

RAPID COMMUNICATION

Family history of irritable bowel syndrome is the major determinant of persistent abdominal complaints in young adults with a history of pediatric recurrent abdominal pain

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Abstract

AIM: To assess the late outcome of teen-agers with a previous history of recurrent abdominal pain (RAP) or irritable bowel syndrome (IBS).

METHODS: A group of 67 children with RAP referred to the department from January 1986 to December 1995 was followed up between 5 and 13 years after the initial diagnosis by means of a structured telephone interview. We hypothesized that those patients with persistent adult IBS-like symptoms would be significantly more likely to report a family history of IBS in comparison with adults with no persistent abdominal complaint.

RESULTS: Out of the 52 trackable subjects, 15 were found to present IBS-like symptoms at follow-up (29%) whereas the majority (37 subjects) did not. Subjects with IBS-like symptoms were almost three times more likely to present at least one sibling with similar symptoms compared to subjects not complaining (40.0% vs 16.0%), respectively ($P < 0.05$ at Student t test). Subjects with IBS-like symptoms also reported a higher prevalence of extra-intestinal symptoms, such as back pain, fibromyalgia, headache, fatigue and sleep disturbances.

CONCLUSION: The study confirms previous observations indicating that pediatric RAP can predict later development of IBS. The latter appears to be greatly influenced by intrafamilial aggregation of symptoms, possibly through the learning of a specific illness behavior.

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INTRODUCTION

Recurrent abdominal pain (RAP) is characterized by three or more episodes of abdominal pain that occur over at least three months and are severe enough to interfere with activities, such as school attendance and performance, social activities, and participation in sports and extracurricular activities^[1].

RAP is common, affecting between 7% to 25% of school-aged children and adolescents^[2,3], and may be responsible for 2% to 4% of pediatric office visits^[4]. RAP becomes more prevalent with increasing age into adolescence^[1,5-7] and is more common in girls^[2,8] with an equal gender ratio in early childhood^[3,9], but greater female symptom reporting in late childhood and adolescence^[1,7,10]. Specific structural, infectious, inflammatory, or laboratory abnormalities are unusual in RAP, particularly in the absence of "red flags" such as weight loss, gastrointestinal bleeding, pain awakening the child at night, systemic symptoms such as fever, or laboratory evidence of anemia or inflammation^[11].

Medically unexplained RAP is often considered to be a functional gastrointestinal disorder (FGD), a condition defined as a variable combination of chronic or recurrent gastrointestinal symptoms in the absence of explanatory structural or biochemical abnormalities^[12]. Irritable bowel syndrome (IBS) is a FGD characterized by recurrent abdominal pain or discomfort occurring over a 3-month period, where the symptoms are relieved by defecation and/or are associated with changes in stool frequency or consistency^[13].

Implications of pediatric RAP across the lifespan are not well understood. Early follow-up studies have reported

persistence of recurrent abdominal pain into adulthood for one third to one half of affected children^[14-16], but are limited by the lack of standardized assessments and formal diagnostic criteria. In more recent studies using standardized assessments and control groups, former RAP patients reported significantly greater abdominal pain, other somatic symptoms, functional impairment, health service use, and internalizing psychiatric symptoms in comparison to controls at 5-year follow-up, and females with a history of RAP are significantly more likely to meet diagnostic criteria for IBS^[17,18]. A large, population-based cohort study of adults born in 1946 in the United Kingdom compared the 2% of the sample who consistently reported medically unexplained abdominal pain at ages 7, 11, and 15 years with study participants without a history of chronic abdominal pain on the basis of standardized assessments when participants were 36 years old. Persistent abdominal pain in childhood is significantly associated with an increased risk of psychiatric disorder in adulthood, but not with abdominal pain or headache once psychiatric disorder is controlled for in the regression^[19].

In this study, a group of children with RAP or IBS was followed up between 5 and 13 years after the initial diagnosis. We hypothesized that those patients with persistent adult IBS-like symptoms would be significantly more likely to report a family history of IBS in comparison with adults with no persistent abdominal complaint.

MATERIALS AND METHODS

Case identification and recruitment

Potential patients were identified from clinical records of the Pediatric Department at the "L. Sacco" University Hospital of Milan. Charts of children referred to the department from January 1986 to December 1995 were retrieved, searching those children aging between 4 and 14 years at the time of index visit and referred because at least three episodes of medically unexplained abdominal pain occurred and they had an established a diagnosis of RAP or IBS. Criteria for inclusion included: Those proposed for RAP by Apley & Naish in 1958 and revised by Hyams JS *et al*^[6], e.g. at least 3 episodes of medically unexplained abdominal pain occurring during a period of at least 3 months that were severe enough to affect the activities of the child or those proposed for IBS by the Rome II Working Party^[13], e.g. in children old enough to provide an accurate pain history, at least 12 wk, even not consecutive, in the preceding 12 mo of abdominal discomfort or pain with two out of the following three features: relieved with defecation, and/or onset associated with a change in frequency of stool, and/or a change in form (appearance) of stool, and no structural or metabolic abnormalities^[13].

