

Role of Synbiotics in Improvement of Feed Tolerance and Weight Gain in the Newborns

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Abstract

Objective: To study the effect of Synbiotics on weight gain and feed tolerance of newborns. **Methods:** This prospective interventional trial included 50 newborns treated with a dietary supplement containing Synbiotics in addition to the routine treatment and 48 newborns served as control without Synbiotics supplement. The primary outcome was weight gain and feed tolerance. **Results:** Newborns in the Synbiotics group reached the full feeds earlier as compared to those in Control group (7.5 ± 4.26 days Vs 14.02 ± 7.88 days $p=0.532$) along with better weight gain (14.61 ± 9.6 grams per day Vs 2.97 ± 3.81 grams per day $p=0.0000001$). **Conclusions:** Newborns receiving Synbiotics are more likely to reach full feeds earlier and show better weight gain.

Keywords: Newborns; Probiotics; Prebiotics; Synbiotics; Feed tolerance; Weight gain.

1. Introduction

Probiotics are defined as “Live microorganisms which, when administered in adequate amounts, confer a health benefit on the host”¹. Prebiotics are defined as “Nondigestible substances that provide a beneficial physiological effect for the host by selectively stimulating the favourable growth or activity of a limited number of indigenous bacteria”¹. Synbiotics contain both prebiotics and probiotics¹.

Many Probiotics help in the digestive process by producing lactase. The bacteria used as starter cultures in yogurt (*Streptococcus thermophilus* and *Lactobacillus*

delbrueckii subsp. *bulgaricus*) produce lactase, and when consumed with dairy products can improve lactose digestion and symptoms in those with lactose intolerance². A number of studies have demonstrated better lactose digestion, as well as a decrease in gastrointestinal symptoms, in people with this condition who consume yogurt with live cultures³. This lactose digestion can improve feed tolerance and thereby may help in weight gain of a neonate.

Published literature indicates that addition of prebiotics to probiotics results in prolonged colonization with probiotics as compared to when probiotics alone are used⁴⁻⁶.

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Historical data suggests that by and large probiotics can be safely employed for use in newborns and infants for various indications⁷⁻¹⁹ and these organisms are considered as GRAS (Generally Regarded as Safe).

Synbiotics have been shown to be safe in newborns in a 2 year follow up study.

2. Material and Methods

This was a Prospective Interventional Study to evaluate the effects of synbiotics in terms of weight gain and feed tolerance in newborns admitted to the neonatal intensive care unit (N.I.C.U.) of Dr. Vasantrao Pawar Medical College, Nashik from January 2011 to October 2012. All the cases admitted in N.I.C.U. excluding those mentioned in exclusion criteria, were included. Newborns who were kept nil by mouth (NBM) for any reason for more than 7 days, born to HIV positive Mothers and having less than 14 days of hospital stay were excluded from the study. Informed written Consent was taken from the parents of the patient. The clinical evaluation of the selected newborns included detailed history, examination and necessary investigations for the relevant problem for which they were admitted.

The patients were randomly divided in two groups: Synbiotic group and Control Group, using a computer generated randomization table. The Synbiotic group newborns were given Synbiotic in the form of Ecobion sachet [a mixture of Lactobacillus acidophilus 0.24 billion, Lactobacillus rhamnosus 0.24 billion, Bifidobacterium longum 0.24 billion, Bifidobacterium bifidum 0.24 billion, Saccharomyces boulardi 0.05 billion, Sterptococcus thermophilus 0.24 billion and Fructo Oligosaccharides 300mg] ½ sachet twice a day mixed with the milk (Breast milk/ Formula Milk) in addition to the therapeutic measures for the medical condition for which they were admitted. Newborns in Control Group were not given synbiotics and received only the treatment for the relevant medical condition and were considered as control group. During their stay in NICU, synbiotics and control groups were compared for their birth weight, gestational age, sex, mode of delivery, no. of days required to reach full feeds and average weight gain per day.

Weight gain was compared as average daily weight gain between two groups. The feed tolerance was decided on the basis of no. of days required by baby to achieve full feeds.

A record of the final outcome was also made. Findings were then analyzed and subjected to statistical analysis.

