I PROBIOTICI E LE FORMULE: PER QUALE OBIETTIVO?

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Piacenza

colonizzazione intestinale neonatale da parte d

lora intestinale e vaginale materna (bifidobatteri

batterioidi, enterobatteri, clostridi e bacillococch

gram +)*(Heine 1998)*

Molecular characterization of intestinal microbiota in infants born by caesarean delivery

Biasucci G[1], Benenati B[1], Morelli L[2], Bessi E[3], Boehm G[4,5]

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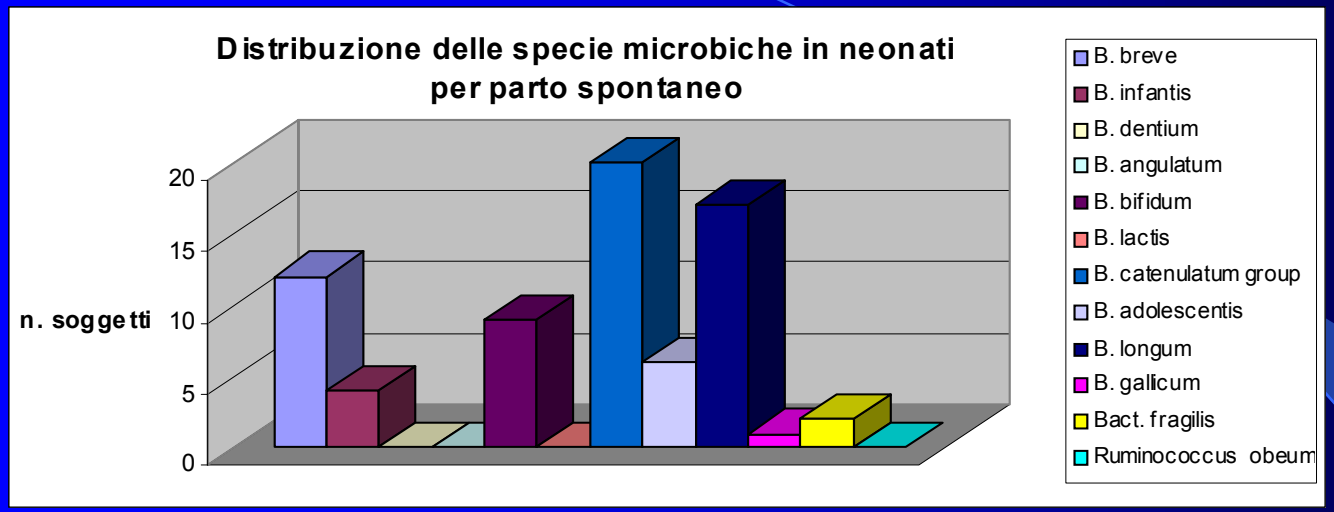
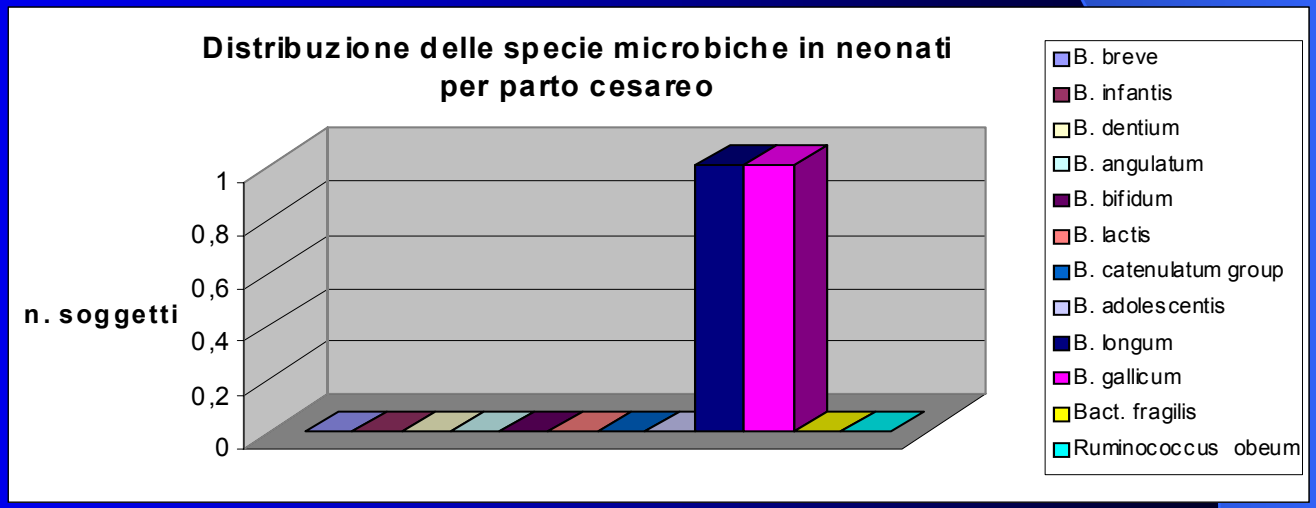
Neonati da parto spontaneo



