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An integrated approach with bovine colostrum and vitamins improving IBS-D care parameters: a case series

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ABSTRACT

BACKGROUND

Bovine colostrum is full of growth factors and is classified as a health food supplement. The aim of this data collection, referred to a patients population, was to describe the clinical response after taking food supplement consisting of bovine colostrum, Vitamins C, D, E and A.

METHODS

Out of a total of 430 patients suffering from IBS-D with leaky gut syndrome, 36 with serum zonulin ≥38 ng/ml and initial value of fecal calprotectin ≤50 µg/g have taken IMOpro COLOSTRUM Plus® for 30 days and were considered in the present observation.

RESULTS

In this case series, among 36 patients were observed a statistically significant reductions zonulin levels (112.1 ng/ml was reduced to 45.7 ng/ml), BCS value (from 6.06 to 5) and VAS value (from 7.64 to 4.58).

CONCLUSIONS

The complex interaction between host factors in IBS-D, such as microbial dysbiosis, immune activation, impaired intestinal epithelial barrier function and motility, can be modulated by integrating different therapeutic strategies, such as bovine colostrum enriched with fat-soluble and water-soluble vitamins.

KEYWORDS

Bovine colostrum, vitamins, IBS-D.

INTRODUCTION

Bovine colostrum is an important secretion, that is produced right away parturition happens by the mammary gland and provides newborns sustenance as well as growth, maturation, and repair of a large number of tissues. It also enhances protection against pathogens and ensures the development of immune system development. Bovine colustrum composition and properties – specifically physical – may vary a lot because of many factors, among which are individuality, ethnicity, prepartum nutrition and time postpartum. It contains less lactose than milk but, at the same time, more elements like fat, protein, peptides, non-protein nitrogen, vitamins and minerals, hormones, growth factors, cytokines and nucleotides. For plenty of time the composition of human and Bovine Colostrum (BC) has been studied, in order to point out the referred higher concentrations of many biologically active substances than mature milk. BC is rich in immunity, growth and antimicrobial factors, useful to guarantee tissue growth and the maturation of digestive tract and immune function in neonatal animals and humans. In both colostrum and milk it's possible to find immunoglobulin antibodies, which are the main immune components of the acquired immune system. However, immunoglobulin G (IgG) is fully concentrated in colostrum, and particularly important as it confers passive immunity to the neonate after parturition.[1,2] All the elements above-mentioned keep their activity during the passage in the gastrointestinal tract: this produces several beneficial effects on the intestinal functions, surely due to immune-modulatory, antimicrobial and anti-inflammatory activities. Efficacy of bovine colostrum has been evaluated for a large series of clinical disorders of stomach and intestine. In the context of an experimental model of NSAID-induced mucosal damage, gastric wound narrowed down by up to 60% by BC.[3] In addition, in a small study in human volunteers BC was able to prevent the rise in permeability induced by indomethacin treatment, even if it was noticed that, in long-term use, the rise in permeability is lower.[4] The production and release of zonulin represents one of the most important mechanisms that regulate intestinal absorption. Zonulin is in fact a protein that relaxes intestinal tight junctions, allowing paracellular transport through the intestinal mucosa: in addition, its activity allows paracellular transport in the intestines at the physiological level, and high concentrations of zonulin may indicate pathologically increased intestinal permeability.[5-7] Evidence was given about promising results of Bovine colustrum in reducing inflammation and symptoms in animals and humans. Then again, in murine models of colitis BC, as well as its components, prevented or reduced chemically induced colitis. In a different study by Khan et al,[8] BC was observed in improving symptoms and histological scores of patients affected by distal colitis who were administered the colostrum enemas in addition to mesalazine, in comparison to those controls who only received mesalazine. Some benefits were also shown in children with Crohn's disease who receive nutritional supplements rich in TGF – that is one of the main growth factors that can be found in colostrum. These results may state the potential benefit of BC as an adjunct therapy in patients with inflammatory bowel disease (IBD). Evidence is increasing for bovine colostrum to be one of the promising and effective nutraceuticals to anticipate or lower diseases of different kind, both in newborns and adults. An additional element that should be considered when it comes to gastrointestinal disorders (GI) is vitamin D: decreased serum vitamin D (VD) levels are considered linked to GI, such as IBS. In addition, VD may be useful in order to modulate the intestinal barrier. IBS population is often characterized by lack of VD: the successful treatment of diarrhea-predominant IBS (IBS-D) and its associated symptoms, with high oral doses VD supplementation, has lately inspired the notice, in terms of therapeutic option for the IBS-D management, for this hormone.[8-11] Nutraceutical composed by "nutrition" and "pharmaceuticals" is a food or food product that benefits health as an adjuvant or alternative therapy, such as the treatment and prevention of infectious diseases in both children and adults. The aim of reporting this data collection was to verify the clinical response,