3. Results

A total of 98 newborns were studied. With random selection, 50 were included in the synbiotics supplemental group and 48 in the control group. The neonates randomized to the synbiotics and control groups were comparable in terms of birth weight, gestational age and gender and there was no significant difference between the two groups (Table 1 to 3 and Figure 1).

Table 1. Distribution of babies according to birth weight in Synbiotics & Control Group

Group	Synbiotics group		Control Group		P-value
	N	%	N	%	
<1 kg	4	8%	4	8.34%	0.976
1-1.49 kg	21	42%	19	39.58%	
1.5-1.99 kg	11	22%	12	25%	
2-2.49 kg	6	12%	7	14.58%	
>2.5 kg	8	16%	6	12.5%	
Total	50	100%	48	100%	

Table 2. Distribution of babies in Synbiotics Group and Control Group according to gestational age

Group	Synbiotics group		Control Group		P-value
	N	%	N	%	
<28wks	2	4%	1	2.08%	0.565
28-32wks	6	12%	6	12.5%	
32-36wks	25	50%	30	62.5%	
>36wks	17	34%	11	22.92%	
Total	50	100%	48	100%	

Table 3. Gender wise distribution of babies in Synbiotics and Control Group

Gender	Synbiotics group		Control Group		P-value
	N	%	N	%	
Male	32	64%	28	57%	0.712
Female	18	36%	20	43%	
Total	50	100%	48	100%	

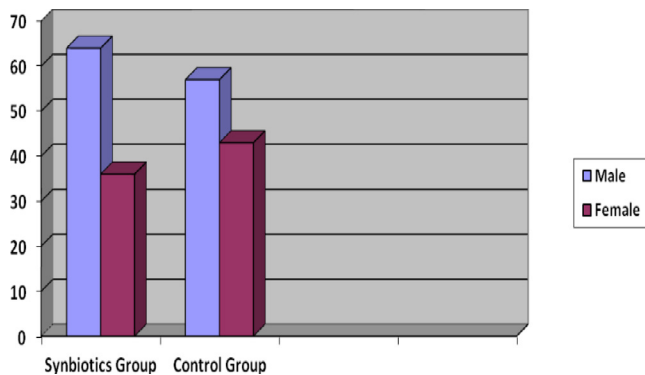


Figure 1. Average Gender wise distribution of babies in Synbiotics and Control Group

3.1 General Demographic Data

There was no significant difference in the weight distribution [p=0.9], gestational age [p=0.56], gender distribution [p=0.712] and mode of delivery [p=0.89] in the two groups as can be seen from Table 1-4. 61% (n=60) were males and 39% (n=38) were females. Most of the newborns in our study had gestational age of 32-36 wks. Majority of the babies in both groups were males.

3.2 Average Weight Gain per Day

The average weight gain /day was found to be significantly more in Synbiotic Group as compared to Control Group in our study (p=0.0000001). (Figure 2 and Table 5)

On further analysis it was found that the effect of synbiotics on weight gain was not confined to a particular weight group but it was present in all the different weight subgroups as can be seen in Table 6 and Figure 3.

3.3 No. of Days to Reach Full Feeds

No. of days to reach full feeds was 7.5 ± 4.26 days in Synbiotics Group; whereas it was 14.02 ± 7.88 days in

Control Group. This difference between the groups was highly significant (p=0.000004).

This difference in the time to reach full feeds was found to be statistically significant in babies in all weight groups except those weighing <1 kg as shown in Table 7 Figure 4.

Table 4. Mode of delivery of babies in Synbiotics Group and Control Group

Group	Synbiotics group		Control Group		p-value
	N	%	N	%	
Vaginal	35	70%	32	66.67%	0.890
LSCS	15	30%	16	33.33%	
Total	50	100%	48	100%	

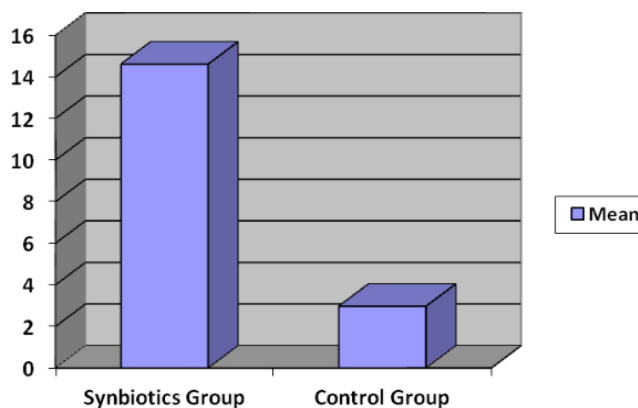


Figure 2. Average weight gain per day of babies (mean) in Synbiotic and Control Group.

