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Original Article / Оригинални рад

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Effect of Early Introduction of Minimal Enteral Feeding on Growth and Rate of Achieving Optimal Nutritive Intake in Very Low Birthweight Preterm Infants

Утицај ране минималне ентералне исхране на раст и брзину постизања оптималног нутритивног уноса превремено рођене деце веома мале телесне масе

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SUMMARY

Introduction/Objective Minimal enteral nutrition (MEN) has an important stimulative effect on morphological and functional development of gastointestinal system in preterm infants.

The aim of this study was the assesment of effect of early introduced MEN on rate of achieving optimal enteral nutritive intake and on body weight, body lenght and head circumference gain in very low birthweight (VLBW) premature infants.

Methods Prospective study included 45 VLBW newborns (1010–1450; 1350±305 g), in 30 newborns MEN was introduced within 3 days after birth, and in 15 newborns enteral intake was introduced after 5 days due to hemodynamic and metabolic instability. Assesment of effect of early MEN introduction on rate of achieving optimal nutritive intake and gain in basic antropometric parameters was based on comparison with group of subjects who had a delayed MEN introduction.

Results Subjects in which MEN was introduced early had a better weight gain ($p<0.05$), reached birthweight sooner ($p<0.05$), and achieved optimal enteral intake much sooner ($p<0.05$), compared to subjects with delayed MEN introduction. Difference in body lenght gain and head circumference gain was not significant.

Conclusion Early introduction of MEN has a significant positive effect on rate of bodyweight gain and on earlier achievment of optimal enteral intake in VLBW preterm infants.

Keywords: very low bodyweight infants; early minimal enteral nutrition; optimal nutritive intake

САЖЕТАК

Увод/Циљ Минимална ентерална исхрана (МЕИ) има битан стимулативни ефекат на морфолошки и функционални развој гастроинтестиналног система код превремено рођеног детета.

Циљ рада је процена ефеката ране МЕИ на брзине постизања оптималног ентералног нутритивног уноса и раст телесне масе, телесне дужине и обима главе код превремено рођене деце веома мале телесне масе (ВМТМ).

Методе Проспективном студијом је обухваћено 45 новорођенчади ВМТМ (1010–1450; 1350±305 г), 30 код којих је МЕИ започет унутар три дана по рођењу и 15 код којих је због хемодинамске и метаболичке нестабилности ентерални унос започет након 5 дана. Процена ефекта ране МЕИ на брзину постизања оптималног нутритивног уноса и раст основних антропометријских параметара заснива-на је на поређењу са групом испитаника код којих је ентерални унос започет касније.

Резултати Испитаници са рано започетом МЕИ у односу на оне код којих је ентерална исхрана одложена су боље напредовали у телесној маси ($p<0.05$), брже достизали порођајну телесну тежину ($p<0.05$) и знатно раније успостављали оптимални ентерални унос ($p<0.05$), док разлика у расту телесне дужине и обима главе између ове две групе испитаника није била значајна.

Закључак Рана МЕИ има сигнификантно позитиван ефекат на брзину пораста телесне тежине и раније успостављање оптималног ентералног уноса код превремено рођене деце ВМТМ.

Кључне речи: новорођенчад веома мале телесне масе; рана минимална ентерална исхрана; оптимални нутритивни унос

INTRODUCTION

With perinatal care improvement in last few decades, incidence of neonatal morbidity and mortality was significantly decreased. Very important role goes to adequate nutrition of this very vulnerabile children, and its positive effects reflect not only on survival rate and optimal growth and development, but in adulthood as well [1].

Development of gastrointestinal system starts early in intrauterine period and continues postnatally. Although highly immature, morphologically and functionally, gastrointestinal system partially meets, initially very poorly, basic nutritive needs of premature infant. In a very complex

process of progressive postnatal functional maturation of gastrointestinal system, early introduction of enteral feeding has a key role as a physiological stimulus [1, 2].

During the eighties of the last century, the new tendencies arise advocating the early initiation of enteral nutrition, that led to abandonment of long-standing practice of delayed enteral feeding of premature infants in intensive care units [1, 2]. Minimal enteral nutrition (MEN) implies early intake of primarily mother's milk in small amounts (up to 25 mL/kg/day) in premature infants [2]. This kind of nutrition doesn't primarily provide optimal nutritive balance in premature infant. Its basic role is contained in trophic influence on immature gastrointestinal system, i.e. on development of process of food digestion and apsorption, coordination of motility, gastrointestinal hormone activity, and on preservation of intestinal barrier integrity. In that manner better feeding tolerance is achieved, as well as faster postnatal growth and development, lower incidence of sepsis and necrotizing enterocolitis, and on shortening lenght of hospitalization [2]. Nowadays, this way of nutrition is generally accepted in most neonatal intensive care units as an integral part of treatment of premature infants [3].

Assessment of the effects of early introduced MEN on bodyweight (BW), body length (BL), head circumference (HD) and rate of achievement of optimal nutritive intake in very low birthweight premature infants.

