Reactions to dietary tartrazine

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SUMMARY Double blind challenges with tartrazine and benzoic acid were performed in hospital in 24 children whose parents gave a definite history of a purely behavioural immediate adverse reaction to one of these substances. The patients, whose ages ranged from 1·6 to 12·4 years, were on a diet that avoided these items, and in all there was a clear history that any lapse of the diet caused an obvious adverse behavioural reaction within two hours. In no patient was any change in behaviour noted either by the parents or the nursing staff after the administration of placebo or active substances. Twenty two patients returned to a normal diet without problems, but the parents of two children insisted on continuing the diet. While popular belief has it that additives may have harmful behavioural effects, objective verification is required to prevent overdiagnosis.

It is becoming common for parents to report that their child's behaviour problem is caused by an adverse reaction to a food additive and in particular to tartrazine. This study is an attempt to verify these observations.

Patients and methods

Between January 1981 and the end of July 1986, out of roughly 700 children referred to a unit with a special interest in eczema and severe atopic disease, 30 children were seen whose parents provided a definite history of a purely behavioural immediate adverse reaction to a food additive. Those whose parents were merely suspicious about food additives were not studied. Children in whom a behavioural change was only one of several features of an adverse reaction to an additive, such as an acute attack of eczema or asthma, were also not studied. This report concerns the 24 patients whose parents were willing for their observations to be exposed to objective validation. In one patient the parents agreed to double blind challenges but then telephoned to report that their child had suddenly grown out of additive intolerance and food allergy. At the time of study, all the patients were on a diet that avoided the additives and any other foods under suspicion, and in all there was a clear history from the parents that any lapse of the diet caused an obvious adverse behavioural reaction within two hours.

In all patients a record was made of the reasons given by the doctor for the referral and of the

specific behaviour problems noted by the parents. The history and observations in the clinic and on the ward were used to see if the child's behaviour problems met the American Psychiatric Association DSM-III criteria for the diagnosis of 314·01, attention deficit disorder with hyperactivity¹ (more commonly simply called hyperactivity in this country). A family and personal history of atopic disease was recorded and details of the diet noted. The parents of all 24 patients reported that tartrazine was the additive that caused the most severe adverse reaction, and in six there was a history of a similar adverse behavioural change to benzoic acid.

With the parents' agreement, the children were challenged double blind with tartrazine and benzoic acid separately. The challenges were performed on a general medical paediatric ward. Twelve children were inpatients and 12 came to the ward as outpatients. The parents of the outpatients knew on which day the challenge was to be performed, but for the inpatients neither the parents nor the nursing staff knew on which days challenges were to be performed, and the child was given the vehicle drink (orange juice or Ribena) throughout admission.

Each child was allowed to play normally on the ward, in both the play room and the corridor, and was allowed to mix freely with inpatients and visitors. Each child was observed by at least one parent and by the nursing staff, each of whom were asked to keep a timed but separate record of any change in the child's behaviour. No specific scoring system was employed. While the parents knew what symptoms to look for, the nursing staff were not

given specific details about an individual patient and were just asked to record any change at all in the child's behaviour. Challenges with tartrazine were performed by dissolving 50 mg in a coloured drink to which the child was said to be tolerant, which in 19 cases was pure orange juice from a carton and in five was Ribena, a blackcurrant drink that also contains sodium benzoate and sodium metabisulphite. A second tartrazine challenge using 250 mg was performed at least two hours after the first challenge. After the challenge with tartrazine, but on a separate day, all patients were challenged with benzoic acid, the procedure and dosages being the same as for tartrazine. All drinks were administered by a member of the medical staff, the child used a straw, and neither the parents nor the nursing staff were allowed to see the drink at close quarters. Despite these precautions one 10 year old child accidentally spilled orange juice containing tartrazine and immediately noticed the colour staining his skin.

Results

Nineteen of the 24 patients (79%) were boys, a sex ratio of 3.8. Their ages ranged from 1.6 to 12.4 years, with a mean age of 5.2 years. Formal developmental assessments were not performed, but none of the patients was mentally retarded. One patient was seen in 1981, one in 1982, one in 1983, four in 1984, seven in 1985, and 10 in 1986. Twenty three of the 24 patients were on a diet excluding a mean of 23 food items, ranging from two (colouring agents and preservatives each counted as one food) to 38. The other child was on a diet comprising only three foods. In nine children the only exclusions from the diet were colouring agents and preservatives. The patients had been on a diet for a mean of 24 months, ranging from one to 36 months.

