN: Hypertension, UTI: Urinary Tract Infection, Hge: Antepartum Hemorrhages, PROM: Premature Rupture of Membranes.

Table 2: Comparison between lactoferrin & control groups as regards some clinical aspects:

		Lactoferrin group N = 40	Control group N = 40	Test value	P-value
Diagnosis on admission	RDS Low birth weight	33(82.5%) 7(17.5%)	40(100%) 0	7.671*	**0.006**
Ventilation mode	NCPAP	33 (82.5%)	40 (100.0%)	7.671*	**0.006**
Duration of ventilation (days)	Mean ± SD. Range	4.70 ± 1.80 2-8	7.10 ± 2.13 4-12	-5.437•	**0.000**
Age on achieving full feeding (days)	Mean ± SD. Range	7.15 ± 1.88 3 – 11	8.38 ± 1.66 5 – 12	-3.094•	**0.003**
Neonatal sepsis (LOS + EOS)	Positive (yes)	11 (27.5%)	13 (32.5%)	0.238*	0.626
	Negative (no)	29 (72.5%)	27 (67.5%)		
Age on diagnosis of sepsis (days)	Median (IQR) Range	5 (3 – 7) 3-7	3 (2 – 4) 2-4	-2.366≠	**0.018**
Sepsis duration (days)	Mean ± SD. Range	4.50 ± 0.97 3-6	6.62 ± 1.19 4-8	4.557•	**<0.001**
Duration of hospital stay (days)	Mean ± SD. Range	10.55 ± 4.01 4-20	10.28 ± 2.48 6-16	0.369•	0.713

*: Chi-square test; •: Independent t-test, ≠: Mann-Whitney test; RDS: Respiratory distress syndrome, NCPAP: Nasal continuous positive airway pressure, EOS: Early onset sepsis, LOS: Late onset sepsis

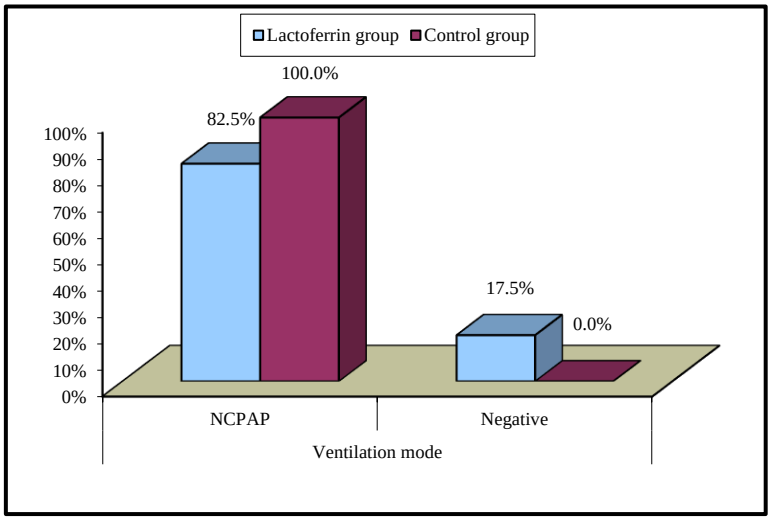

Figure 1: frequency of nasal CPAP use in Lactoferrin group and control group, P: 0.006.

Table 3: Comparison between Lactoferrin group and control group as regards NNNS at 36 weeks corrected gestational age.

Age of examinations of NNNS at 36 weeks corrected gestation		Lactoferrin group N = 40	Control group N = 40	Test value•	P-value
Stress/abstinence (range 0-1)	Mean ± SD	0.00 ± 0.00	0.00 ± 0.00	NA	NA
	Range	0 – 0	0 – 0		
Hypotonicity (range 0-10)	Mean ± SD	1.00 ± 0.00	1.00 ± 0.00	NA	NA
	Range	1 – 1	1 – 1		