Neonati da parto cesareo



colon: > 400 specie diverse di batteri ad effetti potenzialmente patogeni e/o favorevoli per l'ospite, stabili già in 10° giornata di vita, influenzati da patologie, farmaci e *alimentazione*

Flora batterica fecale

LM	*formula*
Bifidobatteri(>90%)	Bacteroidi
Lattobacilli	Bifidobatteri
	Stafilococchi
	E. coli
	Clostridi

Possibili cause: differente qualità e quantità proteica, oligosaccaridi, fattori immuno-modulatori cellulari e umorali

Satokari RM, Vaughan EE, Favier CF, et al. Diversity of *Bifidobacterium* and *Lactobacillus* spp. in breast-fed and formula-fed infants as assessed by 16S rDNA sequence differences. *Microb Ecol Health Dis* 2002;14:97–105.

Harmsen HJ, Wildeboer-Veloo AC, Raangs GC, et al. Analysis of intestinal flora development in breast-fed and formula-fed infants by using molecular identification and detection methods. *J Pediatr Gastroenterol Nutr* 2000;30:61–7.

Rubaltelli FF, Biadaioli R, Pecile P, et al. Intestinal flora in breast- and bottle-fed infants. *J Perinat Med* 1998;26:186–91.

Heine W, Mohr C, Wutzke KD. Host–microflora correlations in infant nutrition. *Prog Food Nutr Sci* 1992;16:181–97.

Ouwehand A, Isolauri E, Salminen S. The role of the intestinal microflora for the development of the immune system in early childhood. *Eur J Nutr* 2002;41(Suppl 1):132–7.

Kunz C, Rodriguez-Palmero M, Koletzko B, et al. Nutritional and biochemical properties of human milk. Part I: General aspects, proteins, and carbohydrates. *Clin Perinatol* 1999;26:307–33.

Probiotici – nuova definizione

Preparazioni di cellule microbiche o componenti di cellule microbiche che hanno effetto benefico sulla salute ed il benessere dell'ospite

Salminen 1999

i probiotici

Requisiti generali

provenienza intestinale

biosicurezza /assenza di patogenicità

resistenza a basso pH, succo gastrico e pancreatico

I LATTI FORMULATI

i probiotici

Requisiti tecnologici

- **capacità di sopravvivenza durante la conservazione del latte acidificato**
- **assenza di effetti metabolici secondari con aumento acidità o proteolisi durante la conservazione**

Requisiti funzionali

- **capacità di adesione alla mucosa intestinale con azione di barriera** ("spiazzamento" recettoriale flora patogena)
- ↓ **enzimi intestinali con azione procarcinogenica**
- **stimolazione sistema immunitario: IFN gamma, GALT**
- **colonizzazione intestinale → equilibri microbiologici**
- **inibizione di microrganismi patogeni:** batteriocine, competiz.per nutrienti

LE FORMULE E

i probiotici

Obiettivi nella prima infanzia:

) **influenzare la crescita di un ecosistema intestinale "favorevole"**
Latti acidificati ed arricchiti con bifidobatteri (con parzial
idrolisi e fermentazione proteica) sembra riducano la carica d
clostridi, bacilli e Bacteroides fragilis ed aumentino quella d
bifidobatteri, potenziando inoltre la barriera intestinale, co
azione simile al latte materno.

) **proteggere il lattante da infezioni intestinali: *L.casei GG* s**
diarrea da rotavirus; *Bifidob.bifidum e Str.thermophilus* i
profilassi enteriti virali acute, *L.acidophilus e casei* su enteriti d
E.Coli, salmonelle e shigelle, *Bifidob.breve* su enteriti d
campylobacter.

Come può, la flora intestinale, avere un ruolo nell'effetto protettivo del LM (↓ gastroenteriti ed infezioni) ?:

Bifidobatteri e lattobacilli:

produzione di:

ac.acetico, lattico, acidi organici

riduzione pH

competizione per:

nutrienti e

siti adesione epiteliale

Inibizione della crescita di batteri potenzialmente patogeni

Howie PW. Protective effect of breastfeeding against infection in the first and second six months of life. *Adv Exp Med Biol* 2002; 503:141–7.
Howie PW, Forsyth JS, Ogston SA, Protective effect of breast feeding against infection. Br Med J 1990;300:11–16.

