THERAPEUTICS

L. Ciocîrla, L. Crivceanschi, G. Şcerbacova

THE USE OF EUBIOFLOR IN ORGANISING THE INTESTINAL FLORA IN NEW BORNS

SUMMARY

Up to 30% of the pregnant women present urogenital infections; every 4th pregnant woman is affected from a chronic disease, the rate of caesarean births is high, the incidence of infected new-borns is also increased as well as the number of new-borns fed artificially.
The clinical effects of probiotics are: inhibition of the potentially pathogenic Escherichia coli, Staphylococcus aureus, and Clostridium perfringens; prevention of diarrhoea; reduction of fungal infection (Candida).
We have designed this cohort prospective study in order to evaluate in catamnesis the new-borns with intestinal dysbiosis.
The study included a total number of 68 new-borns having the following gestational age (gestational weeks): 26 g.w. - 4%; 27- 28 g.w.- 13%; 30-32 g.w. - 31%; 33 -36 g.w.- 32%; 37- 42 g.w. - 20%.
A growth deficiency has been attested in 45%.
Their body mass was: 500 - 999 g- 4%; 1000-1999g.- 39%; 1999- 2499g.- 33%; 2499- 4000 g.- 24%.
All subjects have been divided into two Groups.
Group I – 38 children with certified diagnosis of intestinal dysbiosis who received Subtil;
Group II - 30 children also with confirmed diagnosis of intestinal dysbiosis who received Eubioflor.
The current study has shown that in the Group I (Subtil), positive results was attested at the 4th day in 64% of the children, while at the 10th-30th day in 78% of the children the gastrointestinal disturbances had disappeared.
In Group II (Eubioflor) positive results have been obtained at the 4th day in 82% of the children and at the 10th-30th day in 89% of the children.

KEY WORDS **INTESTINAL FLORA, DYSBIOSIS, IMMUNE SYSTEM, *BIFIDOBACTERIA*, EUBIOFLOR**

BACKGROUND

During the last decades an increased incidence of metabolic syndrome, allergic diseases, autoimmune diseases, diabetes mellitus, chronic gut diseases have been reported.
The disturbances of intestinal flora are considered to be among the main risk factors of these pathologies.
In the intestinal tract microorganisms play a very important role in the differentiation and activation of the Immune System in children.

A healthy intestinal flora determines the physiological differentiation and activation of immune cells and thus can prevent pathologic immune problems.

THE IMMUNE-MODULATING ROLE OF THE INTESTINAL FLORA

The colonization of the gastrointestinal tract in new-borns determines the formation of a protective barrier and the activation of the Immune System. The prevalence of *Bifidobacterium* among the intestinal microorganisms stimulates the non-specific immune response, increases the phagocytes activity, increases the secretion of IgA and protects the child from endogenous infections and diarrhoea, blocks the growth of pathological microorganisms by reduction of the intestinal pH, reduces overweight, removes the toxins, stimulates the production of B vitamins and of some enzymes, protects the enterocytes against Zn insuffi-

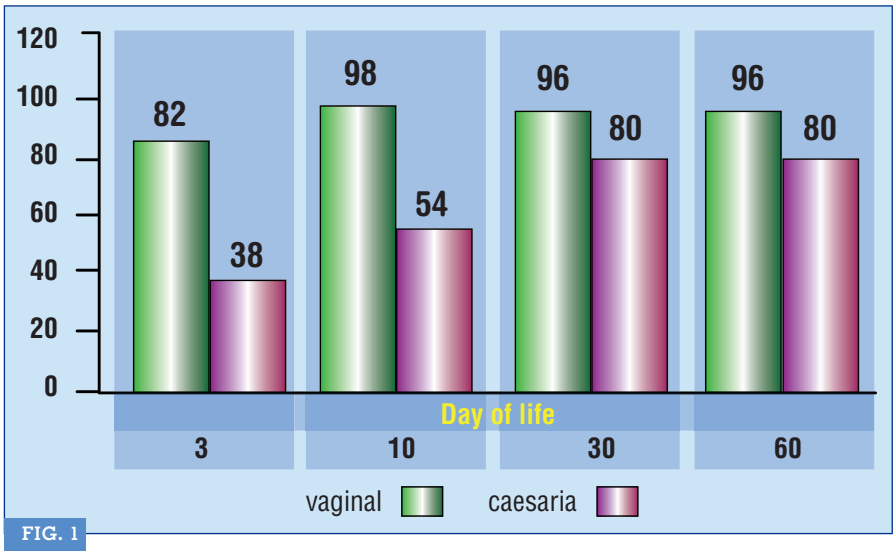


FIG. 1

The component of intestinal microflora regarding the type of birth (the level of colonization with *Bifidobacterium*) (S.Nutten, 2007).

