Mental health problems of children in the community: 18 month follow up

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In a recent national survey, the prevalence of psychiatric disorder in children and adolescents in Great Britain was more than 9%.¹ Parents and doctors commonly think that these disorders are transient, but longitudinal studies show otherwise.² We followed up children from the national survey to examine persistence in a large sample of children in Britain.¹

Participants, method, and results

The original survey studied a sample of 10 438 British children aged 5-15 years.¹ We sent the parents of all children with a psychiatric disorder (936) and a third of those without a psychiatric disorder (3029) a questionnaire. It included the strengths and difficulties questionnaire, a well validated measure of childhood psychopathology and its impact on the child.^{3 4}

A total of 73% of parents responded; most losses were non-contacts, not refusals. The response rate was lower among those with a child with a disorder than those without (66% *v* 76%). Non-responders at follow up had had significantly more symptoms initially (analysis of variance adjusting for initial diagnosis, $F=39.9$, 1 df, $P<0.001$: the mean symptom score for non-responders was greater, by 1.2, than for responders, matched by diagnosis). Responders' and non-responders' initial impact scores did not differ significantly. Overall, differential non-response will not have led us to overestimate the persistence of psychopathology.

The figure shows symptom and impact scores in children initially diagnosed with hyperkinetic, conduct, emotional, or no disorder. We used paired *t* tests to test whether the changes in symptom and impact scores in children with hyperkinetic, conduct, emotional, or no disorder were significant. For conduct disorder, neither symptoms nor impact changed significantly. Symptoms ($P<0.05$) but not impact fell significantly in children with hyperkinesia. For emotional disorder, there were significant falls in both symptoms and impact ($P<0.001$ for both), though the follow up scores were still substantially greater than in the group with no initial disorder ($P<0.001$, independent samples *t* test).

We defined "caseness" from the combination of raised symptom (≥ 14) and impact scores (≥ 2).³ Caseness at follow up was considered informative for only the 86% (2487/2901) of participants in whom caseness was congruent with the initial psychiatric diagnosis. For example, when a child was initially diagnosed as having conduct disorder solely on the basis of symptoms reported by a teacher, and when the initial questionnaire, completed by the parents, described their child as normal, then the diagnosis (disorder present) and the caseness (negative) were not congruent. So, caseness was not considered informative at follow up, since the parent's answers to the questionnaire would probably not change whether or not the conduct disorder persisted or was resolved. Similarly, if the initial diagnosis of depression in a teenager was based on self reported symptoms (not reported by a parent), the follow up parent questionnaire is unlikely to be informative.

Caseness criteria at the 18 month follow up were met by 3% (67/2249) of children who did not initially have a psychiatric disorder, compared with 62% (147/238) of children who did (relative risk 20.7; 95% confidence interval 16.0 to 26.7). Persistence at 18 months varied with initial diagnosis: 36% (25/70) for children who had an emotional disorder initially, compared with 73% (122/168) for children with other disorders initially (mostly conduct and hyperkinetic disorders, sometimes with coexistent emotional disorders) ($P<0.001$, χ^2 test).

Comment

Childhood psychopathology is often persistent, particularly among children with conduct disorder and hyperkinesia. Although emotional disorders have a better prognosis than conduct or hyperkinetic disorders, they are not always benign: their resolution over 18 months is far from complete, and recent work suggests an increased risk of similar disorders recurring in adulthood.²

Everyone in contact with children should take the symptoms of emotional distress, behavioural difficulty, and hyperactivity seriously, as they may impair the child's function and development and are unlikely to be transient. This is particularly important as evidence

Mean symptom and impact scores initially and at 18 month follow up from the strengths and difficulties questionnaire, completed by parents, for children with and without initial psychiatric disorder

based interventions can alleviate distress and minimise the secondary handicap that results from disrupted education and impaired social development.⁵

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Drug points

Severe myalgia from an interaction between treatments with pantoprazole and methotrexate

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A 59 year old man with a folliculotropic cutaneous T cell lymphoma had been receiving treatment with interferon alfa-2a. After the treatment was discontinued because his tumour had relapsed, he started taking low dose pulse methotrexate (15 mg intramuscularly, once a week). Concomitantly he also had a Barrett oesophagus, which was treated with pantoprazole (20 mg/day, orally), and arterial hypertension, which was treated with atenolol. After the first injection of methotrexate the patient had severe generalised myalgia and bone pain. This led to partial immobility that began three to four hours after the injection and continued—albeit to a lesser degree—for several days. The symptoms recurred over the following four methotrexate cycles. Multiple clinical and laboratory examinations excluded clinical causes such as an underlying focal or disseminated infection and the systemic exacerbation of the cutaneous T cell lymphoma. A drug interaction with methotrexate was suspected because the symptoms arose when the drug was given. After pantoprazole was replaced by ranitidine, the symptoms subsided dramatically and finally disappeared.

The patient was rechallenged with pantoprazole eight weeks later, having given his informed consent. Treatment with pantoprazole was started six days before the weekly dose of methotrexate was given so that the maximum effect could be attained. Serum concentrations of methotrexate and its metabolite 7-hydroxymethotrexate were monitored with and without pantoprazole by a high performance liquid chromatography-fluorescence assay.¹ The two study periods were separated by a washout phase of six weeks. Atenolol, clemastine to treat local itching, and ascorbic acid to treat a temporary deficiency of vitamin C were given concomitantly.

The symptoms reappeared in response to the challenge but did not reappear without pantoprazole. The concentration-time curves (figure) are identical for methotrexate in both periods, but they differ considerably for 7-hydroxymethotrexate. The area under the curve between 0 and 144 h after drug administration was nearly 70% higher for 7-hydroxymethotrexate plus pantoprazole than without pantoprazole (1929 ng·h/ml *v* 1131 ng·h/ml); the half life of 7-hydroxymethotrexate was doubled when methotrexate was given with pantoprazole (81.4 h *v* 36.4 h). This indicates an interaction in renal elimination, rather than a metabolic interaction.

About 30% of all patients discontinue the low dose pulse methotrexate because of adverse effects. Drug interactions contribute considerably to the number of patients who stop using the drug.²⁻³ Reactions after dosing occur in

Serum concentration of methotrexate and 7-hydroxymethotrexate with and without pantoprazole

about 10-15% of patients with rheumatoid arthritis receiving this treatment.⁴⁻⁵ This report shows for the first time a link between methotrexate post-dosing reactions and an interaction of 7-hydroxymethotrexate and concomitantly given pantoprazole. The German Federal Institute for Drugs and Medical Devices and the Drug Commission of the German Medical Profession were informed about the case. The manufacturer of methotrexate (Medac GmbH, Wedel, Germany) was not aware of this drug interaction.

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