Kelleher SL, Casas I, Carbajal N, et al. Supplementation of infant formula with the probiotic *Lactobacillus reuteri* and zinc: impact on enteric infection and nutrition in infant rhesus monkeys. *J Pediatr Gastroenterol Nutr* 2002;35:162–8.
Sudo N, Sawamura S, Tanaka K, et al. The requirement of intestinal bacterial flora for the development of an IgE production system fully susceptible to oral tolerance induction. *J Immunol* 1997; 159:1739–45.

Eur J Nutr (2006) 45 [Supplement 1]:I/1–I/18
DOI 10.1007/s00394-006-1101-1

ORIGINAL CONTRIBUTION

W. Allan Walker
Olivier Goulet
Lorenzo Morelli
Jean-Michel Antoine

Progress in the science of probiotics: from cellular microbiology and applied immunology to clinical nutrition

The regulatory constraints in Europe differ widely from those in the USA and Japan, probably due to the influence of sociocultural traditions. In Europe there is as yet no legal definition of "functional foods" and no legislation on their use in health claims. With regard to probiotic products, there has been no legislation on the use of microorganisms in human food and no prohibition of functional claims with regard to promoting health. In contrast, important health claims for probiotics are prohibited if they suggest disease treatment or disease prevention. Furthermore, the use of probiotics in animal feed is closely controlled. In the USA, all types of health claims (for health and disease prevention are authorized for functional products if the benefits have been demonstrated. Probiotics are

EUROPEAN COMMISSION
HEALTH and CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate C - Scientific Opinions
C2 - Management of scientific committees; scientific co-operation and networks

Scientific Committee on Food

SCF/CS/NUT/IF/65 Final
18 May 2003

Report of the Scientific Committee on Food on the Revision of Essential Requirements of Infant Formulae and Follow-on Formulae

(adopted on 4 April 2003)

oint FAO/WHO Expert Consultation on Evaluation of Health nd Nutritional Properties of Probiotics in Food Including owder Milk with Live Acid Bacteria (2001)

probiotic strains must survive the passage through the digestive tract and roliferate in

he gut;

they belong primarily to two genera: *Lactobacillus* and *Bifidobacterium*;

there are no *in vitro* tests to predict the probiotic activity of a strain;

strains should be named according to the International Code of Nomenclature

probiotic strains should be deposited in an internationally recognised culture

ollection;

strain identification should be performed by phenotypic tests followed by enetic

lentification with methods as DNA/DNA hybridisation, 16SRNA sequencing Blaut

t al., 2002) or similar methods;

effects considered and evaluated comprised prevention and therapy of infectious
arrheal diseases and of sequelae of antibiotic treatment, *Helicobacter pylori*
fection, inflammatory bowel diseases, prevention or delaying the onset of cancer,
leviation of constipation, modulation of mucosal or systemic immune responses
cluding allergic diseases, benefits on cardiovascular diseases and urogenital
sorders and infections, possible beneficial or adverse effects in healthy subjects;
the necessity for well designed in vivo trials was underlined;

safety considerations should include transmission of antibiotic or dru
esistance inherent in some probiotic microorganisms; the exclusion o
***nterococcus* strains as probiotic microorganisms was recommended;**

labelling should include the microbial species or strain and its viabl
oncentration, claims would have to be substantiated;

dried milk powders with live lactic acid bacteria should preserve adequat
umbers of viable probiotic bacteria with stable probiotic properties throughou
helf-life;

the regulatory status of probiotics as a component in food should be established on ar
ternational level.

The Committee recognises the necessity to come to a decision at Community level on the use of bacteria generally considered as probiotics in infant formulae and/or follow-on formulae. The Committee consulted previous expert reports, but in view of time restrictions was unable to perform a full review of the available evidence on the inclusion of probiotic bacteria into infant formulae and follow-on formulae, and it recommends that a full review should be performed in the future. The Committee notes that the available information is still limited, and many studies in young infants have been done in non-European countries and in selected subpopulations of infants that are at increased risk of infectious or atopic diseases. The Committee recommends that infant formulae with microorganisms regarded as probiotics should only be introduced into the market if their benefit and safety have been evaluated according to the principles outlined in chapter XI of this report.

Follow-on formulae with added bacteria regarded as probiotics have been for since abou three years. The Committee has no reason to object to the addition of bacteria regarded as probiotics to follow-on formulae, provided the requirements described below are fulfilled.