METHODS

This prospective study included 45 VLBW premature infants hospitalized in Institute for Neonatology, Belgrade since June 2012. Until September 2013. Subjects were divided in two groups according to time of MEN introduction: group A, n=30, in which after establishing hemodynamic stability, normal blood pressure, blood pH above 7.30 and FiO_2 under 40%, MEN was introduced within 3 days after birth, and group B, n=15, in which MEN was introduced from days 5 to 10 (average 6.07) after birth due to hemodynamic and metabolic instability and/or meteorismus ($t=0.02$, $p<0.05$). Basic characteristics of both group of subjects are presented in Table 1. Distribution of

Table 1. Basic characteristics of subjects at birth (n=45)

Characteristics	Group A (n=30)		Group B (n=15)	
	Range	($\bar{x}$±SD)	Range	($\bar{x}$±SD)
Birth weight (g)	1000–1500	1274.0±144.6	1000-1500	1250±152.2
Gestational age (weeks)	26–32.5	29.5±1.6	27-31.5	29.0±1.2
Apgar score 1'	1–8	4.9±1.9	2-8	5.53±1.9
Apgar score 5'	2–8	5.9±1.5	4-8	6.33±1.5

subjects according to sex was identical in both groups. Group A had 14 male subjects (46.7%) and 16 female subjects (53.3%), and group B had 7 male (46.7%) and 8 (53.3%) female subjects.

Basic way of meeting nutritive needs in both group of subjects during the first days of life was via parenteral nutrition, while enteral feeding via nasogastric tube was introduced according with above mentioned criteria. Enteral nutrition in all newborns was started with human milk, whereas it was donor milk or mother's milk. Daily intake volume in first 5 days was 25 mL/kg/day, and was

increased gradually according to feeding tolerance. When enteral volume intake of 80 mL/kg/day was achieved, fortified human milk was introduced (FM 85 Nestlè, Nestlè, Switzerland) in dose of 5g/100mL and/or specialized milk formula for premature infants (Impamil Mil PRE, Serbia).

Following subjects were followed in all subjects: daily gain in body weight, day of achieving birthweight, weekly increase in body lenght and head circumference, and day of achieving of optimal enteral intake.

All data obtained during research was analysed with SPSS Windows 10.0 software package. Both parametric and non-parametric statistical test were used to analyse data. Comparison of two groups was done using Student's *t*-test and Mann-Whitney's *U* test, depending on data homogeneity. Comparison of data between more than two groups was done with Kruskal Wallis test. Statistical significance was set at $p<0.05$.

RESULTS

Subjects with early introduced MEN (group A) compared to subjects with delayed introduction of MEN (group B) had a significantlly better body weight gain (10.88±3.25 g vs 7.73±1.85 g daily; t=0.017, p<0.05), and achieved birthweight sooner (16.38±3.36 days vs 21.00±7.16 days; t=0.017, p<0.05) (Figure 1). Also, group A subjects achieved optimal enteral intake significantlly sooner compared to group B (25.70±7,20 days vs 28.33±7.35 days; t=0.021, p<0.05) (Figure 2).

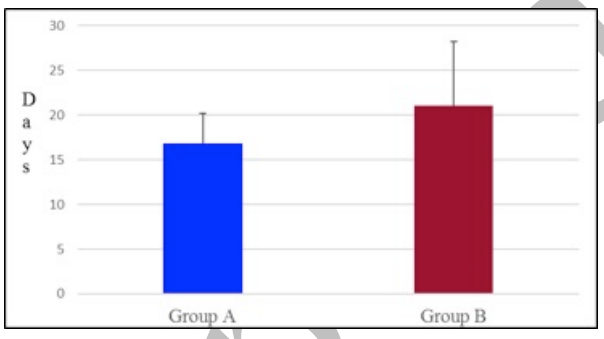

Figure 1. Achievement of birth weight (day), A:B; *p*<0.05.

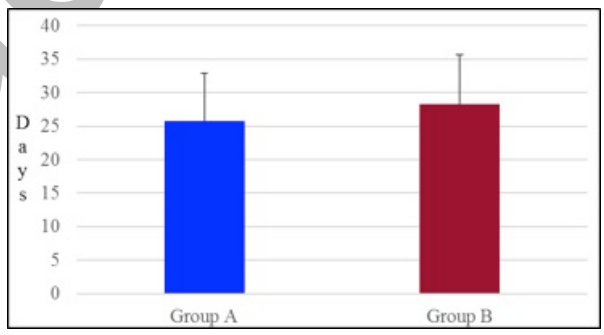

Figure 2. Achievement of optimal nutrition intake (day), A:B; *p*<0.05.

Difference in weekly gain in body lenght (BL) during the observed period between subjects in group A (0.45-0.58; 0.51±0.35 cm) and group B (0.45–0.53; 0.49±0.33 cm) was not significant (t=0.025, p>0.05).

