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 an addition 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 muscle tone were not affected. Between attacks plasma potassium levels were normal. He was given oral supplementation of potassium (5 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; Norwellithium, Laboratory) 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, 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 electrolyts 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 shown in vitro studies. Results are contradictory, depending on the study design and the patient’s psychiatric state. No noticeable and consistent systematic effect of lithium on body potassium has been reported. Nevertheless, 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.14 To the best of our knowledge, there is only one other report concerning lithium therapy in a patient with FHPP.13 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 who are resistant to standard therapies. It is safe and can be beneficial on rate of attack.

We are grateful to Drs N Daitz and S Siroi from LABCAT Laboratories for their help in the trial design and the provision of the drug, and to Professor Guy Chazot for his helpful comments. 

CHRISTIAN CONFAVREUX PAUL GARASSUS* ALAIN VIGGETTO GILBERT AIMARD Clinique de Neurologie, Hôpital Neurologique, and Service de Neurologie,* Hôpital de l’Antiquaille, Lyon, France

Correspondence to: Professor Confavreux, clinique de Neurologie, Hôpital Neurologique, 59 boulevard Pinel, 69003, Lyon, France.

**Hyperphagia in dementia: fluvoxamine takes the biscuit**

Marked overeating has been described in a number of conditions which involve brain damage.1 Such overeating can cause management difficulties, but there have not been any reports of effective drug treatment for this problem. We describe the case of a man with probable Pick’s disease whose marked 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 fatalistic bonhomie. 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,2 but repeated examination over the next three years showed clear and increasing impairment in sequencing, 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 SPECT 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 blocker.

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 from a window from the adjacent room. The stock of biscuits was replenished if required and observations 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) at 100 mg/day for four weeks. The medication was tapered off and observations continued for a further 11 weeks.

Three baseline observations were made 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 method. After four weeks of 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 whilst 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 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.4 Fluvoxamine is a selective 5-HT uptake blocker. However, this case 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 uptake blocker can work. On restarting the fluvoxamine the patient’s overeating 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.

My Music—a case of musical reminiscence diagnosed courtesy of the BBC

Musical reminiscence is a disorder characterised by formed auditory hallucinations of a musical nature. This case is unusual in that the patient made the diagnosis and was subjected to NMR and SPECT studies.

On Christmas Eve 1985, an active 73 year old widow retired to bed in a particularly distressed state. She had just learned that her son and daughter-in-law were about to separate. On Christmas Day she was surprised to find her “elderly” neighbours playing Christmas tunes loudly on what she presumed to be a new music centre.

She was reluctant to open the door as she felt her old neighbours “had so few pleasures left to them”. After a few days the continuous and repetitive tunes became so irksome that she asked her home-help to make discrete enquiries. She was dismayed to learn that her neighbours had not bought a new music centre. Sometime later her son visited and she described to him the sounds she was hearing. He realised that these sounds were the basis for his mother’s complaints and initiated a series of medical referrals through the family doctor.

The ENT surgeons prescribed a tinnitus