FIG. 2

The influence of antibiotics on the intestinal flora (S.Nutten, 2007).

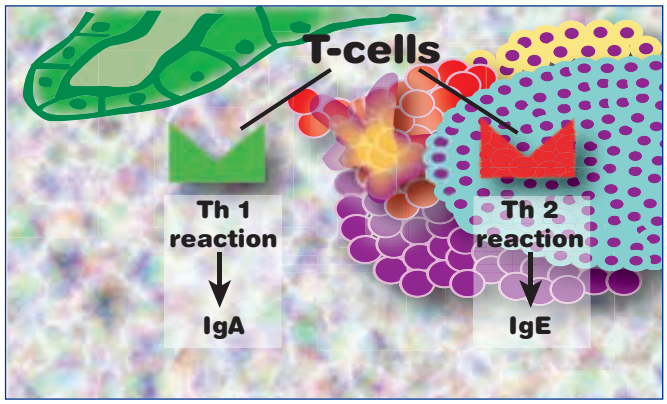
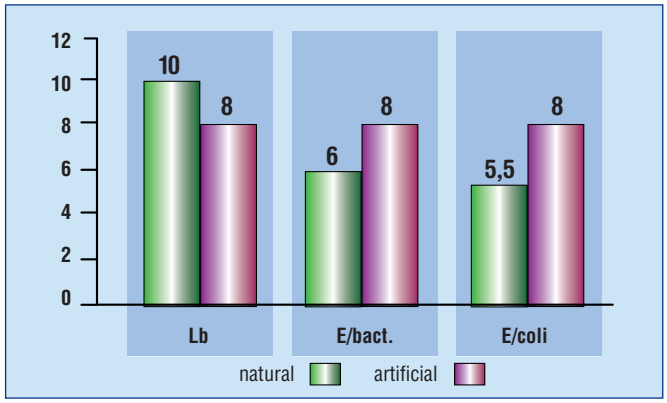


FIG. 3

Intestinal microflora in children depending on diet.



ciency, inhibits the activation of Th, determines tolerance to foods, blocks the pro-inflammatory cytokines, and helps the Th2 - Th1 switch.

The immune modulating role of *Bifidobacterium* is very important, especially during the most critical postnatal period.

WHICH FACTORS DETERMINE THE INTESTINAL FLORA IN THE NEW-BORN?

After birth many factors influence the type and concentration of intestinal microflora in new-borns (FIG. 1): mother's health, mother's intestinal flora, pregnancy evolution, quality of diet, type of birth, intake of antibiotics during the postnatal period, living environment, etc. (FIGG. 2, 3, 4, 5).

The intake of *amoxicillin* has demonstrated to increase the number of specific intestinal cells, to decrease the food tolerance, and increase the incidence of inflammatory diseases.

The beneficial role of breast feeding in the organisation of intestinal microflora compared to artificial feeding has been confirmed due to the presence of *Bifidobacterium* in the human milk.

HOW IMPORTANT IS THE PROBLEM OF DYSBIOSIS AND THE INTAKE OF PROBIOTICS?

Up to **30% of the pregnant women** presents urogenital infections; every 4th pregnant woman is affected from a chronic disease, the rate of caesarean births is high, the incidence of infected new-borns is also increased as well as the number of new-borns fed artificially.

The clinical effects of probiotics are: inhibition of the potentially pathogenic *Escherichia coli*, *Staphylococcus aureus,* and *Clostridium perfringens*; prevention of diarrhoea; reduction of fungal infection (*Candida*).

Moreover probiotics have a favourable effect on cholesterol level; prevent/

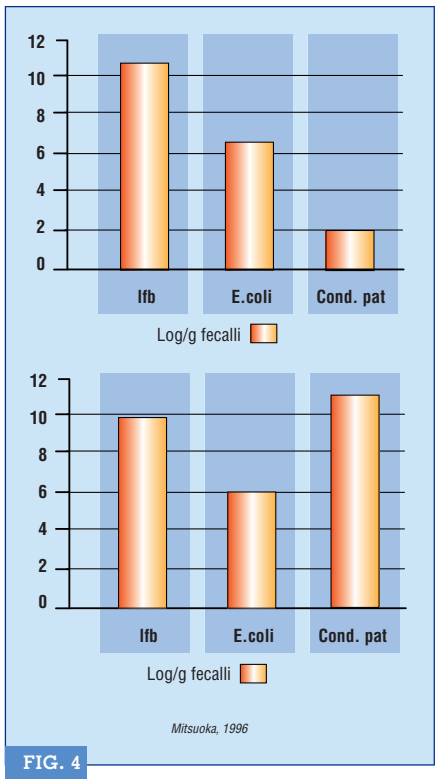


FIG. 4

The evolution of intestinal microflora during the 1st year of life.