Difference in weekly head circumference (HC) gain between group A (0.46-0.67; 0.49±0.21 cm) and group B (0.44–0.53; 0.50±0.21 cm) during the observed period was also not significant (t=0.022, p>0.05).

DISCUSSION

Because of its stimulating effect on motphological and functional development of gastrointestinal system, MEN introduced during first 24 to 72 hours within birth is also known in

literature as „trophic feeding“ [4]. Some authors consider early introduction of MEN to be within 4 days after birth [5].

In our subjects, MEN was introduced within first 72 hours as advocated by most authors [4]. Amount of enteral intake was also problem in everyday work, because it varied greatly among studies. Therefore, MEN was defined as small volume enteral intake, up to 25mL/kg/day, or less than 20 kcal/kg/day [6]. MEN was introduced in our subjects in accordance with forementioned recommendation.

Precondition for initiation of MEN is clinical state of a patient, its metabolic and hemodynamic stability. Precaution should be taken in case of severe perinatal asphyxia, sepsis, severe hemodynamic instability, absence of end-dyastolic flow, indomethacin therapy and hemodynamically significant persistent ductus arteriosus, because of possible necrotizing enterocolitis development [7]. In all our subjects before enteral feeding was introduced, mean arterial pressure was in reference range for BW and gestational age, there was no meteorismus, and pH was more than 7.30.

It is fully understood nowadays, that MEN should be initiated with mother's milk, using colostrum whenever possible [3]. Otherwise, when mother's milk is not available, human donor milk from milk bank is an optimal choice [8]. Current tendencies show the need for establishing of human milk banks which will be the foundation of nutritive support of premature infants and will contribute greatly to lactation preservation [9]. It is general attitude that mother's milk, with appropriate supplementation represents the foundation of nutrition of preterm infant. Unfortunately in most cases, production of human milk is inadequate or lactation is not established at all, in which case nutrition with donor milk is an appropriate choice [9, 10]. In all our subjects, MEN was conducted with human donor milk, in which in 5 subjects colostrum was used.

Duration of MEN and further increase in volume intake are also not precisely defined. There is a need for a unique protocol considering increase in volume intake which would have primarily practical role in everyday neonatologist's work [11]. In our subjects, MEN was conducted during 5 days, with a volume up to 25 mL/kg/day. After that time, increase in volume intake was 15-20 mL/kg/day, adjusted to individual feeding tolerance.

Measurement of body weight, lenght and head circumference represent basic antropometric indicators of growth in neonatal period. Skinfold thickness and subscapular test are far less significant in neonatal clinical practise, considering very small changes in neonates [12]. Proper technique of measurement and adequatly trained personnel perform measurement in intervals instructed by the protocol or research methodology. During this study, body weight was measured on digital scales incorporated in incubators or on classic mechanical scales (accuracy range ±5 g). Proper way of measuring body lenght is by using a stadiometer, but depending on clinical state of a patient, various forms of adapted flexible plastic coated tape measure are used. Use of tape measure made from impregnated unstrechable cloth is the most optimal way of measuring head circumference [13].

Time of birthweight achievement is also an indirect indicator of nutritive support, and it is three weeks in VLBW preterm infants, but according to clinical condition it can be even longer [14]. Our subjects in whom MEN was introduced early reach birthweight on day 17, which is significantly shorter compared to day 21 in group with delayed enteral nutrition ($p<0.05$).

Body weight gain during intrauterine growth is about 15-20 g/kg/day, while postnatal growth of 10-20g/kg/day is considered to be appropriate [15]. Average body weight gain in group with early introduced MEN was 10.88g/kg/day, which is significantly more compared to 7.73g/kg/day in group with delayed enteral intake ($p<0.05$).

Increase in BL and occipitofrontal HC of 0.9 cm per week is ideal, and represents a goal of adequate nutritive support, although that value is far less and hard to reach in clinical practice. Monitoring of early postnatal growth through series of BL measurements in preterm infants shows a value of 0.5-0.9cm per week, and occipitofrontal HC of 0.5-1.1cm per week [16, 17, 18]. Average weekly gain in BL in our subjects was 0.45-0.58cm, and in HC 0.46-0.67cm. Studies conducted weren't coherent considering the question of effect of minimal enteral nutrition on short term growth, while analysis of long term growth and its developmentall effects was not analysed [19]. There is a need for new randomised studies that will include extremely low birthweight infants in this research, as well as infants with intrauterine growth restriction [20, 21].

CONCLUSION

Minimal enteral nutrition with human milk as an addition to parenteral nutrition represent a very important practical approach in treatment of VLBW premature infants, naturally stimulating development of gastrointestinal functions. Minimal enteral nutrition introduction within 72 hours compared to 5 or more days since birth significantly contributes to rate of BW gain and to earlier achievement of optimal nutritive intake, so it should be practised whenever possible.

NOTE

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