

GUT-BRAIN AXIS-ORIENTED INDIVIDUALISED HOMOEOPATHIC MANAGEMENT IN CHILDREN WITH AUTISM AND GASTROINTESTINAL DYSREGULATION: A PROSPECTIVE OBSERVATIONAL CASE SERIES

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Abstract:

Autism Spectrum Disorder (ASD) is frequently accompanied by gastrointestinal disturbances, and growing evidence supports the role of the microbiota-gut-brain axis in modulating behavioural severity. This prospective observational case series explored the clinical effect of individualized homoeopathic management in children with ASD presenting with prominent gastrointestinal dysregulation. Six children were followed over six months in a tertiary homoeopathic clinical setting. Baseline and follow-up assessments were conducted using the Indian Scale for Assessment of Autism (ISAA), Autism Spectrum Disorder Gastrointestinal and Related Behaviours Inventory (GIRBI), and ordinal severity scores (0–3) for constipation, abdominal pain, sleep disturbance, and irritability. Mean ISAA scores reduced from 101.67 ± 9.33 to 73.67 ± 6.53 (27.54% improvement; $p = 0.0355$), while GIRBI scores decreased from 34.17 ± 4.02 to 16.00 ± 2.37 (53.17% improvement; $p = 0.0355$). Significant reductions were observed in constipation, abdominal pain, sleep disturbance, and irritability (mean reduction = 1.83 points each; $p = 0.0263$). A moderate positive correlation was noted between gastrointestinal and behavioural improvement (Spearman $\rho = 0.515$). These findings indicate parallel improvement across gut and behavioural domains and suggest a clinically relevant association between gastrointestinal stabilization and behavioural changes. Although limited by small sample size, the study provides preliminary observational evidence supporting integrative gut–brain axis–oriented therapeutic approaches.

Keywords: Autism Spectrum Disorder; Gut–Brain Axis; Individualised Homoeopathic Therapy.

INTRODUCTION

Autism Spectrum Disorder (ASD) is a complex array of neurodevelopmental disorders that are characterized by persisting social interaction deficits, communication problems and repetitive behaviour. More recently, there has been growing investigation into the biological links between gut function and neurobehavioral presentations of ASD⁴. Many children with autism have comorbid GI problems that include constipation, abdominal pain, dyspepsia, abnormal stool frequency and poor sleep. These are not random symptoms, increasing evidence suggests the microbiota-gut-brain axis as a key modulation system in behavioural and neurodevelopmental disturbances where immune, metabolic, neural, and endocrine routes work as players. Children with ASD commonly have disturbances in the gut microbiota, gut permeability, and a chronic low-level mucosal inflammation¹¹. These alterations are believed to affect central nervous system signalling via vagal afferents, as well as neuroimmune function and the metabolism of microbial metabolites. As a result, GI dysfunction has become recognized as an implicated contributor to variability of behaviour, irritability, sleep disturbances and cognitive engagement in autism. This has fostered interest in potential therapeutic approaches targeting both gut dysfunction and behavioural symptoms¹.

Another often-raised factor in gut microflora development is the method of delivery. Caesarean section (LSCS) is associated with perturbed early microbial colonisation compared to normal vaginal delivery (NVD), which may have implications for immune programming and microbiome diversity. It is believed that children born via LSCS have a higher prevalence of ASD and GI complaints, however there is evidence from epidemiological studies to support this theory⁶. This relationship, albeit intricate and bidirectional in nature, does deserve attention clinically within studies of gut-related symptom burden. Homeopathic therapy Individualized homoeopathic medicine is often prescribed after careful evaluation of physical, behavioural and constitutional parameters. Systemic dysregulation and functional symptom patterns are often targeted in clinical homoeopathic approaches. For individuals with ASD who have pronounced GI symptoms, interventions tested for both behavioural and gut-related outcomes may provide more comprehensive symptom relief¹. Despite anecdotal clinical observations and case descriptions, systematic observational studies on the event of contemporaneous alterations within GI and behavioural domains are scarce.