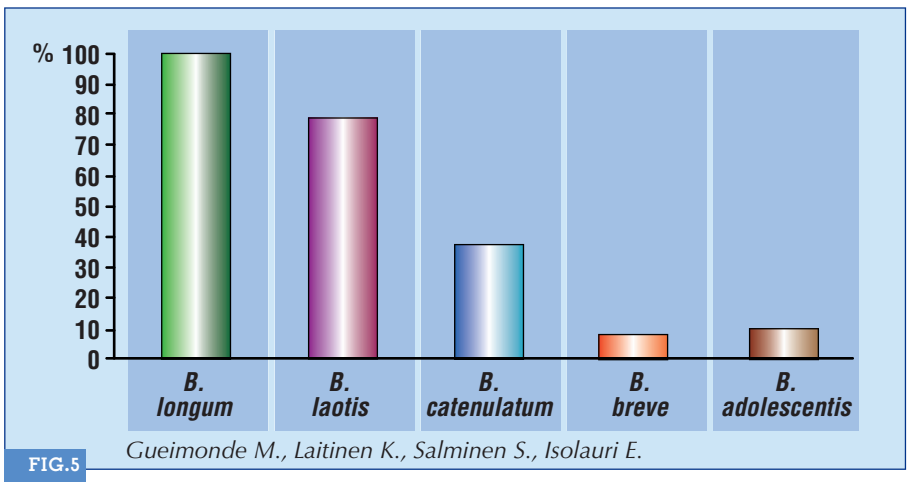


FIG.5

Breast-feeding determines a predominance of *Bifidobacterium* up to 99%.
- There are different species of *Bifidobacterium* in human milk.

decrease the incidence of colon cancer; stimulate the Immune System; synthesize vitamins; decrease constipation frequency; improve the absorption of minerals - especially Calcium; improve the digestion of lactose (in subjects with intolerance to lactose).

Types of *Bifidobacteria* (geno-molecular assessment)	Infants, breast-feeding (N=27)	Infants after 6 months, breast-feeding plus compliments (n=17)
B. bifidum (1)	66.6%	88.2% (2)
B. infantis (2)	51.9%	52.9 (3)
B. longum (3)	44.4%	29.4%
B. adolescentis	29.6%	23.5%
B. dentium	29.6%	23.5%
B. breve	Not attested	100% (1)

TAB. 1

The frequency of detecting different types of *Bifidobacteria* in infants during the 1st year.

Disease	N level of evidence	Probiotic
Allergy (atopic eczema, allergy associated to cow-milk protein)	A	*LGG, B. lactis*
therapy	A	*LGG, Lactobacillus acidophilus, L. plantarum, Bifidobacterium lactis, Lactobacillus johnsonii*
prevention		
Immune response	A	
Irritable Bowel Syndrome	B	*Bifidobacterium infantis*
	C	*Bifidobacterium animalis, VSL#3, Lactobacillus plantarum*
Diarrhea	A	*LGG, Lactobacillus reuteri*
• infection in children (treatment)		
• prevention ADD	A	*S. boulardii, LGG, L. casei, L. bulgaricus, S. thermophilus*

TAB. 2

Clinical recommendation for probiotics use.

- Recommendations for Probiotic Use—2008; Floch *et* Al.

Antibiotics	SUBTIL during and after antibiotic therapy %		EUBIOFLOR during and after antibiotic therapy %	
Peniciline im	10,5	8	9,0	7
Semisintetic	42,5	34	43	33
Cefalosporine	52,1	65	53,4	69
Macrolide	7,8	4,8	6,9	3,9

TAB. 3

Frequency of antibiotic intake in the 2 groups (Subtil or Eubioflor).

THE CLINICAL TRIAL

- The aim of the trial is to attest the efficiency of probiotics in the prevention and treatment of dysbiosis.

MATERIALS AND METHODS

We have designed this cohort prospective study in order to evaluate in catamnesis the new-borns with intestinal dysbiosis. Some important data on the topic are present in the scientific literature (TABB. 1, 2).

The study included a total number of **68 new-borns** having the following gestational age (gestational weeks): 26 g.w.- 4%; 27- 28 g.w.- 13%; 30-32 g.w. - 31%; 33 -36 g.w.- 32%; 37- 42 g.w. - 20%.

