LETTERS TO THE EDITOR

Familial hypokalaemic periodic paralysis: prevention of paralytic attacks with lithium gluconate

The clinical course of familial hypokalaemic periodic paralysis (FHPP) is characterised by transient paralytic attacks associated with decreased serum potassium and chronic progressive muscular weakness. Hypokalaemic attacks are usually prevented with oral administration of potassium, spironolactone or acetazolamide. We report a case where such treatments became progressively ineffective. The episodic character of the disease led us to test lithium gluconate as add-on therapy in so far as lithium effects on cellular potassium fluxes are known. The drug was first introduced in an open trial and a reduction in the frequency of attacks was observed. A randomised, placebo-controlled, cross-over study was then carried out.

A 45 year old mechanic had experienced periodic paralytic attacks since the age of 15 years. The investigation of his pedigree revealed 15 comparable familial cases among four generations. During paralytic attacks hypokalaemia as low as 2·3 mmol/l was confirmed. Thyroid function tests were normal. Limbs and trunk muscles were involved but respiratory, facial and oesophageal musculature were not affected. Between attacks plasma potassium levels were normal. He was given oral supplementation of potassium (5 to 8 g daily) and there was an improvement in the severity of attacks. Acetazolamide and spironolactone were then successively introduced without serious effect. For the past two years, paralytic attacks occurred at a mean rate of once a week. Permanent muscular weakness increased progressively and socio-professional adjustment became necessary.

Lithium gluconate (5 ml ampoules: Li 4·95 mmol and NaCl 0·05 g; Neuroliothium, Labcatal laboratories) was introduced. To begin with, the patient was given lithium during an open trial, potassium being continued as before. The lithium daily dose was one ampoule from week 1–6, two ampoules from week 7–12, two and three ampoules each other day from week 13–23, and one ampoule from week 24–34. The medication was well tolerated and the attacks less frequent. During the whole trial, the patient noted the following daily: motor attack, if any, defined as a paralytic deficit of variable severity; motor deficit tested at 9 am, with a 20-point scale testing neck and limbs muscles; global daily working ability; oral potassium supplementation dosage; other medications; potential side-effects.

Systematic examination was performed weekly on the same day at 9 am. Functional deficits were assessed and potential side-effects were registered. Blood sample was withdrawn for lithium, urea, creatinine, glucose and electrolytic assays. RBC, WBC and platelet counting were performed monthly. The open-phase treatment lasted 34 weeks. Before the introduction of lithium, frequency of attacks was about one per week.

During lithium treatment, 11 attacks were observed (fig a), that is, a mean of 0·32 attacks per week. Serum lithium levels were found in the range of 0·30 to 0·80 mmol/l. The frequency of attacks were analysed according to serum lithium levels and an inverse correlation was found between them. When the lithium level was between 0·30 and 0·59 mmol/l, frequency of attacks per week was 0·42. Between 0·60 and 0·66 mmol/l, frequency was 0·33 and no attacks were observed during the seven weeks with lithium levels higher than 0·67 mmol/l. Permanent muscular weakness did not appear to be modified by lithium treatment (data not shown). No side effects were noted.

With informed consent of the patient, a randomised, placebo-controlled, cross-over, double-blind study was undertaken. It was designed with two six week test periods, each preceded by a two week wash-out. Ten millilitre ampoules were prepared for lithium (Li 9·90 mmol and NaCl 0·1 g) and placebo (NaCl 0·1 g), with identical appearances. During the randomised trial, the patient was asked to take one ampoule per day. The patient and the clinical examiner were blind to treatment and biological results. A second examiner surveyed blood data and possible adverse side effects.

The benefit of lithium therapy on paralytic attacks, suspected during the open trial, was confirmed by the randomised trial. Only one attack occurred during the six week lithium treatment phase to be compared with seven attacks observed during the placebo phase (fig b). Due to the design of the controlled trial, a period-order effect cannot be discounted. Such an interpretation, however, would be difficult to reconcile with the positive and long term improvement of the immediately preceding open trial. By contrast, no improvement was observed on permanent motor weakness at self-evaluation and medical examination (data not shown).