Only bacterial strains with identity and genetic stability demonstrated by cultural and molecular methods should be used, if they can be considered as generally safe when added to the individual food and have been shown to survive the gastrointestinal passage, have the capacity to proliferate in the gut for the duration of consumption and can modify the intestinal milieu (for example pH, short chain fatty acids). The identity of the probiotic strain should be described by molecular methods in a dossier and be available to the food control authorities. The content of viable bacteria should be such throughout shelf-life as to achieve 10^6 to 10^8 colony forming units per gram of formula prepared as ready for consumption. Processing, packaging and storage should not impair the viability of the bacteria.

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38:365–374 © April 2004 Lippincott Williams & Wilkins, Philadelphia

Medical Position Paper

Probiotic Bacteria in Dietetic Products for Infants: A Commentary by the ESPGHAN Committee on Nutrition

ESPGHAN Committee on Nutrition: *Carlo Agostoni, †Irene Axelsson, ‡Christian Braegger, §Olivier Goulet, ||Berthold Koletzko, #Kim F. Michaelsen, **Jacques Rigo, ††Raanan Shamir, ‡‡Hania Szajewska, §§Dominique Turck, and |||Lawrence T. Weaver

Revisione sistematica al 2003 di studi relativi a formule addizionate con probiotici:

Fonti:

EMBASE, MEDLINE, COCHRANE

Risultati:

6 RCT finalizzati alla valutazione di efficacia clinica su end poin
levanti

basati su formule di partenza e di proseguimento

basati su formule ipoallergeniche

Author	Study	Allocation concealment	Age (mo)	Patients/ Setting	Intervention	Main results	Jadad score
Infant and follow-on formulas							
Saavedra et al.[25]	RCT	Adequate	5–24	Chronic medical care hospital (USA)	FOF with *Bifidobacterium* bifidum (1.9×10^9 CFU/g) and *Streptococcus thermophilus* (0.14×10^7 CFU/g of powder) (n = 29) or control formula (n = 26), mean duration 81 days	Reduced number of patients with diarrhea (RR 0.2 [0.06–0.8]; NNT 5 (3–20)	5
Phuapradit et al.[26]	RCT*	Unclear	6–36	Orphanage (Thailand)	FOF with *Bifidobacterium* lactis Bb12 (10^8/g of powder, n = 62) or with Bb12 + *Streptococcus thermophilus* (ST) (dose not reported, n = 56) or cow's milk formula (n = 57) for 8 mo	Episodes of observed diarrhea; control 25%, Bb 65%, Bb + ST 52% (significance not reported)	1

*No details on randomization given.

RCT = randomized controlled trial; IF = infant formula; FOF = follow-on formula; CFU = colony forming units; RR = relataive risk; NNT = number needed to treat; SCORAD = score of atopic dermatitis.

Langhendries et al.[27]	RCT*	Unclear	0–2	Home (Belgium)	IF + *Streptococcus thermophilus* and *Lactobacillus helveticus* (*Bifidobacterium bifidum*) 10^6/g of powder, (n = 20) or control (n = 20) or breast-fed infants (n = 14; not randomized)	Colonization with bifidobacteria at 1 month, similar in Bb formula (12/20) *v* breast-fed (8/14), but significantly higher ($P < 0.05$) than in the group fed standard infant formula(4/20) Mean bacterial count of bifidobacteria similar in all colonized infants. Fecal pH significantly lower in the breast-fed infants than in the nonacidified bottle-fed infants.	3
Nopchinda et al.[28]	RCT*	Unclear	6–36	Orphanage (Thailand)	FOF (?) with *Bifidobacterium bifidum* Bb12 (3×10^7 CFU/g of powder, n = 51) or with Bb12 + *Streptococcus thermophilus* (ST) (3×10^7 CFU/g of powder n = 54) or cow's milk formula (FOF) (no details given) (n = 43) for 6 mo	Nutritional status (mean Z score of: weight; change of weight; height; height change; weight/height during 6 mo of intervention) Significant differences between groups at entry; no data on the amount of formula consumed and on the duration of intervention in each group. At 6 mo, data of 84/184 (57%) subjects enrolled (Bb12 71%; Bb12 + ST 43%, FOF 58%)	2

*No details on randomization given.

RCT = randomized controlled trial; IF = infant formula; FOF = follow-on formula; CFU = colony forming units; RR = relataive risk; NNT = number needed to treat; SCORAD = score of atopic dermatitis.

