

Intestinal inflammation in nursing infants: different causes and a single treatment... but of protected origin*

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Abstract. Three case histories of nursing infants suffering from different forms of intestinal problems, who underwent special dietary therapy in order to solve situations that would be difficult to deal with using the special artificial milk varieties on the market, are presented. These children were administered a homemade food consisting of Parmigiano Reggiano cheese seasoned for at least 36 months, rice or maize custard and tapioca, sugar, maize oil. In the first case the diagnosis of “widespread nonspecific acute colitis” was made compatible with “antibiotic-associated colitis” and *Clostridium difficile* was isolated from the feces. The second case, under the suspicion of cow’s milk allergy, was fed by soya and hydrolyzed milk with persistent disturbed alvus with greenish feces and mucus. The third case was represented by a nursing child with persistent diarrhoic alvus after an acute episode with subsequent intolerance to rice milk. After the introduction of the food based on Parmigiano Reggiano cheese, all cases showed a rapid and progressive improvement of symptoms and alvus characteristics and were discharged with increased weight. The Parmigiano Reggiano cheese shows a high concentration of easily absorbed amino acids and oligopeptides like a hydrolyzed proteic preparation. As regards the lipoid component the medium and short chain fatty acids are directly absorbed in the bowel and immediately usable as a significant source of energy. Finally, another relevant characteristic of Parmigiano Reggiano cheese is the complete absence of lactose. The use of Parmigiano Reggiano cheese as a dietary therapy is appropriate not only for its high nutritional value, but also for its characteristics as a functional food that produces beneficial effects on health with regards to the gastrointestinal tract and the inflammatory problems resulting from alimentary intolerance, post-therapeutic antibiotic dismicrobism, or post-infective conditions. Moreover, its efficacy on these pathologic conditions is further improved by the prebiotic and probiotic effects resulting from the oligosaccharides and the bacterial flora of this natural food product, only derived from the nature and the work of skilled artisans closely tied to tradition. (www.actabiomedica.it)

Key words: Parmigiano Reggiano, intestinal inflammation, dietetics treatment

Introduction

Maternal milk is a unique milk, inimitable, specific for the child, with an ideal composition for the child’s total needs, not only his nutritional. It is high in a variety of bio-active substances which are only present in minimal amounts in artificial milk. These substances show multiple effects: they help the child’s di-

gestion, permanently reinforce the immune system, develop the nervous system and other organs, stimulate the production of blood, and regulate the sensation of satiety. A long list of diseases are less frequent when children are breast fed. In other words breast feeding shows a health bonus not only with reference to infective diseases (respiratory and diarrhoea in particular), but also for conditions such as allergies, obesity, and

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harmonious neuro-intellectual and immune development. However, different conditions that may lead to a precocious interruption of breast feeding with the need to proceed with artificial milk may be present. This condition can be problematic when gastrointestinal problems arise when the different varieties of artificial milk on the market, though balanced for the needs of the child and easily digested, are not tolerated.

In this study examples are given of certain pathological conditions that may occur in the first few months of life which are difficult to deal with from an alimentary perspective, even with the increasingly numerous special artificial milk varieties available. In the experience of the authors these conditions may be resolved with a "very natural" and well tolerated solution. A few emblematic cases are presented along with their solutions in order to analyse and explain these results.

Case histories

Three case histories are presented of nursing infants suffering from different forms of intestinal problems, who underwent special dietary therapy in order to resolve situations that would be difficult to deal with using the special artificial milk varieties on the market. These children were administered a homemade food consisting of 40 g of Parmigiano Reggiano cheese seasoned for at least 36 months, 40 g of rice or maize custard and tapioca, 40 g of sugar, 10 g of maize oil, all added to a litre of water. This compound, known as NO (Nuovo Olivi from the researcher that first invented this composition), is capable of providing around 60Kcal/100ml. It is prepared daily and warmed up like any milk in the required quantity at meal times.

The first case is a baby girl of 1 month and 16 days who came to our attention due to the appearance of feces containing blood and mucus. The mother reported greenish feces for about a week without vomiting and without crying attacks associated with the evacuations. The case history recorded antibiotic therapy with Amoxicillina at the age of 10 days for an infection of the urinary tract, and mixed feeding with type 1 formula since birth with good weight gain.