A growth deficiency has been attested in 45%.

Their body mass was: 500 - 999 g- 4%; 1000-1999 g.- 39%; 1999- 2499 g.- 33%; 2499- 4000 g.- 24%. All subjects have been divided into **two** groups.

Group I – 38 children with certified diagnosis of intestinal dysbiosis who received **Subtil**;

Group II - 30 children also with confirmed diagnosis of intestinal dysbiosis who received **Eubioflor**.

- Examination methods

For the examination, clinical and catamnestic data were used.

The laboratory parameters taken into account were: total blood and urine analysis, intestinal biocenosis.

The data have been collected at the 1st, 7th and 30th day.

In TAB. 3 the antibiotic therapy is showed for both groups. All the data have been statistically processed using the *student-t test* and the significance has been evaluated by means of the *p* value.

RESULTS

The current study has shown that in the Group I (**Subtil**), positive results was attested at the 4th day in 64% of the children, while at the 10th-30th day in **78%**

%	Appetite 1st day	4st day
GrI	80	36
GrII	81	24

%	Regurgitation 1st day	4st day
GrI	24	12
GrII	23	10

%	Pain 1st day	4st day
GrI	34	11
GrII	33	8

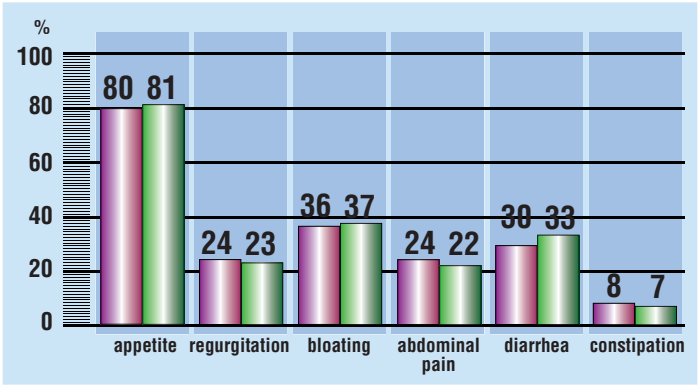
%	Diarrhea 1st day	4st day
GrI	44	12
GrII	48	5

TAB. 4

Follow-up of the features of gastrointestinal disturbances in new-borns.

FIG. 6

The features of gastrointestinal disturbances in new-borns at the base-line in both Groups.



Stage Patients %	Before treatment		10th day		30th day		P– (10th and 30th day)	
	Group I	Group II	Group I	Group II	Group I	Group II	Group I	Group II
I	-	-	24	28	9	5		
II	36,7	37	29	24	-	-	<0,001	<0,001
III	33,3	31	17	2	-	-	<0,001	<0,001
IV	30	32	-	-	-	-	<0,001	<0,001
normal	-	-	30	46	91	95		

TAB. 5

The stage of the intestinal dysbiosis during the follow-up period.

of the children the gastrointestinal disturbances had disappeared.

In Group II (**Eubioflor**) positive results have been obtained at the 4th day in 82% of the children and at the 10th-30th day in **89%** of the children.

The monitoring of the new-borns has demonstrated that the administration of Subtil or Eubioflor reduces the gastrointestinal disturbances in both groups, but faster results were obtained in group II,which included the administration of Eubioflor.

All children have been controlled also according to the stage of the intestinal dysbiosis (FIG. 6; TABB. 4, 5).

Both probiotics used have been well tolerated by new-borns without any adverse effect in 100% of the children included in the study.

CONCLUSIONS

1. Intestinal flora in new-borns depends on mother's health, mother's microflora, pregnancy evolution, type of feeding, type of birth, use of antibiotics after the postnatal period, environment and microflora present in the intensive care department.

2. The colonization of gastrointestinal tract of new-borns determines the protection and the activation of the Immune System.

3. The immunemodulatory function of *Bifidobacterium* is very important, especially during the most critical period – early postnatal life.

4. **Subtil** treatment has shown positive results at the 4th day in 64% of children, while at the 10th-30th day in **78%** of children the gastrointestinal disturbances had disappeared.

5. During the treatment with **Eubioflor** positive results have been obtained at the 4th day in 82% and at the 10th-30th day in **89%** of children.

6. The medications tested in this trial have been well tolerated in both groups without any adverse effect in 100% of the cases. ■

First author's address

L. Ciocîrla, MD
– Department of Paediatric and New-Born Diseases
State University of Medicine and Pharmacy, *Nicolae Testemitanu*, (chief Department: P. Stratulat).
Chisinau - Republic of Moldova