The area is of biotechnological interest because there is a functional gut-brain connectivity. Clinical studies which identify coincident variations in GI burden and behavioural symptom severity provide insight into modes of gut-brain signalling. Small observational studies can also provide hypothesis-generating data regarding biological associations deserving of further exploration through molecular, microbiome and metabolomic methodologies². The present prospective observational case series was undertaken to assess clinical presentations in children with ASD and co-morbid severe GI dysregulation. This study aims to document differences in the severity of autism as measured by the Indian Scale for Assessment of Autism (ISAA), GI burden using the ASD-GIRBI scale and accompanying functional symptoms of constipation, abdominal pain, sleep problems and irritability at 6 months follow-up. Further, the between-group differences are examined in the relation of mode of delivery to proxy baseline GI load and in how improved GI scores relate to behavioural changes.

By reporting the accompanying alterations in behavioural and gut measures, the present study hopes to offer clinically pertinent insights that contribute to ongoing scientific dialogue on bidirectional connections between the gut and the brain during neurodevelopmental conditions.

MATERIALS AND METHODS

STUDY DESIGN AND SETTING

Prospective observational clinical case series for a period of six months in tertiary care hospital homoeopathic clinic is the design of this research work. The purpose of this study was to capture differences in behavioural and gastrointestinal severity in a sample of children with Autism Spectrum Disorder (ASD) which originally presented with an impaired gut under individualized homeopathic treatment. Participants were followed over time and a standardized clinical assessment was carried out at the baseline and end of the six month observation period.

STUDY PARTICIPANTS

Six children with a clinical history of Autism Spectrum Disorder were recruited into the trial due to gastrointestinal problems such as constipation, abdominal pain, bowel movement dysfunction, sleep disturbances and irritability. Routine clinical practice patients were recruited, and they were followed up closely over the study period. Patients with severe neurologic co-morbidities, serious systemic diseases requiring pharmacological intervention on a regular basis, and poor follow-up were excluded. Parental or guardian informed consent was provided and confidentiality of patient data was respected.

BASELINE CLINICAL ASSESSMENT

All participants received a full clinical examination at the time of their entry into the study. Age, sex and type of delivery in demographic data were evaluated. Type of delivery was classified as NVD and LSCS given the evidence that the mode of delivery may be associated with early microbial colonization patterns, as well neurodevelopment⁸. The severity of autism was measured by Indian Scale for Assessment of Autism (ISAA), a validated and standard instrument to assess a range of behavioural and developmental domains in children with ASD⁹. Gastrointestinal symptom load was estimated with the Autism Spectrum Disorder Gastrointestinal and Related Behaviours Inventory (ASD-GIRBI) in frequency of occurrence and severity of gastrointestinal symptoms, as well as their behavioural correlates⁵. In addition to the standardised scales, symptoms were scored individually using an ordinal scale for severity from 0 to 3 (0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms). The parameters evaluated were constipation, abdominal pain/sleep disturbances and irritability, as these are common symptoms in children with ASD related to gut dysregulation.

THERAPEUTIC INTERVENTION

All were treated with individualized homoeopathic prescriptions following simillimum principles on totalities of symptoms, constitution, behavioural aspects and general physical state. Prescription of remedy was based on classical homoeopathic principles along with clinical experience. The prescriptions were modified in follow-up visits according to the development of symptoms and curative effect. Most commonly prescribed remedies during the study period were Carcininum, Baryta carbonica, Sulphur, Tuberculinum and Tarentula hispanica that were given in potentized preparations tailored to clinical status of the patients. Interventions Treatment was administered as part of normal clinical care, and no other external interventions were introduced during the study.

FOLLOW-UP AND OUTCOME MEASURES

The subjects were followed up for 6 months and the clinical observations were made at the time of routine follow-up visits. Post-intervention assessments took place at the end of the study period and the same evaluation instruments as used at baseline were administered to warrant comparability. The primary outcome measures were improvements in autism symptom severity as measured by ISAA scores and reductions in gastrointestinal symptom burden measured using ASD-GIRBI scores¹³. Secondary outcomes measures assessed changes in scores for individual symptoms among constipation, belly pain, and sleep and irritability. Differences in values at baseline and follow-up for each patient were calculated and expressed as percentage reduction of clinical improvement over time.