Physical examination revealed good general conditions and hydration, with a tractable abdomen that was clearly nontender. Blood tests were normal, abdominal echography was negative for signs of invagination, and pediatric surgical investigation did not reveal the presence of surgical disease underway and nor rhagades. In the suspicion of cow's milk protein allergy the diet was modified to hydrolyzed milk, eliminating milk and eggs from the mother's diet. During treatment the child remained in good general conditions, did not present significant problems during physical examination, and continued feeding regularly though still producing 7 to 8 evacuations with blood and mucus per day. On the basis of the persistence of the symptoms and the negative results of the culture tests on the feces, further diagnostic investigation with colonoscopy was programmed. The investigation was carried out under sedation and revealed a clinical picture of "widespread nonspecific acute colitis" and the outcome of the histological examination confirmed a clinical picture compatible with "antibiotic-associated colitis". The examination of the feces for the *Clostridium difficile* toxin was positive, confirming this hypothesis. On the eighth day of recovery the diet was substituted with "NO". No specific antibiotic therapy towards *Clostridium difficile* has been carried out given the rapid and almost complete recovery of the patient following the appropriate diet therapy. The second case was a baby boy of 1 month and 25 days, referred to us for inconsolable crying since the age of about two weeks, both during meals and away from mealtimes, with alimentary difficulties. The medical history revealed breast feeding for three weeks and then integration with type 1 formula due to maternal hypogalactia, with good weight gain. Familial allergy was noted. Six days earlier, due to suspected GER (Gastroesophageal Reflux), ranitidine was administered and the adapted milk was substituted with soy milk for two days followed by hydrolyzed milk due to the appearance of disturbed alvus with greenish feces and mucus, but without improvement of the clinical picture.

On admission to the department the child presented good general conditions, and the physical examination was normal. Blood tests were performed (mild anemia) and urine tests were normal. During

hospitalization, feeding was initially continued with hydrolyzed milk without improvement of symptoms. Various tests were carried out (culture tests on the feces and urine, abdominal echography due to the suspicion of invagination, radiology of the initial tract with barium meal) all within normal range. Due to the persistence of symptoms and to the difficulty in feeding, the diet was substituted with "NO".

The third case was a nursing child of 3 months and 20 days referred to us for persistent diarrhoic alvus (10-12 liquid and greenish evacuations) for about 20 days. Previous episodes of infective gastroenteritis in the brother were reported. The case history revealed breast feeding for 15 days and then, due to maternal fever, replacement with adapted type 1 milk. During the acute episode rice milk was initially administered but after 2 to 3 days, due to the partial rejection of the food, normal alimentation was resumed. Physical examination revealed good general conditions, with mild signs of hypotrophy, and a certain degree of dehydration; moreover the persistence of diarrhoic alvus with 8 to 10 greenish evacuations per day preceded by crying were observed. The patient was therefore hospitalized for assessment. With regards to the possible development of a clinical condition of chronic post-enteric diarrhoea associated with lactase deficit and/or possible intolerance to the protein of cow's milk, once infective agents were excluded in the feces, the diet was substituted with "NO".

Results

After the introduction of the food based on Parmigiano Reggiano cheese, which was well tolerated, all our cases showed a rapid and progressive improvement of symptoms and alvus characteristics and were discharged with increased weight. In the first case there was a reduction in the number of evacuations, that were more consistent, without further observation of blood and mucus; moreover she presented good consciousness at discharge. After a month the child was fed again with formula 1 milk which was well tolerated. In the second case, after the introduction of NO a rapid and progressive improvement of symptoms with disappearance of the crying crises and increase in the con-

sistency of feces was observed. At discharge the general conditions were good. After six months the child underwent a provocative test with type 1 milk which resulted in a relapse confirming the suspicion of cow's milk protein allergy. The third case, after 2 days on NO, began producing feces that became progressively more normal with improvement of general conditions and disappearance of crying fits. The reintroduction of type 1 milk after 20 days of dietary therapy was tolerated, permitting normal feeding.

Discussion

In order to investigate the reasons for the clinical advantages achieved with a food as important and complex as Parmigiano Reggiano cheese, we need to take a step back and try to understand where the culture of using this product for dietary therapy came from. In the 1970s Prof. O. Olivi of the Pediatric Unit of the University of Modena was given the task of assessing Parmigiano Reggiano cheese seasoned for at least 24 months from a nutritional point of view. Various analyses were carried out with the purpose of determining its nutrient composition: proteins, carbohydrates, and lipids.

