Hyperventilation tetany: effect of carbamazepine

Schaaf and Payne first reported the use of diphenylhydantoin to treat tetany in 1966.1 We decided to try anticonvulsant therapy with carbamazepine in hyperventilation tetany. Carbamazepine was administered to 211 women and 77 men aged 18-42 (mean 28) in a dose of 600 mg daily for three months. Chvostek's sign was found in 70%, carpopedal spasms and paraesthesiae occurred in 28% and nonspecific features such as headache, fatigue and anxiety in 72%.

Electromyography was performed on all patients after two minutes of hyperventilation and all showed repetitive double, triple and multiple discharges typical of tetany. Carbamazepine significantly improved many of these features and Chvostek's sign disappeared in 31%.

A general reluctance to use anticonvulsant medication to treat hyperventilation tetany is probably due to the belief that tetany is due to ionic imbalance. Our results have shown that the stabilising effects of carbamazepine on neurons, probably implemented at the level of the brainstem reticular formation which is responsible for the integration of tetanic activity, was the reason for the improvement. The effect on the limbic system was shown by the decrease in anxiety.

Our experience suggests that carbamazepine may be useful in the treatment of hyperventilation tetany.


Reversible pituitary stalk enlargement in cranial diabetes insipidus

Infiltrative disease or neoplastic involvement of the pituitary stalk results in the CT appearance of stalk thickening often accompanied clinically by diabetes insipidus. Some patients, however, with cranial diabetes insipidus of no identifiable cause may also exhibit stalk enlargement.1 The natural history of this radiological abnormality in so-called idiopathic cranial diabetes insipidus has not been previously reported. We report on the follow-up of two patients with cranial diabetes insipidus whose CT findings at initial presentation revealed gross stalk enlargement.

CT scan showed gross thickening of the pituitary stalk in a 14 year old boy who presented three months after onset of symptoms. Water deprivation test with parallel assessment of thirst sensation confirmed the diagnosis of diabetes insipidus with concomitant adipsia. Treatment comprised water restriction (2 l/day) and intranasal desmopressin. Three years later a repeat CT scan showed no abnormality of the stalk. Serial CT and MRI over an eight year follow up have excluded a mass lesion.

In a second case a 24 year old female presented with a two week history of polyuria and polydipsia of sudden onset. Water deprivation testing confirmed cranial diabetes insipidus. Anterior pituitary function was intact. CT findings in this patient at initial presentation are shown in fig 1. The normal pituitary stalk (PS) is smaller than or equal to the size of the basilar artery (BA), but as illustrated in fig 2, was considerably enlarged in this patient.

MRI performed after three months of treatment with intranasal desmopressin confirmed that the stalk was still thickened. One year after presentation, however, repeat CT showed that the stalk was then of normal size (fig 3).

Structural involvement of the pituitary stalk in a number of pathological states such as histiocytosis, sarcoidosis, primary and secondary neoplasms may result in diabetes insipidus. Our patients with diabetes insipidus had gross stalk enlargement at presentation but resolution of the abnormality without treatment other than desmopressin in these cases confirmed that stalk enlargement may occur in the absence of any progressive infiltrating or neoplastic process.

The MRI findings in case 2 (fig 2) three months after presentation are noteworthy. There was no abnormalities of the hypothalamus. Stalk thickening was still obvious, though less marked than at presentation suggesting a slowly resolving process. The fact that the lesion was still present at this time excludes the possibility of ischaemic infarction of the stalk since the effects of infarction

Table Agreement with ultrasonographer's assessment of stenosis in 37 arteries

<table>
<thead>
<tr>
<th>Clinician</th>
<th>No arteries correctly identified</th>
<th>Agree on stenosis n (%), CI*</th>
<th>Disagree by 1 category of stenosis**</th>
<th>Disagree by 2 categories of stenosis</th>
<th>Uninterpretable</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>36</td>
<td>14 (50, 33-67)</td>
<td>15</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>C</td>
<td>29</td>
<td>11 (36, 21-58)</td>
<td>15</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>D</td>
<td>28</td>
<td>13 (46, 28-66)</td>
<td>12</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>E</td>
<td>26</td>
<td>11 (42, 23-63)</td>
<td>9</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>

*the proportion of correctly identified arteries in which the clinicians' assessment of stenosis was in the same category as the ultrasonographer and 95% confidence intervals. **categories of stenosis: Normal, 1-24%, 25-49%, 50-74%, 75-99% and occluded.
do not persist for more than three weeks.\(^4\)

Likewise, there was no evidence of haemosiderin deposition in the stalk which might be expected after haemorrhage. Stalk enlargement could have been an effect of untreated diabetes insipidus, in which the first case might have expected resolution of the abnormality with treatment. However, the swelling persisted for three months despite adequate treatment of the diabetes insipidus. It is possible that unrecognised injury or infection with ensuing inflammation resulted in the swelling observed initially. It is known that insults to the stalk can lead to reorganisation and proximal enlargement.\(^5\) We may have observed the resolution of such changes.

We conclude that pituitary stalk enlargement may occur in idiopathic cranial diabetes insipidus, persist for months, and eventually disappear. Serial imaging with CT or MRI will exclude progressive infiltrative or neoplastic causes.

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Ropinirole (SK and F 101468) in the treatment of Parkinson's disease

Ropinirole (4-[2-[(dipropylamino)ethyl]-1,3-dihydro-2H-indol-3-yl]methyl), a selective dopamine D2 agonist has been shown to have anti-Parkinsonian effects at doses between 0.5 mg twice a day and 2 mg twice a day in an open inpatient study.\(^1\) We report the results of a further open-label study in fourteen patients with idiopathic Parkinson's disease.

