Weight loss in people with Alzheimer's disease: a prospective population based analysis.

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Weight loss in people with Alzheimer's disease: a prospective population based analysis.

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Comments
Article starts on page 8 of full text.

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Retrospective study of concussive convulsions in elite Australian rules and rugby league footballers: phenomenology, aetiology, and outcome

Paul R McCrory, Peter F Bladin, Samuel F Berkovic

Abstract

Objectives: To study the ictal phenomenology, aetiology, and outcome of convulsions occurring within seconds of impact in violent collision sport.

Design: Retrospective identification of convulsions associated with concussive brain injury from case records from medical officers of football clubs over a 15 year period.

Subjects: Elite Australian rules and rugby league footballers.

Main outcome measures: Neuroimaging studies, electroencephalography, neuropsychological test data, and statistics on performance in matches to determine presence of structural or functional brain injury. Clinical follow up and electroencephalography for evidence of epilepsy.

Results: Twenty two cases of concussive convulsions were identified with four events documented on television videotape. Convulsions began within 2 seconds of impact and comprised an initial period of tonic stiffening followed by myoclonic jerks of all limbs lasting up to 150 seconds. Some asymmetry in the convulsive manifestations was common, and recovery of consciousness was rapid. No structural or permanent brain injury was present on clinical assessment, neuropsychological testing, or neuroimaging studies. All players returned to elite competition within two weeks of the incident. Epilepsy did not develop in any player over a mean (range) follow up of 3.5 (1-13) years.

Conclusions: These concussive or impact convulsions are probably a non-epileptic phenomenon, somewhat akin to convulsive syncope. The mechanism may be a transient traumatic functional decerebration. In concussive convulsions the outcome is universally good, antiepileptic treatment is not indicated, and prolonged absence from sport is unwarranted.

Methods

We retrospectively identified convulsions associated with concussive brain injury from case records of all club medical officers in elite Australian rules football competition over a 15 year period. The league is a national football competition, and in the 15 year period about 200 000 player games occurred. Twenty episodes of concussive convulsions were identified, and all cases were followed up. This probably represents total ascertainment of cases because of the dramatic nature of the episodes concerned. We also included two additional cases of concussive convulsions that occurred in elite rugby league football during the time frame of the study.

In all 22 cases eyewitness accounts of the episodes were obtained from medical officers. In four of the 22 cases, television videotape of sufficient quality was available for detailed analysis of the event. These cases allowed the detailed ictal phenomenology of the convulsive episodes to be determined.

The routine management after concussion in Australian rules football entails clinical and brief neuropsychological assessment. This assessment includes questions of memory, orientation, digit symbol substitution test (from the Wechsler adult intelligence scale), and choice reaction time. These...
measures have been found to be sensitive markers of mild traumatic brain injury in football.\textsuperscript{5-7} The concussed player's results are then compared with his preseason baseline assessment. Seventeen players were followed up in the period after injury by serial clinical and neuropsychological testing. Functional measures of performance from match statistics were recorded before and after injury. These were available for all 22 Australian football cases. The mean number of ball possessions per quarter was calculated over four games before and after injury. Match statistics from an equal number of randomly selected controls matched for age were used for comparison. The control data were derived from a prospective database of football statistics recorded for ongoing research in head injury related to football.\textsuperscript{6,89}

All players in the study were followed up clinically. In all cases, neuroimaging data and the original electroencephalographic records were sought from the treating neurologists and neurosurgeons.

Results

The 22 identified episodes occurred in footballers aged 19-30 years (mean 23.4 years).

Case report—A 24 year old footballer was struck on the left side of the face by an opponent's elbow during a collision (fig 1 (left)). As he fell towards the ground loss of consciousness was apparent, and he developed tonic arm posturing with both clenched fists in a “bear hug” position (fig 1 (centre)). His legs were extended and his head and eyes were turned to the right. After 20 seconds of tonic posturing, a series of generalised symmetrical myoclonic jerks occurred for 30 seconds (fig 1 (right)). His loss of consciousness was 2 minutes, and he had 45 minutes of post-traumatic amnesia. Results of subsequent neurological examination, electroencephalography, and cerebral magnetic resonance imaging studies were normal. He returned to football the following week without further effects and has continued his football career for a further six years without problem.

Ictal phenomenology

Table 1 shows separate analyses of all 22 eyewitness accounts and of the four videotaped cases. Typically, after a violent collision the player lost consciousness and started convulsive movements within 2 seconds of impact. The mean (range) time to onset in the video cases was 0.75 seconds (range 0.2-2.0 seconds). The convolution usually entailed a brief tonic phase followed by bilateral myoclonic jerking. Asymmetrical posturing and versive head movements were seen in all video cases but recalled less often (31\%) by the eyewitness accounts. The episodes ceased spontaneously within 150 seconds, and the players woke with behavioural and neuropsychological features indistinguishable from mild concussion.