Author	Study	Allocation concealment	Age (mo)	Patients/ Setting	Intervention	Main results	Jadad score
Foods for special medical purposes							
Isolauri et al.[30]	RCT*	Unclear	Mean age 4.6 (age range not given)	Infants with atopic eczema during breast feeding (Finland)	Extensively hydrolyzed whey formula (H) (n = 9) Extensively hydrolyzed whey formula + *Bifidobacterium* lactis Bb-12 (HBb12) (1×10^9 CFU/g) (n = 9); Extensively hydrolyzed whey formula + *Lactobacillus* GG (HLGG) (3×10^8 CFU/g) (n = 9) Duration of intervention not reported (2 mo?)	After 2 mo: SCORAD significantly decreased in both groups treated with probiotic supplemented hydrolysates (HBb12 before treatment: 12 (5.5–18); after treatment: 0 (0–3.8); HLLG before treatment: 14.5 (6–25.3); after treatment: 1 (0.1–8.7); no significant difference in HS group; before treatment: 10 (6.5–26.5); after treatment: 13.4 (4.5–18.2). SCORAD significantly improved in 9/9 in HS-Bb-12 group after 2 mo *v* 9/9 in HS/LGG group *v* 4/9 in HS group; RR: 2.2 (95% CI: 1.5–5). After 6 mo: no difference in SCORAD.	2
Majamaa and Isolauri[29]	RCT*	Unclear	2.5–15.7	Infants with atopic eczema and cow's milk allergy (Finland)	Extensively hydrolyzed whey formula (n = 14) or extensively hydrolyzed whey formula + *Lactobacillus* GG (5×10^8 CFU/g) (n = 13) for 1 mo; follow-up for 2 mo	SCORAD after 1 mo significantly [from 26 (17–38) to 15 (7–28)], but no change in controls (from 21 (14–31) to 19 (13–31)]. After 2 mo: no significant difference between the study groups.	2

*No details on randomization given.

RCT = randomized controlled trial; IF = infant formula; FOF = follow-on formula; CFU = colony forming units; RR = relataive risk; NNT

CONCLUSIONS

Our review of available clinical trials found only limited data on the safety and clinical effects probiotic preparations added to infant formulas, follow-up formulas, and special medical foods. There is no published evidence for any long-term clinical benefit of infant formulas supplemented with probiotic bacteria. No data are available on possible long-term effects on intestinal colonization and its effects on long-term gastrointestinal and immune functions. Acquisition of such data would be highly desirable given the suggestion that bacteria ingested during early infancy are more likely to permanently colonize the intestine than those ingested during later life (84). There are some data supporting a short-term benefit of some probiotic strains in infants and young children with infectious diarrhea.

The Committee recognizes that there is evidence that some probiotic preparations have benefits on health and well-being. Reported benefits include a reduced severity of diarrhea, potential preventive effects on diarrhea, promising results of in vitro and animal studies on digestive and immune functions, and indications from human studies on possible short-term preventative and therapeutic effects on atopic eczema. In view of the potential for benefits on child health that might be achieved by the use of some probiotic bacteria, major efforts on their thorough evaluation are justified.

Probiotics in Clinical Practice: an Overview

GV Zuccotti, F Meneghin, C Raimondi, D Dilillo, C Agostoni, E Riva and M Giovannini

The Journal of International Medical Research 2007; in press

PROBIOTICI

(30 anni di studi clinici)

La maggior parte dei ceppi batterici con

- dimostrata efficacia probiotica
- sicurezza d'uso

appartiene ai generi

Lactobacillus e Bifidobacterium

PROBIOTICI NELLE FORMULE: Gastroenteriti

AUTHOR AND YEAR PUBLISHED	POPULATION STUDIED	TYPE OF TRIAL	TYPE OF PROBIOTIC	PROBIOTIC(s) DOSE	OUTCOME	TYPE OF EVIDENCE
Thibault H, 2004	971 healthy infants (4-6 months)	**randomized**, double-blind, placebo-controlled trial	**Bifidobacterium breve Streptococcus thermophilus**	formula fermented with Bb and St for 5 months	**reduce the severity of acute diarrhea** among healthy young infants	**I**
Eduardo Salazar-Lindo, 2004	male infants aged 3-36 months with acute watery diarrhea; 89 received placebo, 90 LGG.	double-blind, **randomized**	**Lactobacillus casei strain GG (LGG)**	milk formula with 10^9 cfu/ml of LGG	**no significant difference** between two groups (placebo vs LGG).	**I**

Journal of Pediatric Gastroenterology and Nutrition
33:S17–S25 © October 2001 Lippincott Williams & Wilkins, Inc., Philadelphia

Probiotics in the Treatment and Prevention of Acute Infectious Diarrhea in Infants and Children: A Systematic Review of Published Randomized, Double-Blind, Placebo-Controlled Trials

*Hania Szajewska, and †Jacek Z. Mrukowicz

**Department of Pediatric Gastroenterology and Nutrition, The Medical University of Warsaw, Warsaw, Poland; and †Medycyna Praktyczna, Cracow, Poland*

Methods: A systematic review of published, randomized, double-blind, placebo-controlled trials on probiotics in the treatment or prevention of acute diarrhea defined as >3 loose or watery stools per 24 hours in infants and children.