Hypertonicity (range 0-10)	Mean ± SD	2.00 ± 0.00	2.00 ± 0.00	NA	NA
	Range	2 – 2	2 – 2		
Asymmetrical reflexes (range 0-16)	Mean ± SD	16.00 ± 0.00	16.00 ± 0.00	NA	NA
	Range	16 – 16	16 – 16		
Nonoptimal reflexes (range 0-10)	Mean ± SD	3.60 ± 0.50	3.48 ± 0.51	1.116	0.268
	Range	3 – 4	3 – 4		
Lethargy (range 0-15)	Mean ± SD	10.48 ± 1.60	10.80 ± 1.42	-0.961	0.339
	Range	8 – 13	8 – 13		
Excitability (range 0-15)	Mean ± SD	8.95 ± 0.68	8.83 ± 0.68	0.827	0.411
	Range	8 – 10	8 – 10		
Quality of movements (range 1-9)	Mean ± SD	4.05 ± 0.81	4.15 ±0.77	-0.564	0.574
	Range	3 – 5	3 – 5		
Handling (range 0-1)	Mean ± SD	0.00 ± 0.00	0.00 ± 0.00	NA	NA
	Range	0 – 0	0 – 0		
Regulation (range 1-9)	Mean ± SD	6.50 ± 1.20	6.58 ± 1.01	-0.303	0.763
	Range	4 – 8	5 – 8		
Arousal (range 1-9)	Mean ± SD	4.15 ± 0.77	4.15 ± 0.77	0.000	1.000
	Range	3 – 5	3 – 5		
Orienting (range 1-9)	Mean ± SD	4.25 ± 0.67	4.15 ± 0.74	0.636	0.527
	Range	3 – 5	3 – 5		

• Independent t-test

Table 4: Comparison between Lactoferrin group and control group regarding laboratory investigations initial and at 36 weeks corrected gestational age.

Laboratory investigations initial and discharge		Lactoferrin group N = 40	Control group N = 40	Test value	P-value
Initial					
CRP mg/l	Negative Positive	38 (95.0%) 2 (5.0%)	39 (97.5%) 1 (2.5%)	0.346*	0.556
WBCs 10^3/uL	Mean ± SD Range	12.61 ± 4.89 6.2 – 27.1	13.12 ± 4.48 6.5 – 21	-0.484•	0.630
Hb g/dL	Mean ± SD Range	16.28 ± 2.46 10.6 – 22.3	15.92 ± 3.46 7.2 – 22	0.528•	0.599
HCT %	Mean ± SD Range	44.51 ± 9.55 4.1 – 62.6	42.96 ± 9.99 20.8 – 60.8	0.707•	0.482
PLT 10^3/uL	Mean ± SD Range	261.30 ± 98.63 32 – 404	252.73 ± 85.80 32 – 404	0.415•	0.679
36 weeks					
CRP mg/l	Negative Positive	40 (100.0%) 0 (0.0%)	40 (100.0%) 0 (0.0%)	-	-
WBCs 10^3/uL	Mean ± SD Range	11.48 ± 3.86 6.2 – 24.7	12.82 ± 4.28 6.9 – 20.7	-1.466•	0.147
Hb g/dL	Mean ± SD Range	15.21 ± 1.89 12 – 19.8	14.45 ± 2.33 8.6 – 18.5	1.591•	0.116
HCT %	Mean ± SD Range	44.59 ± 5.62 35.9 – 60.4	41.46 ± 7.53 25.8 – 54.6	2.107•	**0.038**
PLT 10^3/uL	Mean ± SD Range	273.73 ± 79.25 100 – 436	257.35 ± 70.75 100 – 436	0.975•	0.333

• Mann Whitney test; independent t-test

CRP: C-reactive protein; WBCs: white blood cells; Hb: hemoglobin; HCT: hematocrit; test; PLT: Platelet Count

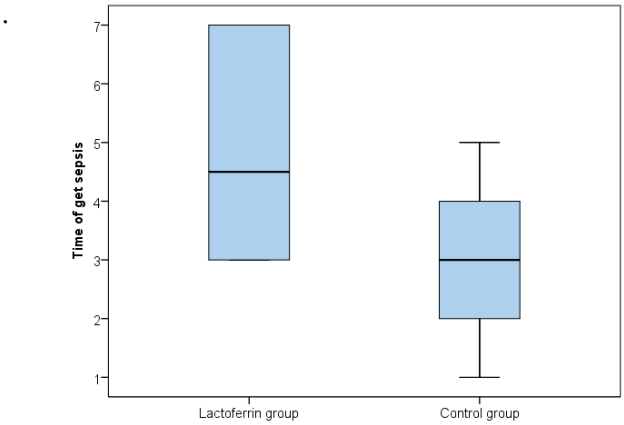

Figure 2: Age of diagnosis of sepsis in the Lactoferrin group and control group. P: 0.018

DISCUSSION:

During the early neonatal period, preterm newborns usually consume little to no milk and have low lactoferrin consumption. Any delays in starting enteral feeding aggravate the poor lactoferrin intake in the early newborn period. Although bovine lactoferrin and human lactoferrin are roughly 70% similar, the former possesses stronger antibacterial properties. Bovine lactoferrin is less expensive than human or recombinant lactoferrin and is sold commercially as a food supplement in a stable powder form [(10)]. Because of this, it can be given to premature neonates without running the danger of causing septic attacks, especially if the babies are admitted to the NICU [(10)].