The primary defect in FHPP may be a
marked reduction of muscle permeability to potassium. Effects of lithium on potassium metabolism have been reported, and lithium could enhance Na-K pump activity, similar to potassium. Lithium therapy has already been proposed in various forms of familial periodic paralysis with varying results. In this case, carbohydrate lithium was administered to reach serum lithium levels up to 1.0 mmol/l. No benefit was observed, notably on attack frequency which remained about one per week. Biochemical homogeneity of FHPP may be questioned on the basis of such discrepant results. Some forms could be lithium sensitive and others, lithium resistant. Further studies are clearly needed to elucidate this problem. Lithium, as an oral potassium add-on therapy, is worth trying in FHPP patients according to standard therapy. It is safe and can be beneficial on rate of attack.

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Hyperphagia in dementia: fluvoxamine takes the biscuit

Marked overeating has been described in a number of conditions which involve brain damage, such as Huntington's disease. Other causes include psychiatric disorders and drug treatment. In this case, we describe the case of a man with probable Pick's disease whose hyperphagia appears to have been reduced by fluvoxamine.

A 69 year old man presented with a four year history of personality change and difficulty in planning tasks. All his personal interactions became bland and his persistent mood was one of fatalism. In addition he became incapable of carrying on his work as a builder. At this stage he scored 29/30 on the Mini Mental State Examination, but repeated examination over the next three years showed clear and increasing impairment in sequences, categorising and problem-solving tasks. A diagnosis of Pick's disease was made on the basis of the history, neurological examination, the neuropsychological tests and brain imaging. His mother had died aged 54 years apparently confused and unable to walk. No further details of her clinical state are known.

Two years ago he began to eat large amounts, selecting 5-HT uptake blockers from his son's plate, from supermarket shelves, and continually searching the house for more food. He was admitted to a residential home but his persistent attempts to obtain food led to admission to a psychogeriatric ward. On the ward he ate all food put in front of him, he took food from other patients and he raided the larder.

To see how much he would eat if given a limitless supply we observed the patient in a standard setting. On a table there were five plates containing a variety of biscuits (40 biscuits in all), a large pot of tea and four magazines. The observations were made from 9–10 am after an overnight fast. Mr C was invited to help himself to whatever he wanted. He was observed through a window from the adjacent room. The stock of biscuits was replenished if five biscuits were made approximately weekly.

On the hypothesis that the marked hyperphagia might be due to reduction in effective 5-HT function he was treated with fluvoxamine (a 5-HT uptake blocker) 100 mg/day for four weeks. The medication was tailed off and observations continued for a further 11 weeks.

Three baseline observations were made in the ward before starting fluvoxamine. These showed that he ate at a constant rate throughout the hour consuming a total of 60 or 61 biscuits (about 5500 kilocalories) on each occasion.

Within one week of starting the fluvoxamine the nursing staff reported a clear improvement in his behaviour. This improvement was confirmed by the standardised observation on the second day after starting fluvoxamine he ate 19 biscuits in the first 30 minutes and then looked through one of the magazines for the remainder of the hour. During this treatment phase we carried out five observations. The median number of biscuits eaten per hour was 21 (range: 15–40).

The patient did not experience nausea while taking fluvoxamine.

On stopping the fluvoxamine there was considerable fluctuation in the number of biscuits eaten, but he did not return to the behaviour observed before treatment. Ward staff reported that, after stopping fluvoxamine, his behaviour worsened, but that it was considerably less of a problem than it had been before treatment. We carried out a further 12 observations during this period. The median number of biscuits eaten per hour was 18 (range: 7–47).

Animal studies have implicated the 5-HT system as crucial in the satiety mechanism. Fluvoxamine is a selective 5-HT uptake blocker. However, in this case it does not prove that the primary defect lies in the 5-HT system. Indeed, it implies that there is sufficient intrinsic 5-HT on which the uptaker blocker can work. On discontinuing the fluvoxamine the patient's binge-like behaviour did not return to the pre-treatment levels. One possible explanation is that the apparent effect of fluvoxamine was purely coincidental. However, the marked change in long-standing behaviour on starting treatment would argue against this. A second explanation is that whilst he was on treatment there was sufficient progression of the disease to cause a change in his eating behaviour. A third explanation is that the fluvoxamine caused long-lasting effects on brain function. Whatever the mechanism, fluvoxamine appears to have had an effect on his hyperphagia which was measurable and clinically important.
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