Conclusions: There is evidence of a clinically significant benefit of probiotics in the treatment of acute infectious diarrhea in infants and children, particularly in rotaviral gastroenteritis. *Lactobacillus GG* showed the most consistent effect, although other probiotic strains may also be effective. Further research is needed. Clinical and statistical heterogeneity of the prophylactic interventions preclude drawing firm conclusions about the efficacy of probiotics in preventing acute gastroenteritis. *JPGN 33:S17–S25, 2001.* **Key Words:** Probiotics—

REVIEW ARTICLE

Lactobacillus Therapy for Acute Infectious Diarrhea in Children: A Meta-analysis

Cornelius W. Van Niel, MD*‡; Chris Feudtner, MD, PhD, MPH‡§; Michelle M. Garrison, MPH§; and Dimitri A. Christakis, MD, MPH‡§

Results. Summary point estimates indicate a reduction in diarrhea duration of 0.7 days (95% confidence interval: 0.3–1.2 days) and a reduction in diarrhea frequency of 1.6 stools on day 2 of treatment (95% confidence interval: 0.7–2.6 fewer stools) in the participants who received *Lactobacillus* compared with those who received placebo. Details of treatment protocols varied among the studies. A preplanned subanalysis suggests a dose-effect relationship.

Conclusion. The results of this meta-analysis suggest that *Lactobacillus* is safe and effective as a treatment for children with acute infectious diarrhea. *Pediatrics* 2002; 109:678–684; *gastroenteritis, infectious diarrhea,* Lactobacillus, *meta-analysis, rotavirus.*

Probiotici nella Pratica Clinica

Gastroenteriti: sintesi

linical condition	Clinical effectiveness	Organisms
iarrhea	A	S. boulardii , LGG , L.reuteri (±L.rhamnosus)

PROBIOTICI NELLE FORMULE: AAD

AUTHOR AND YEAR PUBLISHED	POPULATION STUDIED	TYPE OF TRIAL	TYPE OF PROBIOTIC	PROBIOTIC(s) DOSE	OUTCOME	TYPE OF EVIDENCE
Correa NB, 2005 [68]	double-blind, **randomized,** controlled formula study	80 infants (6-36 months)	**Bifidobacterium lactis Streptococcus thermophilus**	commercial formula containing 10^7 viable cells of B lactis and 10^6 viable cells of S thermophilus at initiation of antibiotics for 15 days	**prevention** against AAD in infants	**I**

Probiotici nella Pratica Clinica

AAD: sintesi

linical condition	Clinical effectiveness	Organisms
ntibiotic-associated diarrhea	A	S.boulardii, LGG, Lactobacilli+Bifidobatteri

Probiotici e allergia: razionale dell'uso

Poiché alla nascita l'intestino è sterile e lo sviluppo della flora intestinale è influenzato anche dalla dieta, la supplementazione con probiotici può influenzare la composizione della flora intestinale ed avere effetti immunomodulanti favorendo lo switch TH2/TH1

AUTHOR AND YEAR PUBLISHED	POPULATION STUDIED	TYPE OF TRIAL	TYPE OF PROBIOTIC	PROBIOTIC(S) DOSE	OUTCOME	TYPE OF EVIDENCE
Xiao JZ, 2006 [185]	**randomized**, double-blind study	57 infants were randomized and double-blindly allocated to the 3 groups before birth	**Bifidobacterium animalis**	prebiotic (GOS/FOS) group (n=19) receive infant formula with FOS and GOS (6g/l), probiotic group (n=19) formula with $6x10^{10}$ viable cells of B animalis, standard group (n=19) non supplemented formula	in probiotic group composition and metabolic activity of the flora were more similar to those of the standard group	I
Isolauri E, 2000 [187]	open study	7 healthy children (15-31 mo)	**Bifidobacterium lactis Bb-12**	a follow up formula containing 10^9 probiotic was given to the subjects for 21 days	The increase in local IgA levels resulting from ingestion of the probiotic formula may contribute to enhancement of the mucosal resistance against gastrointestinal infections	II
Kirjavainen PV, 2002 [193]	double blind **randomized** study	21 infants with early onset atopic eczema	**Bifidobacterium lactis Bb-12**	infants were randomize to receive extensively hydrolysed whey formula (EHF) with (treated group) or without (placebo group) probiotic supplementatio	data indicate that bifidobacterial supplementation appears to modify the gut microbiota in a manner that may alleviate allergic inflammation	I

Nutr. 2007 Mar;137(3 Suppl 2):794S-7S.

Antiallergic effects of probiotics.