DATA PROCESSING

Patient details were tabulated from all structured case sheets for the analysis. The baseline and follow-up measurements were included in a statistical database, and individual changes on each outcome measure were calculated. Percentage improvement was calculated as:

$$(\text{Baseline score} - \text{Follow-up score}) / \text{Baseline score} \times 100.$$

STATISTICAL ANALYSIS

The data was analysed with R statistical software. Non-parametric statistics were used, though power was limited by the small sample size and ordinal scaled outcome. Summary statistics such as mean, standard deviation, median and range were used to describe baseline values and follow-up¹². The Wilcoxon signed-rank test was applied for comparing the baseline and six-month scores of ISAA, ASD-GIRBI, as well as individual symptom-severity parameters. Estimate of effect size was provided by the mean reduction, percent reduction and Cohen's d to measure the effect in terms of magnitude. The correlation between change in GI symptoms and change in behaviour, and between baseline GI severity and the amount of change in behaviour were analysed using Spearman's rank correlation. To examine the effect of mode of birth, Fisher's exact test was used to evaluate categorical associations and Mann-Whitney U tests were used in comparing baseline severity, improvement scores between children born via normal vaginal delivery and those with caesarean section. $P < 0.05$ was considered statistically significant for all statistical analyses. As the study was exploratory, our intention was to record clinical trends and associations that might contribute on a theoretical basis to elucidation of connections between gastrointestinal findings and behaviour in children with ASD.

RESULTS AND DISCUSSION

PARTICIPANT CHARACTERISTICS

Six children who all fulfilled diagnostic criteria for Autistic Spectrum Disorder and who had prominent gastrointestinal symptoms were followed in a prospective fashion for 6 months. The children were of young to pre-adolescent age. Of the 6 babies, 4 (66.7%) were delivered by lower segment caesarean section (LSCS) and 2 (33.3%) by normal vaginal delivery (NVD). This distribution is of interest as LSCS delivery has been the subject of discussion in literature regarding modified early microbial colonization and its possible effects on gastrointestinal physiology and neurological development. (Table.1)

CHANGES IN AUTISM SEVERITY

Baseline mean ISAA score was 101.67 ± 9.33 , suggestive of moderate behavioural severity in the participants. After 6 months of individualized homeopathic treatment the average ISAA score reduced to 73.67 ± 6.53 . The average decrease was 28 points, representing a 27.54% amelioration of autism severity. The Wilcoxon signed rank test demonstrated a significant decrease in ISAA scores at follow-up ($V = 21$, $p = 0.0355$). (Figure.1) This implies that an improvement in behaviour was not restricted to individual cases but was distributed across the group. The large magnitude of change (Cohen's $d = 7.278$) indicates an overall downward-linear shift in severity with little between-subject variability. This clinical improvement was associated with increased attention, decreased irritability and more responsivity as reported by care-givers.

CHANGES IN GASTROINTESTINAL SYMPTOM BURDEN

The gastrointestinal load, measured with the ASD-GIRBI scale, showed a significant decrease throughout the study. The average baseline GIRBI score was 34.17 ± 4.02 , the median was 34.5 and the range was from 28 to 40. At 6-month follow-up, the average score was 16.00 ± 2.37 (median: 16; range: 13-19). The average decrease was 18.17 points, indicating a 53.17% change. This decline was significant (Wilcoxon $V = 21$, $p = 0.0355$) and demonstrated that participants' performance improved over time. (Figure.2) (Table.2) The absolute change effect size was large with a calculated Cohen's d of 8.9. This enema decreased colonic spasms, number of stools and left abdominal pain and normalized the activity of intestine clinically.