During these studies it emerged that the *proteic* component (average content 33%) consisted in a high concentration of easily absorbed amino acids and oligopeptides derived from the degradation of casein, due to the proteolytic effect of enzymes derived partly from the milk itself and partly from the lactic bacteria that develop in the curd. The resulting product is comparable to a hydrolyzed proteic preparation (1, 2). Regarding the *lipoid* component (average content 28%), in addition to a prevalent fraction of saturated fatty acids the product had a relatively high concentration of medium and short chain fatty acids which are directly absorbed in the bowel and immediately usable as a significant source of energy. During the seasoning of the cheese, the lipoid component undergoes significant modifications caused by a partial lipolysis which makes a certain proportion of fatty acids available in the free form, facilitating their absorption. The triglycerides also include a significant percentage (about 25%) of medium and short chain

Table 1. Nutritional characteristics of Parmigiano Reggiano cheese

For 100 g of product:

- protein 33 g
- lipids 28.4 g
- sodium chloride 1300 mg of which 551 mg sodium
- energy value 395 Kcal
- Vit A 270 µg
- Vit E 440 µg
- Vit B₁ 34 µg
- Vit B₂ 370 µg
- Vit B₆ 110 µg
- Vit B₁₂ 4.1 µg
- Vit PP 55 µg
- Biotina 23 µg

fatty acids which are easily absorbed and rapidly usable, thus constituting an immediate source of energy.

Finally, another relevant characteristic of Parmigiano Reggiano cheese is the complete absence of lactose, which disappears during the first hours of life of the product since it transforms into lactic acid, causing the immediate acidification of the product, one of the key factors in the production process.

In the same years a special artificial milk was put on the market in the United States, a hydrolyzed proteic milk, without lactose or saccharose, suitable for infants and nursing children with serious intolerance to cow's milk and soy proteins, intolerance to lactose, or with serious intestinal absorption problems. Having assessed the chemical-nutritional characteristics of the artificial milk and comparing them with those of Parmigiano Reggiano cheese, the idea arose of composing a "food" to replace commercially available milk, consisting in Parmigiano Reggiano cheese, already naturally suitable, with the addition of simple carbo-

hydrates (saccharose), complex carbohydrates (rice or maize custard and tapioca), and essential polyunsaturated fatty acids (maize oil).

It thus became a common practice at the Modena Pediatric Clinic to feed newborn infants (and not only) who could not have maternal milk with this food. It is well tolerated, palatable, nutritionally appropriate and produces a rapid clinical improvement in patients with rapid normalization of alvus. Among the conditions with gastro-intestinal symptoms that may benefit from dietary therapy, a brief mention is given below.

Antibiotic-associated colitis

Various antibiotics alter the equilibrium of the normal intestinal bacterial flora permitting a massive growth of *C. difficile*, a gram positive anaerobic bacillus. The diarrhoea and the colitis are caused by the toxins produced by the pathogenic strains of *C. difficile*. Almost all antibiotics can cause *C. difficile* infection, but Clindamycin, the wide spectrum penicillins, such as ampicillin, amoxycillin, and the cephalosporins are most frequently involved. Diarrhoea is the most frequent symptom following oral antibiotic administration. In mild cases the mucus of the colon may only show inflammation or a modest edema or may appear macroscopically normal. In the most serious cases widespread fragility and ulcerations may simulate, macro- and microscopically, idiopathic ulcerative colitis. In extreme cases yellowish raised exudative plaques are observed, covering the mucus of the colon. Histologically, these pseudomembranes consist of fibrin, leukocytes, and scaling necrotic epithelial cells. The bacterial invasion of the mucus has,

Table 2. Nutritional characteristics of hydrolyzed preparation compared with NO

Nutritional characteristics 100 ml	Hydrolyzed milk preparation	NO
Nutritional value	68 Kcal	60 Kcal
Protein	1.9 g (extensive hydrolysis of casein)	1.3 g (AA and oligopeptides)
Lipids	3.4 g (linolenic acid 0.61 g)	2.1 g (linolenic acid 0.5 g)
Saccharides	7.5 g (glucose and maize starch)	8 g (saccharose and maize or rice starch)
Sodium	32 mg	22 mg (52 mg NaCl)

in fact, never been observed. The symptoms usually begin during antibiotic therapy but in 1/3 of patients they may appear from 1 to 10 days after the suspension of treatment. Therefore, the diagnosis of antibiotic-associated colitis must be considered in any patient that develops diarrhoea up to 6 weeks following exposure to antibiotics.