Duwehand AC

Reduced exposure to microbial allergens as a result of our hygienic lifestyle ha been suggested as one of the possible causes. It has also been suggested tha probiotics may provide safe alternative microbial stimulation needed for th developing immune system in infants. This idea is supported by the fact tha allergic infants have been observed to have an aberrant intestinal microbiota. The were shown to have more clostridia and fewer bifidobacteria and, in addition, t have an adult-like Bifidobacterium microbiota. Clinical trials have shown that th standard treatment of infants with atopic eczema, extensively hydrolyzed infan formula, can be significantly improved through the addition of Lactobacillu rhamnosus GG or Bifidobacterium lactis Bb-12. It has also been shown possible t halve the incidence of allergy in at-risk infants through administration of L rhamnosus GG to expecting mothers and subsequently to their infants during th first half-year of life.

Clin Exp Allergy. 2006 Jul;36(7):899-906

No effects of probiotics on atopic dermatitis in infancy: a randomized placebo-controlled trial.

Prouwer ML, Wolt-Plompen SA, Dubois AE, van der Heide S, Jansen DF, Hoijer MA, Kauffman HF, Duiverman EJ

METHODS: We conducted a randomized, double-blind, placebo-controlled study. After 4 6 weeks of baseline and double-blind, placebo-controlled challenges for diagnosis of cow milk allergy (CMA), infants less than 5 months old with AD received a hydrolysed whey based formula as placebo (n = 17), or supplemented with either Lactobacillus rhamnosus (= 17) or Lactobacillus GG (n = 16) for 3 months. Before, during and after intervention, th clinical severity of AD was evaluated using SCORing index Atopic Dermatitis (SCORAD).

RESULTS: No statistically significant effects of probiotic supplementation o SCORAD, sensitization, inflammatory parameters or cytokine production betwee groups were found. Only four infants were diagnosed with CMA.

CONCLUSION: We found no clinical or immunological effect of the probiot bacteria used in infants with AD. Our results indicate that oral supplementatio with these probiotic bacterial strains will not have a significant impact on th symptoms of infantileAD

Enterocolite necrotizzante

Causa importante di morbilità e mortalità nei neonati prematuri

Prematurità, alimentazione enterale e colonizzazione batterica causano risposta infiammatoria esagerata responsabile della necrosi ischemica intestinale

In modelli animali l'esposizione a Bifidobatteri sembra essere protettiva perché inibisce la crescita di patogeni per esempio i Clostridi

ediatrics International, 2004, 46,5: 569

ffects of bifidobacterium breve supplementation on intestinal flora of low birth weight nfants

udong Li, Toshiaki Shimizu , Atsuto Hosaka , Noritsugu Kaneko , Yoshikazu Ohtsuka and Yuichiro amashiro

ackground: Because bacterial populations develop during the first day of life, the authors xamined whether the early administration of bifidobacteria has a positive effect on the health o ow birth weight infants.

Methods: The effects of **oral administration of *Bifidobacterium breve (B. breve)*** supplemen ere studied in a **controlled trial with low birth weight infants** (average birth weight 1489 g he infants were divided into three groups: Group A and B received a dose of 1.6×10^8 cells . *breve* supplement twice a day, **commencing either from several hours after birth (group A r 24 h after birth (group B). Group C, the control group, received no supplement**.

esults: No significant differences in birth weight, treatment with antibiotics, and the startin me of breast-feeding among the three groups. A *Bifidobacterium*-predominant flora was forme an average of 2 weeks after birth in group A and at an average of 4 weeks after birth in grou , while no *Bifidobacterium* was isolated in eight out of 10 infants in group C during th bservation period of 7 weeks. In comparison between group A and B, *Bifidobacterium* wa etected significantly earlier in group A, and the number of *Enterobacteriaceae* present in th nfants at 2 weeks after birth was significantly lower in group A.

onclusion: The results of the present study suggest that very early administration of *B. breve* ow birth weight infants is useful in promoting the colonization of the *Bifidobacterium* and th

Reduced Incidence of Necrotizing Enterocolitis Associated with Enteral Administration of *Lactobacillus acidophilus* and *Bifidobacterium infantis* to Neonates in an Intensive Care Unit

Angela B. Hoyos, MD*

Int J Infect Dis 1999; 3:197–202.

Methods: Daily doses of 250 million live *L. acidophilus* and 250 million *B. infantis* were given to all 1237 newborns (both inpatients and transfer patients) admitted to the unit during 1 year, until they were discharged from the hospital. In this study, 1282 patients hospitalized during the previous year were used as controls.