SYMPTOM-SPECIFIC SEVERITY REDUCTION

Specific domain scores (measured on an ordinal scale from 0 to 3) showed improvement in all areas with statistical significance. The severity of constipation was significantly reduced from the baseline mean score 2.5 ± 0.55 to 0.67 ± 0.52 at an average decrease of 1.83 points equivalent to a change by (73.33%). This alteration reached statistical significance (Wilcoxon $V = 21$, $p = 0.0263$). Abdominal pain intensity was reduced from a average baseline down to of 2.33 ± 0.52 of 0.50 ± 0.55 , with an average reduction of points and improvement% respectively). This reduction was also statistically significant ($V = 21$, $p = 0.0263$). Initial quality of sleep VAS scores average 2.5 ± 0.55 with significant decrease to a mean score of VAS = 0.67 ± 0.52 (1.83 points reduction and overall improvement by or equal to -73.33%) at the end point assessment ($V: 21$; $p: > 0,0263$). The irritability scoring also decreased from a baseline mean of 2.5 ± 0.55 to the obtained score of 0.67 ± 0.52 , with an average decrease of 1.83 points and a reduction percentage of (73,33%) $V = 21$, $p = 0.0263$). The same V statistic across these symptom dimensions suggests relatively uniform change in all participants, consistent clinical improvement. (Figure.3)

EFFECT SIZE AND MAGNITUDE OF CLINICAL CHANGE

Estimation of effect size revealed large clinical benefit in all domains. Reduction of behavioural severity was 27.54%, gastrointestinal burden was reduced by 53.17%, and symptom parameters as individuals were reduced from 73 to 78%. Large effect size (Cohen's d) values were generally observed across variables, suggesting strong and stable change compared to variance in paired differences³. The interpretation of these values, however, should be done with caution due to the small sample size and similar improvement pattern across all participants.

CORRELATION BETWEEN GASTROINTESTINAL AND BEHAVIOURAL IMPROVEMENT

For correlation analysis between improvement of gut symptoms and changes in behaviour, Spearman's rank correlation was used¹⁰. There was only a tendency toward moderate positive correlation between the decrease in GIRBI-Total scores and decrease in ISAA total scores ($\rho = 0.515$, $p = 0.296$). This indicates that subjects who experienced a larger positive change in GI symptoms were also likely to have some improvement in behaviour. When we next correlated concerns for GI severity with behavioural improvement, we identified a trend towards a moderately positive association ($\rho = 0.638$, $p = 0.173$), meaning that individuals with greater baseline burden of the gut often had greater reductions in ISAA scores over time. A moderate positive correlation was also observed between baseline GI severity and percentage behaviour improvement ($\rho = 0.543$, $p = 0.266$). (Figure.4) While these associations did not achieve statistical significance, likely because of the small sample size, their consistent positive direction supports a potential clinical link between GI stabilization and behavioural improvement.

DELIVERY TYPE AND GASTROINTESTINAL SEVERITY

A primary goal of this study was to perform an analysis on the relationship between modality of delivery and FGT burden. Fisher's exact test was applied and no statistically significant relationship was found between type of delivery and GI severity at the first testing day point ($p = 0.40$) for category of improved patients, nor for delivery type and improvement category ($p = 1.00$). Nevertheless, descriptive observations already showed a trend for a greater percentage of LSCS-born children with significant gastrointestinal symptoms at baseline. Behavioural improvements did not significantly differ between NVD and LSCS animals (Mann-Whitney U test comparisons, $W = 3$, $p = 0.814$). There were also no significant differences between patients in the changes from baseline in GI improvement ($W = 0.5$, $p = 0.158$) and baseline GI severity ($W = 0$, $p = 0.133$). Although not statistically significant, possibly due to the small sample size, these findings may reflect a tendency toward more GI involvement at baseline in LSCS-delivered children.

INTEGRATED INTERPRETATION

There is sustained and statistically significant improvement in both behavioural and gastrointestinal domains at 6 months. Strong decreases in ISAA and GIRBI scores, and in individual symptom severity parameters reflect reliable clinical improvement of the patients. The modest positive associations between GI improvement and behavioural change further support the hypothesis of functional relationships between gut physiology and neurobehavioral domains. While limited by a small sample, the consistent direction of improvements, statistically significant pre-post change and reduction across all symptoms make it clinically very meaningful⁷. These results are consistent with a broader trend focusing on microbiota-gut-brain axis in fields of science and indicate that the stabilization of GI disturbances may correlate with measurable behavioural improvement in children with ASD.