after the use of a supplement based on bovine colostrum (called IMOpro COLOSTRUM Plus®, consisting of 300 mg of bovine colostrum, 80 mg of Vitamin C, 12 mg of Vitamin E, 800 micrograms of Vitamin A and 5 micrograms of Vitamin D3) in adult patients (affected by IBS-D with leaky gut syndrome) of both sexes and aged between 18 and 75 years.

MATERIALS AND METHODS

The aim of this data collection was to describe the clinical response of a patients population, of both sexes and aged between 18 and 75 years, after taking "IMOpro COLOSTRUM Plus®" supplement – consisting of bovine colostrum, Vitamins C, D, E and A (Table 1) – affected by IBS-D with leaky gut syndrome (2 times a day, 1 stick in the morning before breakfast and 1 stick in the evening before bed for 30 days); in particular the examination concerned those who, for suspected IBS-D with leaky gut syndrome, turned to the Clinic of Gastroenterology and digestive endoscopy, Pisa, Italy. Anyway, all patients were seen by the PI in the period from June 2022 through March 2023. The suspicion of leaky gut was investigated through instrumental diagnostic examination – performed as for clinical practice – such as: complete abdominal ultrasound in order to verify the presence of irritable bowel/inflammatory intestinal pathology (IBS-D) and exclude MICI (Chronic Inflammatory Bowel Diseases) as well as other pathologies. About the dosage of serum zonulin patients with serum zonulin ≥ 38 ng/ml were considered eligible. Other inclusion criteria were also considered, such as the dosage of Fecal calprotectin (FCP), including patients with an initial value ≤ 50 µg/g (assuming it as an index value) and excluding patients with calprotectin values from 50 µg/g to 100 µg/g (assuming that it could represent an organic pathology); however, considering that these last are not predictive models but case series, the decision was not to exclude them because it could be helpful to see the different characteristics of those patients, in order to understand if there is a rationale behind the fact that those patients have higher values than normal – unless it is a case of obvious measurement or data entry error. To correctly define the characteristics and consistency of stool according to transit the BSC (Bristol Stool Scale) was adopted, with the aim of evaluating the intensity of pain associated with IBS-D, and the VAS (Visual Analogue Scale). To clinically classify the patients and and to evaluate their intestinal motility disorders as well as visceral hypersensitivity, the Rome V Criteria were adopted. Other criteria clinically evaluated were: alterations in bowel habits, variable between diarrhea and constipation with alternating periods, abdominal pain or discomfort, relief of pain after bowel motility and increase after meals, bloating, feeling of urgency and/or incomplete evacuation, straining to defecate, presence of mucus, stress, anxiety and/or depression. On the other hand patients with organic pathologies, multitreated patients and patients under pharmacological treatment with other therapies (Loperamide, Diphenoxylate and Alosetron) were not included in the chart review. Of this part of the identified population 36 took the supplement IMOpro COLOSTRUM Plus®. The powdered supplement used in the study contained: bovine colostrum 300 mg, Vitamin C 80 mg, Vitamin E 12 mg, Vitamin A 800 µg and Vitamin D3 5 µg. The prescription of this supplement is not clinical practice but the literature shows various evidence of the use of bovine colostrum and Vitamin D to counteract excessive intestinal permeability. Many studies suggest paying particular attention to com-