Results: There were no complications attributed to the daily administration of *L. acidophilus* and *B. infantis*. The study groups were compared for place of origin, clinical, and demographic variables, and there was no statistically significant difference in those variables. In the historic control group, there were 85 NEC cases compared to 34 cases in the group that received probiotic prophylaxis ($P < 0.0002$). In the historic control group, there were 35 NEC-associated fatalities compared to 14 fatalities in the group that received probiotic prophylaxis ($P < 0.005$).

Dani C, Biadaioli R, Bertini G, et al. Probiotics feeding in preven
ion of urinary tract infection, bacterial sepsis and necrotizing en
erocolitis in preterm infants. A prospective double-blind study
Biol Neonate 2002;82:103–8.

RCT su 585 pretermine

Lactobacillus GG dal primo pasto 6 x 10^9 CFU

Nessun effetto significativo su IVU, spesi, NEC

J Hum Nutr Diet. 2006 Feb;19(1):51-8

Growth during the first 6 months of life in infants using formula enriched with Lactobacillus rhamnosus GG: double-blind, randomized trial.

Vendt N, Grünberg H, Tuure T, Malminiemi O, Wuolijoki E, Tillmann V, Sepp E, Korpela R.

BACKGROUND: **The aim of this study was to evaluate the influence of Lactobacillus rhamnosus GG (LGG)-enriched formula on growth and faecal microflora during the first 6 months of life in normal healthy infants.** MATERIALS AND METHODS: **One hundred and twenty healthy infants (up to 2 months) received LGG-supplemented formula or regular formula in a double-blind**, randomized manner until the age of 6 months. Weight, length and head circumference were measured monthly and transformed into standard deviation scores (SDS). Faecal samples were obtained from a random sample of infants (n=25) at entry and at the end of the study. RESULTS: One hundred and five infants (51 in the LGG group) completed the study. Children receiving LGG-supplemented formula grew better: their changes in their length and weight SDS (DeltaSDS) at the end of the study were significantly higher than those receiving regular formula (0.44+/- 0.37 versus 0.07+/- 0.06, P< 0.01 and 0.44+/- 0.19 versus 0.07+/- 0.06, P< 0.005, respectively). The LGG group had a significant, higher defecation frequency 9.1+/-2.06 versus 8.0+/- 2.8 (P<0.05). More frequent colonization with lactobacilli was found in the LGG group, 91% versus 76% (P<0.05) at the end of the study. **CONCLUSIONS Infants fed with LGG-enriched formula grew better than those fed with regular formula. Further studies are necessary to clarify the mechanism of LGG in infant growth.**

Pediatr Res. 2006 Aug;60(2):221-4.

Specific probiotics in enhancing maturation of IgA responses in formula-fed infants.

Rautava S, Arvilommi H, Isolauri E

We hypothesized that specific probiotics might promote mucosal immunologic maturation in formula-fed infants. The numbers of cow's milk-specific and total IgA-secreting cells were measured at 3, 7, and 12 mo of age in a double-blind placebo-controlled study of 72 infants with early artificial feeding. The infants consumed infant formula supplemented with specific probiotics (Lactobacillus GG and Bifidobacterium lactis Bb-12) or placebo during the first year of life. Further analyses of the serum concentrations of the IgA-inducing cytokine TGF-beta2 and the soluble innate microbial receptor sCD14 were conducted. The numbers of cow's milk-specific IgA secreting cells were significantly higher in infants receiving probiotics compared with those receiving placebo ($p = 0.045$, ANOVA for repeated measures). At 12 mo of age, the serum concentrations of sCD14 were 1479 pg/mL [95% confidence interval (CI) 1373-1592] in infants receiving probiotics and 1291 pg/mL (95% CI 1152-1445) in infants receiving placebo ($p = 0.046$). Administration of the probiotics Lactobacillus GG and Bifidobacterium lactis Bb-12 at the time of introduction of cow's milk in the infant's diet results in cow's milk-specific IgA antibody responsiveness that may be the result of increase production of sCD14

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Medical Position Paper

Global Standard for the Composition of Infant Formula: Recommendations of an ESPGHAN Coordinated International Expert Group

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Editorial

The Composition of Infant Formula: A Worldwide Approach

*Alfredo Guarino, MD and †Stefano Guandalini, MD

In this scenario, the recommendations are inevitably "conservative" in that they are rigidly evidence-based, i.e. based purely on consolidated scientific information

Quale obiettivo?

Therefore, the adequacy of infant formula composition should be determined by a comparison of its effects on physiological (e.g. growth patterns), biochemical (e.g. plasma markers) and functional (e.g. immune responses) outcomes in infants fed formulae with those found in populations of healthy, exclusively breast-fed infants.

Riferimento: non la composizione biochimica del latte materno ma la crescita ed i marker biochimici e funzionali dell'allattato al seno

Grazie per l’attenzione!