The clinical signs may vary from simple soft feces to active colitis with hematic diarrhoea, abdominal pain, fever, leukocytosis, and enteropathy with loss of proteins. In the most serious cases there may be dehydration, low blood pressure, or toxic megacolon with perforation. Usually endoscopy is not necessary for diagnosis, but if performed it may reveal a non specific colitis, or in serious cases, pathognomonic pseudomembranes. The diagnosis is confirmed by the identification of the *C. difficile* toxins in the feces. The *C. difficile* pathogen produces two toxins, A and B, both potentially responsible for the disease. The frequency of the positive tests for the toxins increases with the increase of seriousness of the colitis, varying from 20% in the most common form of simple post-antibiotic diarrhoea, without any inflammation visible with sigmoidoscopy, to > 90% in cases of obvious pseudomembranous colitis. From a therapeutic point of view, if there is significant diarrhoea during the administration of antibiotics, they should be immediately suspended, unless their use is absolutely essential. A diarrhoea without complications induced by the use of antibiotics, without evidence of frank colitis or of an Acute Systemic Toxicity, generally clears up spontaneously after 10 to 12 days, after the suspension of the antibiotic. No other specific therapy is necessary. The patients affected by an intractable or fulminant disease may require hospitalization for support treatment with the i.v. administration of fluids, electrolytes, and blood transfusions, according to the same principles that govern the treatment of idiopathic ulcerative colitis (3).

Intolerance to cow's milk proteins

This affects from 1 to 8% of infants that consume cow's milk. Sensitization to the proteins of the milk may occur during the foetal period from mothers who consume milk, but more commonly it occurs with total or partial artificial feeding during the first days of

life, or at the start of weaning. No safe and reliable tests for diagnosis are available and thus symptoms are mainly relied upon, as well as the exclusion of other pathologies that cause similar symptoms, and the improvement obtained by the elimination of milk and the relapse when it is reintroduced.

Different clinical forms are observed:

Acute form generally occurring in the first 3 to 6 months of life in a child who consumes cow's milk. The most common symptoms are: vomiting, liquid diarrhoea, mucus or muco-hematic diarrhoea, abdominal pain, meteoric abdomen with the presence of colics. This may appear immediately after feeding or after 1 to 2 hours. *Chronic form* expressed with mucus diarrhoea, muco-hematic diarrhoea or simply with sidero-penic anemia caused by continuous hematic loss from the colon. Looking for hidden blood in the feces is a good diagnostic guide. In the form of chronic diarrhoea with malabsorption it has similar characteristics with celiac disease showing slowing down of growth, chronic diarrhoea with steatorrhea, atrophy of the intestinal mucus, even though less serious compared with the celiac disease, from which it also differs for its appearance during the first 3 to 6 months of life. Treatment consists in the complete abolition of cow's milk proteins and derivatives from the diet, including dairy products and biscuits or food with added milk or milk proteins. The therapy is based on rice milk or hydrolyzed milk protein formulas, although 10 to 15% of children also begin to manifest intolerance to these substance, when the use of foods in which the proteic portion consists in amino acids must be made. Generally Parmigiano Reggiano cheese is tolerated, as long as it is seasoned for at least 24 months, since the milk proteins have degraded into peptides (4, 5).

Protracted postenteric diarrhoea

A diagnosis of intolerance to lactose after an infective diarrhoea is reasonable in a previously healthy child with persistent diarrhoea, on the return to the normal diet containing lactose. The entity of the diarrhoea is not always correlated with the degree of deficit of disaccharidase. Intolerance to carbohydrates is suggested by an acidic pH in the feces. It is nevertheless necessary to differentiate between intolerance

to lactose and hypersensitivity to the proteins of cow's milk. The appearance of a nonspecific chronic diarrhoea may be preceded by an acute diarrhoic disease, especially between 3 months and 1 year of age (6-8).

The scientific basis for the reported results are shown as follows.

The use of Parmigiano Reggiano cheese as a dietary therapy is appropriate not "only" for its high nutritional value, but also for its characteristics as a functional food that produces beneficial effects on health. With regards to the gastrointestinal tract and the inflammatory problems resulting from alimentary intolerance, post-therapeutic antibiotic dismicrobism, or post-infective conditions, it is important to consider the properties of an easily digested food due to the presence of ready to use proteins and lipids, the absence of lactose, and its prebiotic and probiotic effect, with modulation of the intestinal flora.

With regards to the complete absence of lactose, already from the first hours of the fermentation process, studies were recently carried out to assess the effective complete absence of lactose in order to classify this cheese as a "lactose-free" product. On the basis of the standards of the European Commission (April 2003), regarding artificial milk for newborn infants and nursing children, "lactose-free" is defined as an artificial milk with a lactose content below 10 mg/100 Kcal. An assessment was carried out on Parmigiano Reggiano cheese from different cheese factories and in different stages of seasoning, and the maximum level found was 0.1 mg/100 Kcal. It may thus certainly be defined as a lactose free food.