TABLE 1
Composition of IMOpro COLOSTRUM Plus® supplement

	For 1 stick
FUNCTIONAL INGREDIENTS	Quantity
Acerola Powder	320 mg
Bovine colostrum	300 mg
Vitamin E	12 mg
Vitamin A	800 µg
Vitamin D3	5 µg
NON- FUNCTIONAL INGREDIENTS	Quantity
Sorbitol	1071.77 mg
Calcium salts of ortophosphoric acid	20 mg
Magnesium salts of fatty acids	15 mg
Vanilla flavour	20 mg

pounds with antioxidant properties, such as vitamins A, C and E. Vitamin E supplementation reduced the decrease in ZO-1, thereby affecting the deterioration of intestinal barrier function,[12] Vitamin C deficiency caused a decrease in mucin while it increased IL-6 production and oxidative stress.[13] An intact intestinal barrier requires both vitamin A and vitamin D that act in synergy to regulate ZO-1, Occludin and Claudin tight junction proteins. The ability of vitamin A to regulate the barrier, ILC3 and T cells underlies the impact of this nutrient on the microbiota community structure associated with health.[14] On these patients were evaluated, after 30 days of treatment, the change in serum zonulin, the intensity of pain perceived by the patient, and the BSC values. All data were inserted into an excel spread sheet including elements such as the age and sex of patients, zonulin levels at T0 and T1, BCS results at T0 and T1 VAS results at T0 and T1 and smoking. Data were presented as frequencies and percentages, means, and 95% confidence intervals (CIs) or standard deviations, or medians and interquartile ranges (IQR), when appropriate. Statistical analysis of student's t paired mean test using the SPSS program was performed.

RESULTS

Out of a total of 430 patients, considered in an outpatient setting with a diagnosis of IBS-D with leaky gut syndrome from June 2022 to March 2023, 36 patients (cases) used the supplement and were included in this description, initially meeting eligibility criteria. The most prevalent exclusion criterion was the use of prescription medication. Of the total, 14 were males (38.9%) and 22 females (61.1%) (Figure 1).

The age of cases is mainly concentrated between 40 and 45 years (Figure 2) with an average of 46.3 ± 14.4 (mean ± SD).

Less than half were smokers at the time of diagnosis: in fact, while 10 patients declare themselves to be such smokers (27.8%), 26 are non-smokers (72.2%) (Figure 3).

The baseline and outcome levels of zonulin, values

FIGURE 1
Sex distribution (M/F)

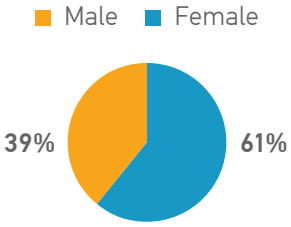


FIGURE 2
Age classes distribution

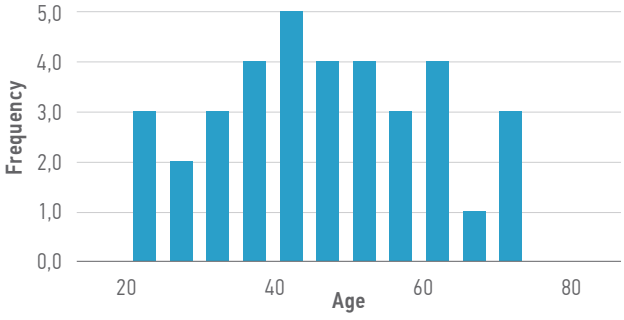
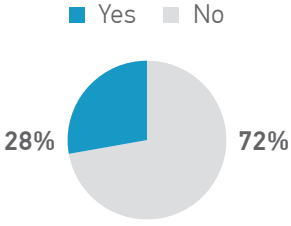


FIGURE 3
Smoking (Y/N)



of BSC and VAS are shown in Table 2. Mean, standard deviation, frequencies, minimum, maximum, median, interquartile range are elements that have also been described for each value.