Criteria for exclusion included: abdominal pain with atypical features, symptoms, or findings suggestive of physical disease (e.g. abnormal physical examination or laboratory findings, persistent vomiting, gastrointestinal bleeding, constitutional symptoms such as fever or weight loss), acute or chronic physical disease, and development disability. There were 67 patients identified who fulfilled the diagnostic criteria for either RAP or IBS.

An effort to contact by telephone the potential partici-

Table 1 Demographic and other clinical features of individuals with or without IBS at follow-up

	IBS symptoms (n = 15)	No IBS (n = 37)	P value
Mean age (yrs) at index diagnosis	7.7	6.2	> 0.05
Female/male	9/6	19/18	> 0.05
Mean duration of follow-up (yr)	8.4	8.6	> 0.05
Siblings with IBS (%)	40	16	< 0.05
Extra-intestinal symptoms (%)	47	13.5	< 0.05
Body mass index	19.9	18.9	> 0.05

pants to the study was made, at an interval between 5 and 13 years after the index visit. However, 13 patients could not be tracked, because of change of address or available number incorrect, 1 because already deceased, and 1 because of interview refusal. Thus, data were available for 52 subjects (contact rate: 88%), with only 1 subject declining to participate (refusal rate: 1.5%).

The telephone interview was done by two of us (ZG and DGS) unaware of the index diagnosis of the subjects. A structured questionnaire was used, developed for the purpose of the study, asking very simple questions, as for example actual weight and height, presence or absence of abdominal complaints, presence or absence of siblings with similar complaints, *etc.* In case of affirmative answer to the question regarding presence of abdominal complaints, the interviewer specifically asked the questions 20 to 27 from the Rome II Modular Questionnaire^[20], relating to a better characterization of bowel and abdominal pain symptoms, respectively, translated and linguistically adjusted for Italian people. Finally, the severity of dominant abdominal symptom as well as the impact on work/school/sport activities were assessed by using an 1-100 analogue scale. If one sibling was identified as suffering from abdominal complaints as well, then an effort was made to verify this information by a subsequent direct telephone to him or her, and the same questions were asked in case of confirmation.

No payment or other revenge was offered to subjects who agreed to participate in the study.

RESULTS

Fifteen subjects were found to present IBS-like symptoms at follow-up (29%) whereas the majority (37 subjects) did not. The demographics and other clinical features of IBS patients and non-patients at follow-up are presented in Table 1.

Subjects with IBS-like symptoms were almost three times more likely to present at least one sibling with similar symptoms compared to subjects not complaining (40.0% vs 16.0%), respectively ($P < 0.05$ at Student *t* test). Not surprisingly, subjects with IBS-like symptoms reported a higher prevalence of extra-intestinal symptoms, such as back pain, fibromyalgia, headache, fatigue and sleep disturbances.

Table 2 shows the features of the 15 subjects with IBS-like symptoms in more detail. Two thirds of the patients reported abdominal pain as opposed by one third only re-

Table 2 Clinical features of the 15 subjects with IBS-like symptoms at follow-up

Symptoms	%
Predominant abdominal pain	67
Predominant abdominal discomfort	33
Alternating diarrhea/constipation	15
Severity of dominant symptom (1-100)	50
Limitation in school/sport/play (1-100)	48
Sleep disturbances	19
Headache	15

porting abdominal discomfort. Approximately half of the patients (53%) reported diarrhea as the main bowel habit abnormality, 32% constipation and 15% an alternating habit, respectively.

The predominant symptom was scored by the subjects as moderate severity (50% severity at the analogue scale) and judged to be the cause of significant limitation in daily activities (48% at the analogue scale). Finally, the more frequent extra-intestinal symptom reported was the presence of sleep disturbances (19%), followed by headache (15%).

DISCUSSION

The major finding of our study is the observation that a considerable proportion of young adults (29%), who suffered from a RAP (or IBS) during their childhood severe enough to be referred to the pediatric department of our hospital, still continue to suffer from abdominal complaints who fulfill the diagnostic criteria for IBS. This finding is in agreement with previous published works, in particular the recent papers by Hotopf *et al*^[19], Walker *et al*^[18], and Campo *et al*^[21]. Hotopf *et al*^[19] did a population-based birth cohort study, assessing the cohort of 3637 individuals born in UK in one week of 1946. These subjects were prospectively evaluated by means of several "waves" of data gathering, in particular at the ages of 7, 11, and 15 years the information was sought concerning abdominal pain. By doing so, the authors were able to diagnose "persistent" abdominal pain as abdominal pain reported at each of these three time-points, suggesting that pain is chronic. They showed that at the age of seven, 20% of survey members were suffering from abdominal pain, at the age of eleven they were 19% and at the age of fifteen they were 17%, whereas at the age of 36 years, only 7% of the subjects still had persistent abdominal pain. Abdominal symptoms in childhood appear to be weakly associated with persistent abdominal pain or headache in adulthood, but are associated with increasing numbers of physical symptoms at this age^[19].