Participating in the study were seven patients with presumed Parkinson's disease (mean age 56-5 years, disease duration 2-5 years and mean Hoehn and Yahr Stage II) and seven patients with disabling levodopa-induced on-off oscillations (median age 66 years, disease duration 10-0 years and duration of levodopa treatment 4-0 years, daily levodopa dose 750 mg, median duration of disabling oscillations 1-0 years, mean Hoehn and Yahr stage when "off" III and when "on" II). Four of the patients treated with levodopa had severe interdose chorea and one patient had biphasic dyskinesias. Three patients were also receiving anticholinergic medication, three were taking L-dephenyl (selegiline); none of the patients had a history of psychiatric disorder or evidence of hepatic, renal or cardiovascular dysfunction.

Both groups were initially treated with 0.6 mg of ropinirole twice daily for one week. The dose was increased to 1 mg twice daily for the second week and by further weekly increments of 1 mg twice daily to a maximum of 7 mg twice a day over an eight week period. If adverse reactions developed, patients continued on the previously tolerated dose for another week. The dose of less than 1 mg twice a day was made; if gastrointestinal side-effects or symptomatic orthostatic hypotension re-occurred, despite modification of ropinirole dosing, domperidone 20 mg twice daily was added (in 2 patients, for the remaining trial period. If interdose dyskinesias increased in the oscillating patients levodopa was concomitantly reduced. After each dose in the study, a standing pulse and blood pressure were made at baseline and then hourly for the following four hours.

Motor assessments were carried out on the day of dose increase before and two hours after dosing, using the Modified Webster scale\(^6\) and tapping and walking tests.\(^7\)

Assessments of motor fluctuations were carried out using self-scoring diaries to record a percentage daily "on" time and severity of dyskinesias.

Of the previously untreated patients two showed improvement comparable with that seen with oral levodopa at doses of 12 mg and 6 mg a day respectively. The first patient had a Webster score which reduced from 14 to 10, a 44% increase in the number of finger taps and a 40% decrease in walking time. The second patient had an increase in numbers of finger taps, but could not increase the dose further because of nausea despite domperidone. Two of the de novo patients dropped out before the treatment period was finished, one because of operations of lying and syncope at 4 mg daily and one following symptomatic orthostatic hypotension after a single dose of 1 mg. Three patients had no response to the drug at daily doses of 10, 12 and 14 mg respectively. However, two of these patients subsequently failed to respond to apomorphine or chronic levodopa treatment raising the possibility of a diagnosis other than idiopathic Parkinson's disease.

Four of the seven patients with levodopa-induced on-off oscillations showed a worthwhile clinical response with a reduction of mean "off" hours per day from 3.9 (1.9-6.5) to 1.3 (0.4-2.0) 6 mg of dose needed to obtain an optimal response was 5.8 mg per day (3.2-8.2 mg), but beneficial effects began at 2.3 mg daily (1.2-4.0). The duration and intensity of interdose dyskinesias increased in three patients, but diminished to even below basal level by a mean reduction of 15% of the total daily levodopa dose in two patients. Two patients treated with up to 10 mg a day in addition to a dose of oral levodopa did not improve. In one, the mean "off" hours remained unaffected, while the other experienced prolonged episodes of disabling biphasic dyskinesias. One patient developed intolerable drowsiness and somnolence at 2 mg a day and discontinued the study and two had nausea and symptomatic orthostatic hypotension controlled by domperidone. Laboratory test results and routine bloods remained normal throughout the eight week period.

We conclude that ropinirole has anti-Parkinsonian effect and that the optimum dose range for most patients may be 4-8 mg a day. Adverse reactions were dose dependent and with other dopamine receptor agonists and can be reduced by the use of domperidone and possibly more gradual dose increments than occurred in this trial. We would recommend in future that oral levodopa and subcutaneous apomorphine tests are carried out on previously untreated patients with Parkinson's syndrome before the treatment of a new dopaminergic agonist, to exclude as far as possible patients with multi-system degeneration unresponsive to this group of drugs.

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Cardiovascular autonomic function tests are three Valsalva and six deep breaths necessary or will singles do?

In the assessment of autonomic neuropathy, two widely used tests of cardiovascular autonomic function assess the heart rate response to three consecutive Valsalva manoeuvres and to six consecutive deep breaths.\(^1\) We aimed to see whether the response to a single Valsalva manoeuvre was significantly different from that averaged from the average of three and whether the response to a single deep breath was significantly different from that from the average of six deep breaths.

The study involved 231 diabetic patients, 25 male and 11 female, 15 insulin treated, mean age 54 years (range 30-82), mean duration of diabetes 17 years (range 3 months-51 years). All had symptoms which may have been due to diabetic neuropathy.

They underwent heart rate monitoring using a computer-assisted system for the collection and analysis of heart rate data for cardiovascular autonomic function tests (RR Medical Electronics, Leeds, UK). A Valsalva manoeuvre was performed by the patient blowing into the tube of a sphygmomanometer and sustaining a pressure of 40 mm Hg for 15 seconds while the R-R interval was recorded, the result being expressed as the Valsalva ratio: the longest R-R interval during the 45 seconds after the manoeuvre divided by the shortest R-R interval during the manoeuvre. All the patients performed the manoeuvre properly and, as far as could be ascertained, achieved an intrathoracic pressure which was adequately raised. Heart rate variability during the manoeuvre was calculated by the patient resting quietly and breathing deeply in over five seconds and