Since these are case series, statistical tests analyzes would not be envisaged; however if it's desirable to apply statistical significance tests, it can be noted that occurred statistically significant reductions ($p < 0.001$) in the following mean variables: levels of zonulin 112.1 ng/ml was reduced to 45.7 ng/ml (–66.4) and the value of BCS moved from 6.06 to 5 (-1,06). Also VAS reduc-

TABLE 2
Baseline, Outcome. Results presented as Mean ± Standard Deviation, Median (MinMax), Interquartile range, p value

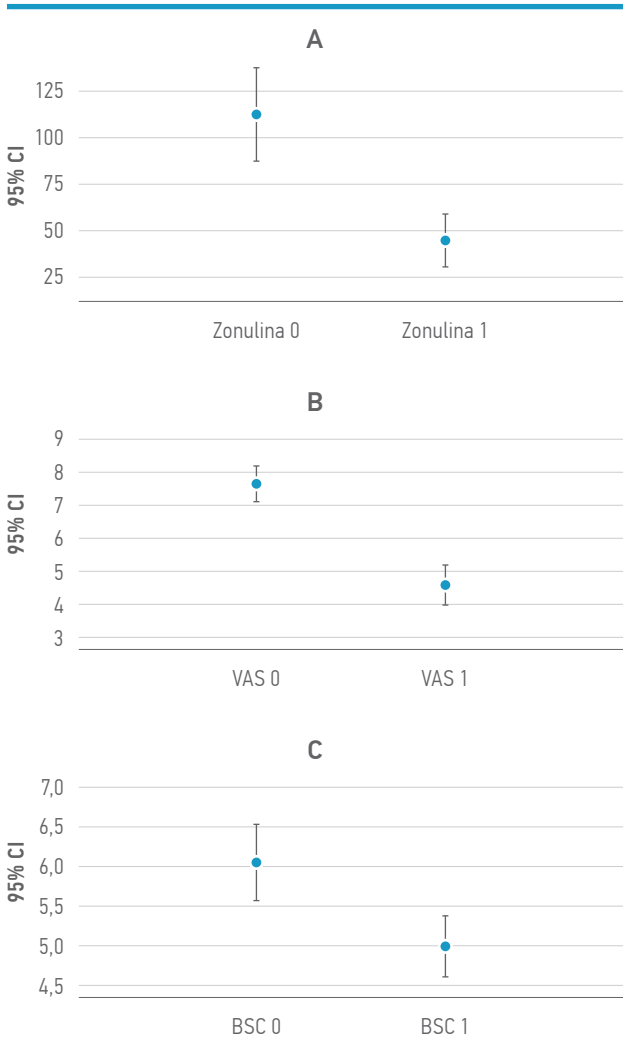
	Mean ± Std.Dev. or frequency (%)	Median	Min	Max	Interquartile Range	p value
AGE (y)	46,3 ± 14,4	46	22	73	35 – 57	
SEX						
M	14 (38,9%)					
F	22 (61,1%)					
Zonulin 0 (ng/ml)	112,1 ± 73,1	87	40	311	63 – 131	
Zonulin 1 (ng/ml)	45,7 ± 40,8	35	7	206	23 – 57	
Zonulin (Difference)	-66,4 ± 52,6	-53	-209	8	-85 – -33	<0,001
VAS 0	7,64 ± 1,61	8	3	10	7 – 9	
VAS 1	4,58 ± 1,81	5	1	8	3 – 6	
VAS (Difference)	-3,06 ± 1,66	-3	-7	0	-4 – -2	
BSC 0	6,06 ± 1,39	6	1	7	6 – 7	<0,001
BSC 1	5,00 ± 1,15	5	2	7	4 – 6	
BSC (Difference)	-1,06 ± 1,17	-1	-3	-2	-2 – 0	<0,001
Calprotectin (pg/g)	40,1 ± 16,9	43	11	92	28 – 50	
SMOKING						
YES	10 (27,8%)					
NO	26 (72,2%)					

es (-3,06) from 7.64 (pre treatment) to 4.58 (post treatment), after 30 days using the product (Figure 4).