In the study by Walker *et al*^[18], 76 patients with RAP and 49 control age- and sex-matched subjects, suffering from acute minor illness or injury, were compared 5 years after their initial evaluation by a structured telephone interview. The subjects constituted a higher proportion of the initial samples, e.g. 84% and 94%, respectively. It turned out that at follow-up frequent (weekly or more often) abdominal pain was significantly more likely to be reported by patients with a history of RAP (45%) than by control subjects (20%)

($P < 0.01$). Patients with a history of RAP were also more likely to report having received a diagnosis of IBS in the 5 years since study entry (5% *vs* 0%). Finally, the former subjects had significantly more school absences and clinical visits because of abdominal pain than the control subjects, while similar levels of school absence and clinical visits for non abdominal symptoms were reported.

Finally, the recent paper by Campo *et al*^[21] compared two small samples of young adults, i.e. 28 subjects were evaluated for RAP between the age of 6 and 17 and 28 matched controls participating at the same age in a study about tonsillectomy and adenoidectomy, an average of 11.1 years after the index visit. In this follow-up study, although approximately one third of the RAP group met the criteria for IBS, patients and controls did not differ significantly on interview measures of IBS (33.3% *vs* 22.2%, NS). One third of RAP patients endorsed a history of migraine, over twice as many as controls, with a trend toward statistical significance (35.7% *vs* 14.3%, $P = 0.07$). The second interesting feature is the familial aggregation of symptoms. In our study, the presence of at least one sibling with IBS was identified in the group developing adult IBS symptoms in a proportion greater than twice that observed in the group not developing adult IBS (40% *vs* 16%, $P < 0.01$). This observation is in keeping with the more recent literature, suggesting the importance of parental reinforcement and modeling in the development of gastrointestinal illness behavior in children and adults. Whitehead *et al*^[22] demonstrated that people with a functional bowel disorder are more likely to report being given gifts or treat foods when they had minor illnesses (cold or influenza) as a child. Levy *et al*^[23] in a case-control study conducted on 631 children of parents with a recent diagnosis of IBS and 646 children matched by parental age, gender and number of children in the family without this diagnosis, found that case children have significantly more yearly visits than controls for gastrointestinal symptoms (0.35 *vs* 0.18, $P < 0.001$) as well as for all causes (mean 12.26 *vs* 9.81, $P = 0.0001$), suggesting an intergenerational transmission of gastrointestinal illness behavior. Finally, Levy *et al*^[24] further explored the relative contribution of genetic and environmental (social learning) influences to the development of IBS by comparing concordance rates in monozygotic and dizygotic twins to concordance between mothers and their children. They found that concordance for IBS is significantly greater in monozygotic than in dizygotic twins (17.2% *vs* 8.4%, $P = 0.03$), supporting a genetic contribution to IBS. In addition, they also found that the proportion of dizygotic twins with IBS who have mothers with IBS is greater than the proportion of dizygotic twins with IBS who have co-twins with IBS (15.2% *vs* 6.7%, $P < 0.001$), suggesting that social learning has an equal or greater influence than heredity.

In our study we did not individually assess the relative contribution of these two factors to abdominal illness behavior, nor measured the influence of this abnormal learned sick role on school or work absenteeism, but were able to explore the subjective impact of IBS complaints on one aspect of health-related quality of life, i.e. the limitation in school/sport or playing activities. We found

that, on a scale from 0 to 100 it weighted 49.2. The last finding we would like to emphasize is the relatively low rate (less than 20%) of extra-intestinal symptoms, such as sleep disturbances or headache, in the group of subjects developing IBS. This finding points toward a very specific type of learned illness behavior in our group of patients, again in keeping with the observation of others, in particular the group of Chapel Hill^[25], who demonstrated that reinforcement of menstrual illness behavior *or* cold illness behavior in parents significantly predicts adult menstrual *vs* cold symptoms and disability days, independent of stress and neuroticism.

Our study has a number of potential limitations. Like most studies of RAP, this was a referred sample from a specialized care setting, which can limit the generalization of our findings. We did not assess the psychopathology of the subjects nor the history of maltreatment, since this was not formally done at the time the subjects were visited the outpatient department because of RAP. Finally, our study was not a case-control one, but merely a follow-up investigation of a cohort of children. We cannot exclude therefore that the rate of adult IBS development observed in our sample is different from that expected in a matched control population. However, to measure the risk of IBS was not our primary aim, which was in fact to compare the individual and family findings of young adults developing or not developing IBS 5 to 13 years after the original diagnosis of RAP or children IBS. On the other hand, valuable features of our study are the large sample investigated (52 subjects tracked compared to 28 in the study by Campo *et al.*^[21], the average 8.5 years of follow-up compared to 5 years in the study by Walker *et al.*^[18], and the use of validated diagnostic criteria for the diagnosis of RAP and IBS).

In conclusion, a large proportion, roughly one third of children referred to the hospital because of RAP or IBS, still presents significant abdominal complaints and can be diagnosed as suffering from IBS 5 to 13 years after this diagnosis, confirming that although RAP is a functional disorder, it should not be dismissed as a completely benign condition or a transient reaction to stress. Furthermore, by comparing young adults presenting or not presenting IBS, the presence of one sibling with IBS is the most important factor associated with IBS development, confirming that functional bowel disorders tend to run in families due to heredity factors and social learning influences.

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