The same studies also identified a secondary aspect, this being the presence of numerous oligosaccharides not only derived from those normally present in cow's milk, but probably also derived from the action of the complex fermentative digestive processes that take place during the production of Parmigiano Reggiano cheese (2).

This leads to the second peculiar aspect of Parmigiano Reggiano cheese, its possible prebiotic effect. A prebiotic (2, 9-11), generally constituted from non-digestible oligosaccharides, is an alimentary ingredient that positively influences the organism, selectively stimulating the growth and activity of bacterial strains already present in the body. In order to have a prebi-

otic effect a nutrient must be neither hydrolysate nor absorbed in the first section of the gastrointestinal tract; be a selective substrate for one or a limited number of bacteria potentially beneficial for the colon, thus stimulating their growth; and finally be able of modifying the intestinal bacterial flora inclining it towards a composition of beneficial effect.

The purpose of their use is to modify the composition of the commensal microflora, stimulating colonization through bacteria of known beneficial action for the organism. This effect has been demonstrated in relation to bifidobacteria and lactobacilli, and more recently towards certain eubacteria, with resulting reduction in the number of *E.coli* and *Clostridia* in feces. Prebiotics act as selective substrates for fermentation and influence microbic activity and the absorption of minerals in the intestine, as well as promoting immune response. A study is currently underway aimed at assessing the prebiotic potential of Parmigiano Reggiano cheese: the preliminary results of the lab tests indicate the effectiveness of Parmigiano Reggiano cheese in promoting the development and maintenance of a positive microflora, in particular of lactobacilli (2).

Furthermore, the probiotic nature of this cheese and its importance in the intestinal and extraintestinal pathologies is also worth noting. Probiotics (2, 10-15) are live micro-organisms, in particular certain strains of bifidobacteria and lactobacilli, of beneficial effect on the host. In order to be considered probiotic a bacterial strain must have certain specific characteristics: be a normal component of the human intestinal microflora; be absolutely safe for use in humans; be active and vital in the conditions present in the intestine; be resistant to gastrointestinal secretions (gastric juice, bile, and pancreatic juice); and be able of persisting, at least temporarily, in the human intestine.

The biological activity of probiotic bacteria is linked to their capacity to adhere to the enterocytes, thus preventing the adherence of pathogenic bacteria through a mechanism of competitive exclusion. Probiotics also influence the commensal micro-organisms in the production of lactic acid and bacteriocine that inhibit the growth of pathogens. Probiotics have been successfully used both in the treatment of gastroenteric conditions (reduction of the seriousness and du-

ration of episodes of Rotavirus enteritis), and their prevention (their effectiveness in preventing antibiotic-associated diarrhoea), without producing adverse reactions. Other important effects of probiotics are shown on chronic inflammation of the intestine, in which recent studies confirm the protective role of certain strains of lattobacilli against episodes of acute-stage relapse of ulcerous colitis. They also act on the primary prevention of atopic diseases when the normal intestinal flora, adhering to the intestinal walls, interacts with them and produces significant effects on the development and regulation of the immune system of the host. Probiotics also promote the intestinal barrier function with the normalization of increased intestinal permeability, and improve secretion of the intestinal IgA, often in deficit in allergic children. They also reduce the antigenic load introduced with the diet through the degradation and modification of macromolecules.

Conclusions

In conclusion, on the basis of its nutritional characteristics of easy digestibility, hypoallergenicity (absence of lactose, proteins hydrolyzed to amino acids, and lipids readily usable) and also for its sodium content which, in addition to restoring losses, reduces the secretions of intestinal cells by inhibition of the AMPc mediated mechanism, the administration of this food proved to be effective in different gastrointestinal pathologies. Furthermore, its effect in improving these pathologic conditions is further accentuated by the prebiotic and probiotic effects resulting from the oligosaccharides and the bacterial flora they contain.

Thus, despite ever increasing knowledge in the nutritional field and the availability of numerous forms of special milk, it is sustained by the authors that, on the basis of decades of experience, gastrointestinal pathologies such as those here described may benefit from a dietary therapy based on a "natural" food product, Parmigiano Reggiano cheese, with the addition of simple sugars, complex sugars, and oil rich in polyunsaturated fatty acids, offering excellent results, thanks to the characteristics of a product derived solely from nature and the work of skilled artisans closely tied to tradition.

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