DISCUSSION

We reported 36 cases of patients suffering from IBS-D with leaky gut syndrome who took for 30 days in their diet, bovine colostrum supplement and vitamins supplement. We investigated the effect of this kind of nutritional supplement by reporting the difference in plasma of zonulin levels as well as BSC and VAS scale values obtained before and after the supplementation period. The observation lead to a reduction in zonulin by 59.3%, in BSC scale values by 17.5% and in VAS scale values by 40.1%. These results appear to provide evidence that bovine colostrum supplementation may have beneficial effects on intestinal permeability; certainly the hypotheses generated in this cases observation should be tested, before generalizing the results, through randomized, placebo-controlled clinical trials. Literature also showed that the active components in BC and Vitamin D counteract excessive intestinal permeability. Eslamian G et al. investigated the effect of early enteral bovine colostrum supplementation on intestinal permeability in ICU-hospitalized patients: this happened in the context of a randomized double blind clinical trial, and results showed that intestinal permeability, as assessed by zonulin concentrations, was improved after a short period of colostrum supplemented enteral feedings.[15] Nevertheless, there's still some uncertainty in the mechanism of intestinal inflammation development, as well as in the correlation between faecal and serum zonulin levels. Strategies to modify intestinal barrier function through negative regulation of the zonulin pathway point to a potential therapeutic application for the treatment of GI disease.[16] Even if there's no doubt about the need for further studies in order to investigate more specifically these effects mechanism of action. The complex interaction between host factors in IBS-D, such as microbial dysbiosis, immune activation, impaired intestinal epithelial barrier function and motility, and environmental factors, including diet and nutritional deficiencies can be modulated by integrating different therapeutic strategies such as bovine colostrum enriched with fatsoluble and water-soluble vitamins. The presence of digestive enzymes in colostrum synergizes the effect of the other constituents present such as lactalbumin, alpha lactalbumin and lactoper-

FIGURE 4
Statistical significance tests (A) Zonulin, (B) VAS, (C) BCS



oxidase or immunoglobulins capable of modulating the digestion processes and therefore being functional for intestinal wellbeing. The presence of performance growth factors (TGF alpha and beta) in bovine colostrum appears to influence the ability to stimulate gastrointestinal growth and repair, inhibit acid secretion and increase gastric mucin concentrations. Combining these high-performance growth factors with the intestinal antioxidant and antiinflammatory effect also induced by vitamins could represent an integrative therapeutic strategy without side effects and pharmacological interactions.[17] In the assessment of case series there are several limitations that could play a role. It should be noted that this analysis was an observation and description of cases, with a small sample size: the aim was not to interpret these results by overestimating their importance: primary limitation was the lack of comparison (control) group. For this reason no causal inferences should be made about the relationship between the treatment and the outcomes. It must be also considered that the prescription of this supplement (or others, in general) is not clinical practice, and patients who did not take the supplement still followed food and nutritional recommendations, such as dietary regime low in galactooligosaccharides (GOS), no other gold standard of reference.

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Institutional Review Board Statement

Ethical review and approval were waived for this study because ethical approval is not required for clinical cases with food supplements in Italy.

Informed Consent Statemen

Informed consent was obtained from all subjects involved in the study.

Data Availability Statement

The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy reasons.

Conflicts of Interest

The authors have no financial interest in any company or any of the products described in this manuscript.

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