The most common reason for referral given in the referral letter was abnormal behaviour (15 cases), followed by a request for supervision of the diet (six), patient's behaviour only partly responded to dietary measures (five), mother requested referral to allergy clinic (three), initial response to diet followed by relapse (two), parents wanted validation of adverse reaction to additive (two), and parents seeking 'underlying reason' for adverse reaction (one). The behaviour problems reported by the parents are given in the Table. Nine of the patients (38%) had a first degree relative with a history of atopy, and 11 patients (46%) had a personal history of atopic disease, which was eczema in six (with rhinitis in one), asthma in four, and urticaria triggered by foods in one. Ten patients (42%) had neither a personal nor a family history of

Table Behaviour problems reported by the parents

Poor sleeping	12
Runs about or climbs on objects incessantly	11
Temper tantrums	10
Aggressive behaviour	8
Unable to sit still	7
Poor concentration	4
Violent outbursts when under stress	4
Uncontrollable	4
Pulls things off shelves in supermarket	3
Accidents/injuries resulting from jumping or rushing	3
Persistent crying as a baby	3
Disobedient or defiant	3
Incessant drinking	2
Often bursts into tears	2
Unable to play constructively	2
Lives in a world of his own	1
Easily led	1
Hysterical if exposed to water	1
Unhappiness	1

atopy. Six of the patients (25%) fulfilled the DSM-III criteria¹ for attention deficit disorder with hyperactivity.

Of the 24 patients, 18 were described by the nursing staff and the parents as behaving quite normally throughout the time of observation, with no detectable change in behaviour with or after placebo or active challenges. There were four children who attended as outpatients, whose parents realised at the end of the first day that there had been no reaction to placebo or active preparation (tartrazine). These four parents suggested that there was no point returning for the second set of challenges and these four children were not challenged with benzoic acid. The other six children, all of whom were studied in inpatients, were regarded by the nursing staff, on clinical grounds, as having behaviour that was in some way abnormal, such as frequent tantrums, aggressive behaviour, or pronounced overactivity. In one of these children, who was admitted to hospital with her mother, the child's temper tantrums (the main complaint) were so gross, prolonged, and frequent that it was initially unclear whether she could be contained on the ward. Her double blind challenges were delayed for four days to see if any spontaneous improvements might occur, but there was no improvement and the challenges were performed without any alteration in the frequency or duration of tantrums with either placebo or active preparations. In the other five the behavioural abnormalities, as observed by the nursing staff and the parents, were unrelated in time to the administration of either placebo or active challenges. In one of these five patients testing was delayed for two days because the child absconded from the ward. In short, in no patient was any change in behaviour noted either by the parents or the nursing staff after the administration of placebo or active substances.

The results of the double blind challenges were analysed in the presence of the parents. Having found a lack of adverse reaction to tartrazine and benzoic acid, the parents were advised to place their child on an entirely normal diet. This was performed in hospital for all 12 inpatients and on the ward for outpatients where the parents were nervous to proceed. Of the 24 patients, 21 returned to a normal diet and remained on it without any food related problems at follow up. The parents of one patient, who was only on three foods at the time of admission, was unable to accept that the child was not food intolerant, and when new items of food were added to the diet they insisted that as a result the child had loose stools, skin rashes, and an adverse behavioural change, although none of these events were detectable to the nursing or medical staff. This child remained on a very restricted diet against our wishes. The parents of a second child were pleased that their daughter was able to eat normal food without adverse effect but continued to insist that she should avoid colouring agents not only in the diet but also in such items as paints. They alleged that on days when the child had been allowed to use paint at school tantrums and aggression were noted in the evening, and at one stage they threatened to withdraw her from school when the teachers would not agree to the child being excluded from painting. After further counselling they agreed to allow the child normal exposure to all forms of colouring agent. The parents of a third child declined to permit resumption of a normal diet and defaulted from follow up. Follow up information was available in all the other patients.