CONCLUSION

This paper presents a prospective observational study in 6 children with ASD, completing six months of the individualized homoeopathic intervention. Statistically significant reductions were observed with respect to severity of autism and gastrointestinal symptoms following implementation of the short-term intervention. Mean ISAA scores decreased by 27.54% ($V = 21$, $p = 0.0355$), and ASD-GIRBI scores were reduced by 53.17% ($V = 21$, $p = 0.0355$). There were also substantial improvements on all four of the individual symptom domains (constipation, abdominal pain, sleep disturbances and irritability), which demonstrated a mean reduction of 1.83 for each domain on a scale of 0-3 severity; this result was statistically significant ($p = 0.0263$). These results suggest that there was evidence of clinical alteration regarding behavioural and gut-related measures during the study. But due to a limited number of patients and the observational character of the study, these results should be interpreted cautiously, new studies with larger patient populations are required in order to confirm these findings.

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Table 1. Baseline Clinical Profile of Study Participants (n = 6)

Patient ID	Age (years)	Sex	Delivery Type	Baseline ISAA	Baseline GIRBI	Constipation Score	Pain Score	Sleep Score	Irritability Score
C1	10	Male	Normal Vaginal Delivery	98	36	3	2	3	3
C2	6	Male	Caesarean Delivery	104	32	2	3	2	3
C3	4	Male	Caesarean Delivery	90	28	3	2	3	2
C4	7	Male	Normal Vaginal Delivery	118	40	2	2	2	2
C5	8	Female	Caesarean Delivery	102	34	3	3	3	3
C6	8	Male	Caesarean Delivery	98	35	2	2	2	2

Scoring note: Symptom variables were recorded on a 0–3 clinical severity scale (0 = absent, 1 = mild, 2 = moderate, 3 = severe). This table presents the demographic profile and baseline behavioural and gastrointestinal severity status of all enrolled participants prior to intervention.

Table 2. Pre–Post Outcome Summary of Clinical Parameters (n = 6)

Variable	Baseline Mean ± SD	6 Months Mean ± SD	Mean Change	% Improvement	p-value
ISAA Score	101.67 ± 9.33	73.67 ± 6.53	28.00	27.54%	0.0355
GIRBI Score	34.17 ± 4.02	16.00 ± 2.37	18.17	53.17%	0.0355

Constipation Score	2.50 ± 0.55	0.67 ± 0.52	1.83	73.33%	0.0263
Abdominal Pain Score	2.33 ± 0.52	0.50 ± 0.55	1.83	78.57%	0.0263
Sleep Disturbance Score	2.50 ± 0.55	0.67 ± 0.52	1.83	73.33%	0.0263
Irritability Score	2.50 ± 0.55	0.67 ± 0.52	1.83	73.33%	0.0263

Note: Mean change represents the average reduction from baseline to six months. P-values were derived using the Wilcoxon signed-rank test for paired comparisons.