Lactoferrin may be important in both the pathophysiology and prevention of neurodegenerative disorders, as evidenced by the increased expression of lactoferrin receptors in the brains of neurodegenerative patients. Environmental and nutritional factors have an essential effect on the neurodevelopment. Sufficient nourishment throughout gestation and early life establishes the groundwork for neuroplasticity, which in turn fosters the growth of cognitive, motor, and socioemotional abilities in children and adults [(11)].

In our investigation, we discovered that, the neurodevelopmental assessment done by NNNS score at 36 weeks corrected gestational age was similar in both groups with no significant difference found. This might be because both groups rely on expressed breast milk as the main source of feeding as our NICU policy. In addition, lactoferrin was given for a brief period (two weeks) with a small sample size and short duration of the follow up; and these are considered limitations to the current study.

Similarly, Ochoa *et al* [(12)] studied a group of low birth-weight neonates who received bovine lactoferrin and they showed that it had no impact on their neurodevelopment and growth outcomes, even with a longer follow-up period and a greater dose of bovine lactoferrin. In very low birth weight neonates, the neurodevelopmental delay was 18.8% (15/80) in the bovine lactoferrin group and 21.2% (18/85) in the placebo group. The growth results at the 2-year follow-up were similar. Mullen's expressive language score on the subscale has been less than the gross motor, visual reception process, fine-motor development, and receptive language scores in both groups.

On the other hand, *Li et al.* [(13)] demonstrated that in the Bovine lactoferrin group's, Bayley-III cognitive composite mean score at day 365 was 8.7 points higher than the control group's (111.0 ± 0.9 vs. 102.3 ± 0.9). The mean scores among the Bovine lactoferrin group in contrast to the controls had been considerably higher in both verbal (122.6 ± 0.9 vs. 110.3 ± 0.9; a difference of 12.3 points) and motor areas

(118.3 ± 1.2 vs. 105.7 ± 1.2; a difference of 12.6 points). There were no discernible group differences in the mean scores for social emotional or general adaptive abilities. When family income, parental education levels and other socioenvironmental factors were considered, the same outcomes continued to be observed. It should be mentioned that breast milk was not used in the prior trial; only artificial milk was used, and the long duration of follow up with long duration of bovine lactoferrin intake.

Neurodevelopmental outcomes assessment at 36weeks corrected gestational age didn't show any significant difference between both groups in our study. Further studies are needed to explain other options as assessment of neurodevelopment outcome at a later age, increasing doses of bovine lactoferrin given and increasing duration of intake. A larger sample size may help in establishing significance in the results.

Despite the absence of significant difference in the neurodevelopmental outcome. Secondary findings were observed and are being highlighted as follows. As regards morbidities our study showed that, although the frequency of neonatal sepsis did not differ significantly between the two groups, neonates in bovine lactoferrin group developed sepsis at an older age and for shorter duration compared to the control group. These highlights the importance of bovine lactoferrin use in neonatal sepsis due to its anti-infective properties. These results were compatible with *Gao et al.* [14] who reported that, subgroup analysis revealed that in neonates with low birth weights or with very low or extremely small birth weight, enteral bovine lactoferrin supplementation significantly decreased the risk of developing sepsis with late onset.

The results of the current study also showed that the need for respiratory support was for significantly shorter duration in bovine lactoferrin group than control group. Similarly, in a study done by *Ochoa et al* [12], who studied the impact of giving bovine lactoferrin in a randomized controlled trial on neurodevelopmental impairment and sepsis prevention in infants under 2000 grams, and their results were consistent with our findings. They stated that compared to the bovine lactoferrin group, the control group's ventilation duration was longer. Furthermore, rat models have demonstrated the protective benefits of bovine lactoferrin against acute lung injury generated by sepsis [13]. It is necessary to start more research to examine these advantages in newborns, particularly preterm neonates.