After resumption of a normal diet the parents were given simple advice about the practical management of the behaviour problems that had been described. Referral to the child psychiatry department was offered to the parents of 16 patients where it was anticipated that the parents might benefit from further counselling. Thirteen accepted this offer, but four later wrote to the psychiatrist and reported that the child's behaviour had improved and that attendance was therefore not needed.

Discussion

A drawback to this study is that it was performed in hospital. It is well known that children often behave differently in new or unfamiliar situations, and the DSM-III criteria for attention deficit with hyperactivity clearly recognise this: 'Because the symptoms are typically variable, they may not be observed directly by the clinician. . . . Signs of the disorder may be absent when the child is in a new or a one-to-one situation'.¹ Thus the failure of the

challenges to elicit a change in behaviour may be attributable to unfamiliarity of the ward environment. Furthermore, it is the belief of certain clinical ecologists that 'allergies' are cumulative, implying that a trigger such as an additive might only operate when the child is also exposed to other antigens such as house dust mites. Against these objections are the patients whose behaviour difficulties continued unabated, the fact that the parents reported that tartrazine had consistently produced adverse reactions under any circumstances, and the absence of adverse reactions on resumption of a normal diet at home. A further objection to the present study is that objective measures of changes in behaviour were not used and that the study relied on the crude and unstructured observations of the parents and non-psychiatrically trained nursing staff. As all the parents had previously reported dramatic and obvious behavioural changes after the administration of tartrazine it seemed reasonable to expect that the parents and nursing staff should be able to recognise such changes had they occurred.

This study was undertaken in hospital because it is almost impossible to disguise tartrazine, which in high concentrations gives a characteristic appearance to food and drink that is quite obvious to an adult who administers it. All drinks were taken through a straw because of the characteristic staining of the skin around the mouth after drinking solutions containing tartrazine. Capsules were not used because of the obvious bright colour of those containing tartrazine. For these reasons, investigations using high doses of tartrazine and performed at home² are likely to be unsatisfactory because the presence of tartrazine is quite evident, even in highly coloured food or drink.

In short, this study of 24 children showed that parents' reports of adverse behavioural changes after ingestion of tartrazine or benzoic acid could not be validated objectively when exposed to the test of double blind challenges. This is consistent with similar previous studies.³⁻⁷ This study does not exclude the possibility that there are rare children who have purely behavioural effects as a result of ingestion of additives such as tartrazine or benzoic acid. It does show, however, that parents' beliefs in the behavioural effects of tartrazine or benzoic acid are often groundless and are unreliable. This is in contrast to the situation in children with atopic disease, such as asthma or eczema, where tartrazine and benzoic acid may act as triggers,^{8,9} and where better control of the disease is often accompanied by a pronounced improvement in behaviour and concentration. Thus in one study of 76 patients where diet was said to contribute to behaviour disorders a large proportion of the children had atopic disease.²

An important feature of this study is that it shows how paediatricians can manage the increasing clinical problem of parents' anxieties about diet without being dismissive or confrontational. Although only two challenges were given, this was convincing to the parents, it allowed them to permit the reintroduction of a normal diet, and it helped them to view their child's behaviour differently and accept management help. Challenges with other food substances may also be required if parents are convinced that these are affecting the child. We need to learn how to help children whose parents insist on keeping them on very restricted diets; there were two such patients in the present series. Our own major effort has been to try and prevent nutritional deficiencies,¹⁰ but this does little to avoid the social isolation and possible emotional harm that results from inappropriate, long term, and extreme dietary measures. It is possible to view such cases as being part of the range of child abuse,¹¹ but this is probably a last resort.

Why do parents attribute behaviour disorders to additives? Many of the parents in this study said that they first learnt of the possible importance of additives through the media, in contrast to the situation in, for example, urticarial allergic reactions to egg, where the parents' observations are the first event. Suggestion as the result of reports in the media is probably combined with an increasing general interest in the nutritional content of food. Most of the children in this study had been labelled hyperactive, although only six met the DSM-III criteria for this disorder. It is understandably attractive for parents of children with behaviour problems to have available a diagnostic label and an exogenous cause. Parents are usually but not always right about a child, and they cannot be objective. While popular belief has it that additives may have

harmful behavioural effects, objective verification is required to prevent overdiagnosis.

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