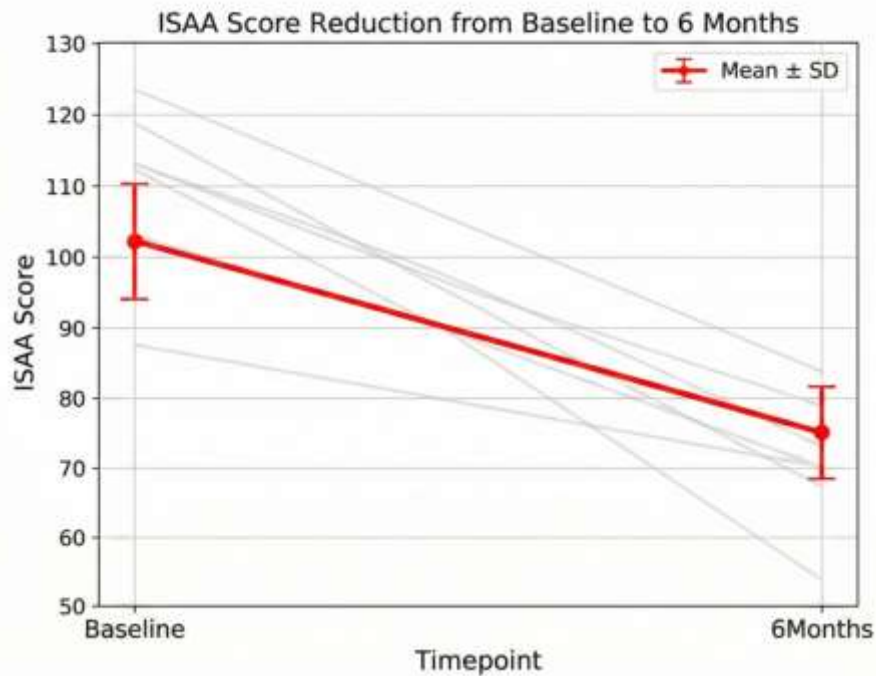


Figure 1. Change in ISAA scores from baseline to 6 months. Grey lines represent individual patient trajectories; red line shows mean ± SD.

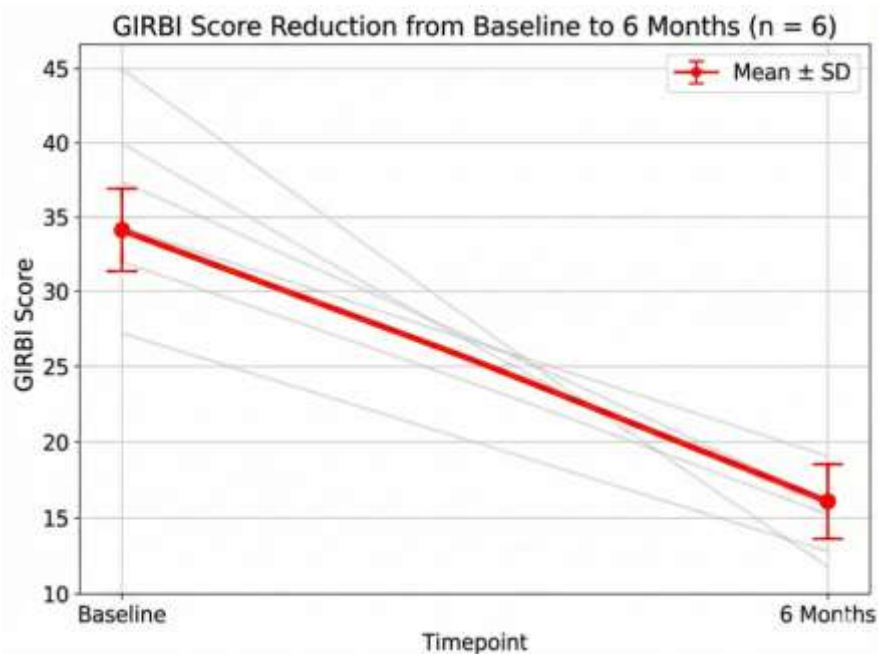


Figure 2. Reduction in gastrointestinal symptom burden measured using GIRBI scores from baseline to 6 months. Grey lines represent individual patient trajectories, while the red line indicates mean ± standard deviation