Table 6. Average weight gain per day in different weight groups in Synbiotics and Control Group

No. of Days to reach full feeds	Groups	Mean	Standard Deviation	P value
	Synbiotics	7.52	4.26	0.000004
	Control	14.02	7.88	

Table 5. Weight gain per day of babies (mean) in Synbiotic and Control Group

Weight(kg)	Synbiotics Group (grams/day)		Control Group (grams/day)		Unpaired t test value	Degree of freedom	P value
	Mean	S.D.	Mean	S.D.			
<1	12.51	4.17	2.78	3.58	3.54	6	p=0.012
1-1.49	10.58	5.49	3.87	3.63	4.5	38	p=0.000061
1.5-1.99	18.23	9.98	3.73	3.7	4.7	21	p=0.00012
2-2.49	18.29	4.82	1.95	2.57	7.8	11	p=0.000082
>2.5	18.48	17.16	0.06	5.23	2.52	12	p=0.026
Overall	14.61	9.6	2.97	3.81	7.82	96	p=0.0000001

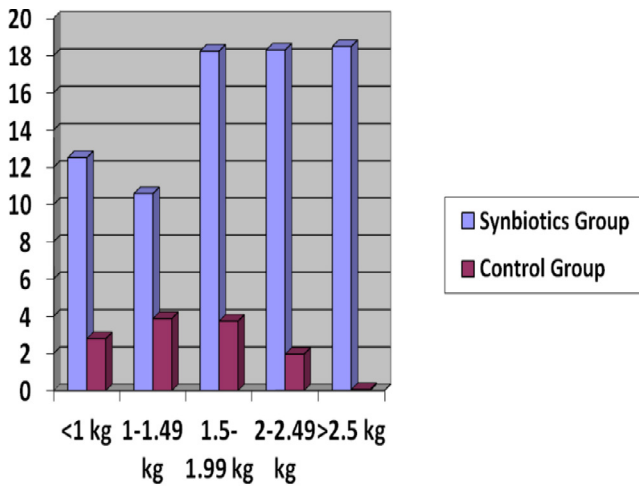


Figure 3. Average weight gain per day (mean) in different weight groups in Synbiotics and Control Group.

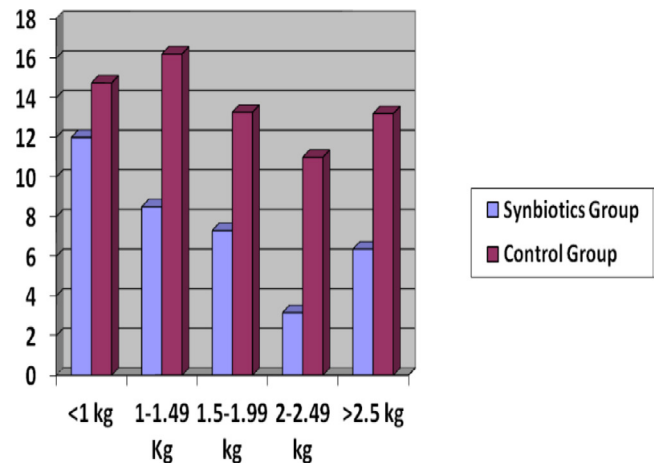


Figure 4. No. of days to reach full feeds (Mean) in Synbiotics Group and Control Group in different weight groups.