In the current study, we found that full volume of enteral feeding was achieved significantly earlier in bovine lactoferrin group than control group, with no difference found between both groups regarding time of initiation of enteral feeding or type of feeding.

In the current study, we found that the hematocrit level was significantly increased in lactoferrin group than control group at 36 weeks corrected gestational age. In agreement with our results, *El Barbary et al.* [15] performed an interventional double-blinded trial on 52 newborns who were randomized into the bovine lactoferrin group (n = 26) and placebo group (n = 26). On day seven, there were no notable distinctions within both groups under investigation in terms of serum ferritin, hemoglobin, hematocrit, mean corpuscular volume (MCV), red cell distribution width (RDW), platelet count, total leukocytes count (TLC), and the C-reactive (CRP). On day 30, however, the Lactoferrin group had significantly lower RDW, TLC, and CRP, and significantly greater serum ferritin, hemoglobin, hematocrit, and MCV than the placebo group.

In the other hand, *Chierici et al.* [16] stated that at day 150 of life, serum ferritin levels were considerably greater in newborns fed the formula enriched with higher amounts of lactoferrin (100 mg/100 ml) than in infants

given supplemented formula or formula enriched with LF (10 mg/100 ml). However, within the first three months of life, there were no appreciable differences in hemoglobin, hematocrit, or serum iron levels across the various feeding groups, indicating that these parameters are not impacted by the type of nutrition that the infants get at this time.

Although our hypothesis suggesting bovine lactoferrin enhances neurodevelopment in preterm infants could not be proven, there were no development of any side effects from the drug given, so bovine lactoferrin is considered safe to be given in preterm neonates and has many other advantages in advancement of feeding, neonatal sepsis and ventilation could be obtained.

Conclusion:

Bovine lactoferrin given to preterm neonates till attaining 36weeks corrected gestational age showed no effect on their neurodevelopment outcomes assessment by NNNS scale. Beneficial effects on time to reach full enteral feeding, shorter duration of later sepsis and increased hematocrit level at 36 weeks corrected GA were detected. Further studies on larger scale for longer duration of lactoferrin intake and longer duration of follow up is required.

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Nil

Conflict of Interest:

Nil.

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تأثير اللاكتوفيرين البقري الجوفى على الأداء السلوكي العصبي لحديثى الولادة المبتسرين

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قسم طب الاطفال- كلية الطب- جامعة عين شمس- القاهرة [1]
المجالس الطبية المتخصصه - القاهره [2]

المقدمة: اللاكتوفيرين هو بروتين سكري الحليب الغني بحامض السياليك، بما في ذلك قدرته على تعديل وظيفة المناعة وتسهيل امتصاص الحديد ، بالإضافة إلى إجراءاته المضادة للبكتيريا والمضادة للالتهابات و أيضاً يلعب دورًا حاسمًا في التطور العصبي.

المرضي والطرق: تم انضمام ٨٠ طفل مبتسر في هذه التجربة العلمية المنضبطة في وحدات الرعاية المركزة لحديثي الولادة في مستشفيات جامعة عين شمس في خلال ٦ اشهر. تم إعطاء لمجموعة اللاكتوفيرين عقار الاكتوفيرين البقري جوفيا لمدة أسبوعين او عند الوصول الي ٣٦ أسبوع عمر رحمي معدل. و تم عمل مقياس للأداء السلوكي العضلي في ذلك الوقت.

النتائج: لا يوجد إحصائيا فرق كبير بين المجموعتين فيما يتعلق بـ NNNS عند 36 أسابيع عمر رحمي معدل. يوجد نسبة اعلي في مدة استخدام الأجهزة الداعمة للتنفس في المجموعة الضابطة عن المجموعة الأخرى. كان المدة الوصول إلى التغذية الكاملة أقل بشكل ملحوظ في مجموعة اللاكتوفيرين عن المجموعة الضابطة.

لم يكن هناك اختلاف في نسبة حدوث الانتان في المجموعتين ولكن مدة العلاج كانت اقل بشكل ملحوظ في مجموعة اللاكتوفيرين.

الخلاصة: اللاكتوفيرين البقري جوفيا لم يؤثر على الأداء السلوكي العصبي لحديثي الولادة المبتسرين عند الوصول الي عمر رحمي معدل ٣٦ اسبوع.