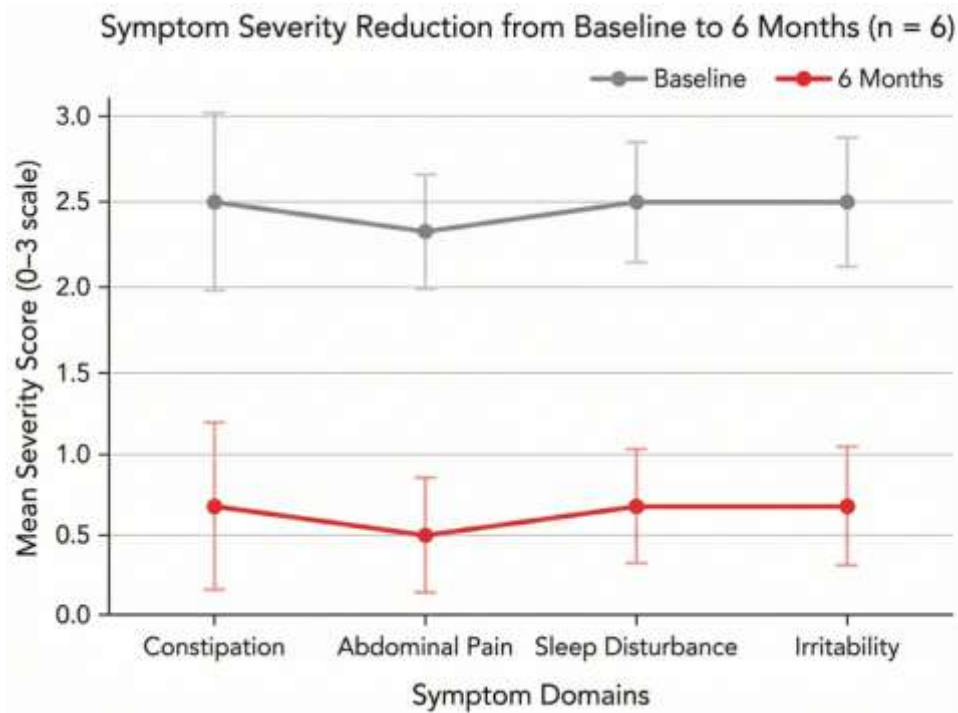


Figure 3. Mean symptom severity scores (0–3 scale) for constipation, abdominal pain, sleep disturbance, and irritability at baseline and 6 months (n = 6). Grey lines indicate baseline values and red lines indicate 6-month scores, showing a clear overall reduction across all domains with SD error bars.

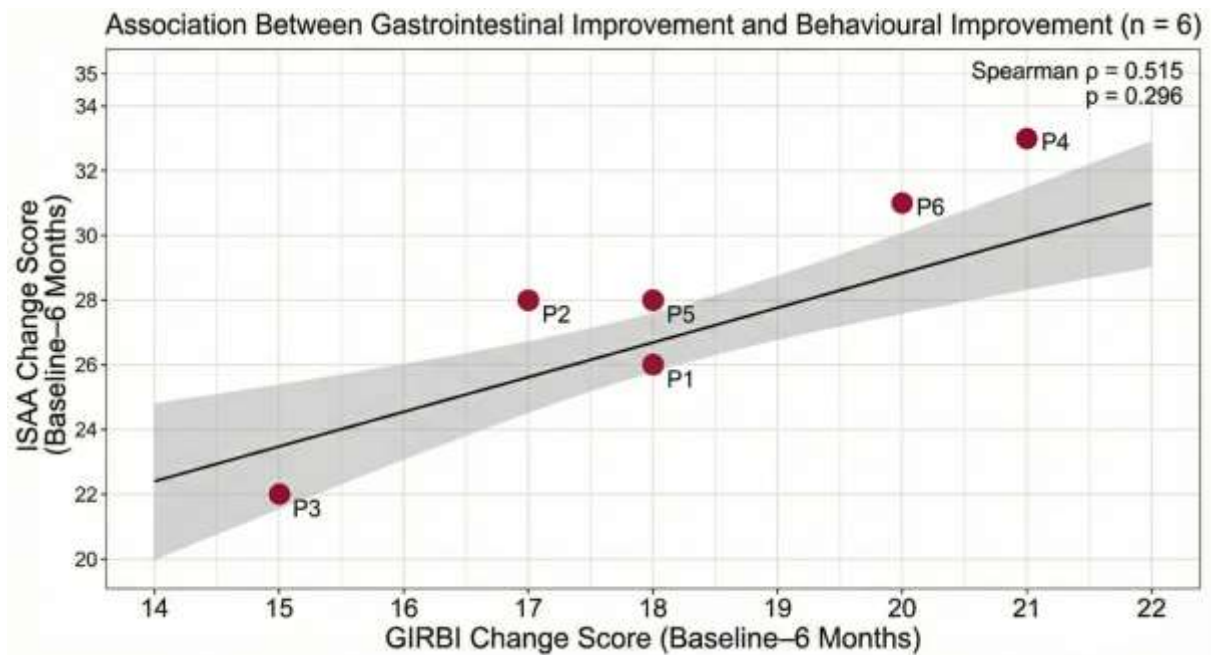


Figure 4. Scatter plot showing the association between gastrointestinal improvement (GIRBI change) and behavioural improvement (ISAA change) from baseline to 6 months (n = 6). A moderate positive correlation is observed (Spearman $\rho = 0.515$, $p = 0.296$), suggesting a parallel trend between GI symptom reduction and behavioural improvement.