Table 7. No. of days to reach full feeds in different weight groups in Synbiotic and Control Groups

Weight(kg)	No. of days to reach full feeds Synbiotic Group		No. of days to reach full feeds Control Group		Unpaired t test value	Degree of freedom	P value
	Mean	S.D.	Mean	S.D.			
<1	12	7.62	14.75	3.30	0.66	6	p=0.532
1-1.49	8.5	3.36	16.21	11.54	2.93	38	p=0.0056
1.5-1.99	7.3	3.91	13.27	5.1	3.12	21	p=0.00508
2-2.49	3.16	0.75	11	4.54	4.15	11	p=0.0016
>2.5	6.37	3.78	13.2	6.94	2.37	12	p=0.0352
Overall	7.52	4.26	14.02	7.88			0.000004

4. Discussion

In our study, 98 neonates were assigned randomly to Synbiotics group (50) and control group (48). The newborn’s demographic and clinical characteristics did not differ between two groups. In the present study, majority of neonates were between 1-1.99 kg (64% in the synbiotics vs. 64.58% in the control) and between 32–36 weeks of gestations (50% in the synbiotics vs. 62.5% in the control).

During their stay in NICU, the synbiotics and control groups were compared for tolerance to feeds (no. of days required to reach full feeds) and average weight gain per day.

4.1 Average weight Gain Per Day

In our Study the average weight gain per day was 14.61 ± 9.6 grams per day in Synbiotics group and 2.97 ±

3.81 grams per day in control group which was highly significant (p=0.0000001). We were unable to find any other study which showed significant effect of prebiotics, probiotics or synbiotics on the weight gain in newborns. Although some studies have shown better weight gain in study group but failed to find any statistical significance.

Kitajima et al.¹⁰ (using *B. breve* with sample size of 88), Costalos et al.¹² (using *S. boulardii*), Indrio et al.²² [using Galacto-oligosaccharides (GOS) and Fructo-oligosaccharides (FOS)] and Mark A et al.²³ (using *L. acidophilus*, *L. rhamnosus* GG, *B. Longum*, *B. Bifidum*, *B.infantis* and FOS with sample size of 90) also found better weight gain in study groups as compared to control/placebo group but the difference was not statistically different. Puccio et al.²⁴ observed similar results in their studies.

In our study, the significant effect on the weight may be due to use of combination of probiotics or due to simultaneous use of prebiotics of our study or due to small sample size.

4.2 Feed Tolerance

In our study, the no. of days to reach full feeds in synbiotics group and control group were 7.5 ± 4.26 days and 14.02 ± 7.88 days respectively which was highly significant ($p=0.000004$) when compared to control group, showing better feed tolerance in Synbiotics group. But when babies were compared according to their birth weights, the difference was not statistically significant in babies of <1kg weight group ($p=0.532$).

Similar observations were found in the study done by Kitajima et al.¹⁰ and Carole Rouge et al.²⁰. Kitajima et al.¹⁰, Kukkonen K et al.²¹ in their study of 88 newborns, demonstrated better feed tolerance (reduced aspirated air volume from stomach) and episodes of vomiting; and found significant reduction of both in the probiotics group. Carole Rouge et al, in their study of 94 babies, found that no. of days to reach full feeds for >1kg babies were significantly less in probiotics group as compared to control (mean 16 vs 19 $p=0.04$) but in babies <1kg it was not significant (mean 34 vs 32 $p=0.12$). Our study confirms this finding. Mihatsch WA et al.²⁵ and Indrio et al.²² who used only prebiotics (combination of FOS and GOS) in their studies also found improvement in feed tolerance in the prebiotics group.

However other authors like Dani et al.⁹, Costalos et al.¹², Bin-Nun et al.¹³, Manzoni et al.¹⁶ and Lin et al.¹⁵ who used probiotics only did not find any significant difference between probiotic and control group as far as feed tolerance was concerned. Also Puccio et al.²⁴ and Underwood et al.²³ who used synbiotics just like our study did not find any significant difference in feed tolerance between synbiotics and control groups. However they used different combination of probiotics in their study as compared to our study.

Groups which found difference have used *Bifidobacterium breve* and combination of *B. lactis* with *L. rhamnosus* GG probiotics while those who haven't found significant difference have used different probiotics (*B.infantis*, *B.infantis*, *B.bifidum*, *S.thermophilus*, *L.acidophilus* and *S.boulardii*) as seen from Table 16. So this difference could be due to use of specific probiotic.

5. Conclusion

On the basis of our study we conclude that Synbiotics can improve feed tolerance and weight gain in newborns, thus enables early discharge. However, it still needs a larger study is needed to establish the standards and dosing in Indian newborns.

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