Of particular interest were two footballers who were alert and orientated within seconds of the termination of the convulsive event. Both cases were documented on videotape. The first of these was an Australian rules footballer whose convulsive event lasted 150 seconds; he then woke up on the stretcher as he was being carried off the ground. The second was a rugby league player in an international test match who sustained an event in the opening minute of the game. After recovery he returned to the field and performed sufficiently well to be voted “man of the match.” In both cases, clinical and neuropsychological assessment after injury yielded normal results, and both players returned to sport the following week without problem.

The mechanism of injury, as determined by the site of impact, was a direct facial blow in all four videotaped cases. Eyewitness reports in the 18 other cases suggested that around half were facial blows, a quarter were occipital, and the remainder were uncertain.

Investigations

All players had either computed tomographic (10 cases) or magnetic resonance (12 cases) brain imaging, which yielded normal results. Twenty one players

Table 1  Details of ictal phenomenology in football players

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Eyewitness (n=22)</th>
<th>Videotanalysis (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (range) onset latency (sec)</td>
<td>Immediate in all</td>
<td>0.75 (0-2)</td>
</tr>
<tr>
<td>Mean (range) duration (sec)</td>
<td>40 (10-150)</td>
<td>78 (30-150)</td>
</tr>
<tr>
<td>No (%) with:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial tonic posturing</td>
<td>6 (28)</td>
<td>3 (75)</td>
</tr>
<tr>
<td>Myoclonic jerks</td>
<td>20 (90)</td>
<td>4 (100)</td>
</tr>
<tr>
<td>Bilateral involvement</td>
<td>17 (79)</td>
<td>4 (100)</td>
</tr>
<tr>
<td>Lateralising features</td>
<td>7 (31)</td>
<td>4 (100)</td>
</tr>
</tbody>
</table>
Concussive convulsions described here in violent collision sport are an uncommon but dramatic association with minor head injury that have been recognised since the time of Gowers.11 12 Our video study showed that these concussive convulsions occurred within 2 s of impact. Moreover, they were not associated with structural brain injury or with ongoing epilepsy or epileptiform electroencephalographic abnormalities and had a universally good outcome. Thus they are unlikely to be epileptic in nature, and other pathophysiological mechanisms need to be explored.

From a phenomenological standpoint, concussive convulsions have more in common with convulsive syncope than with post-traumatic epilepsy. Convulsive syncope is a non-epileptic phenomenon thought to reflect a loss of cortical inhibition coupled with reflex brainstem activation.13 14 Clinical and videoelectroencephalographic analyses have demonstrated a spectrum of convulsive movements ranging from focal myoclonic jerks in mild cases to generalised tonic-clonic events that resemble true epileptic seizures.15 16 In many cases, lateralising features are prominent. The episodes are usually brief, typically lasting for only a few seconds, and occur after a delay of less than 10 seconds. Unlike convulsive syncope, concussive convulsions can last up to 150 seconds and start with a latency of 2.0 seconds or less, making a reflex cerebral ischaemic basis unlikely. Another hypothesis, and the one we favour, is that the concussive impact itself creates a transient functional decerebration akin to the corticomедullary dissociation described above.

In the players suffering concussive convulsions, the universally good outcome and absence of structural injury or long term neuropsychological damage reflects the benign nature of these episodes. From a management standpoint, late seizures do not occur, antiepileptic treatment is not indicated, and prohibition from collision sport is unwarranted. If an episode follows the profile outlined above the treating clinician can reassure the patient that concussive convulsions are benign, and overall management should centre on the appropriate treatment of the concussive injury itself.

We thank Channel 7 Melbourne for provision of TV videotape; the members of the Australian Football League Medical Officers Association; Drs David Maddocks, John B.
Popularity of less frequent follow up for breast cancer in randomised study: initial findings from the hotline study

Tim Gulliford, Magi Opomu, Elena Wilson, Iain Hanham, Richard Epstein

Abstract

Objective: To compare the experiences of patients with breast cancer who were conventionally monitored with those in whom routine follow up was restricted to the time of mammography.

Design: Randomisation to conventional schedule of clinic visits or to visits only after mammography. Both cohorts received identical mammography and were invited to telephone for immediate appointments if they detected symptoms.

Setting: Combined breast clinic, Chelsea and Westminster Hospital.

Subjects: 211 eligible outpatients with a history of breast cancer.

Main outcome measures: Acceptability of randomisation, interim use of telephone and general practitioner, satisfaction with allocation to follow up.

Results: Of 211 eligible patients, 196 (93%) opted for randomisation.

Conclusions: Reducing the frequency of routine follow up has so far proved popular among patients with breast cancer at standard risk in this cohort.

Effectiveness and cost-effectiveness of routine follow up with respect to disease outcomes.

Introduction

Most patients who relapse after treatment for primary breast cancer do so within the first five years of follow up. As curable intramammary relapses are more sensitively detected by mammography than by clinical examination, regular mammography after lumpectomy has now become accepted practice in most centres. Asymptomatic detection of disseminated disease is also achievable by using routine radiological or serologic testing, or both, but objective benefit from this approach has not been shown. Indeed, the only undisputed effect of intensive monitoring is that of diminished relapse free survival. It is therefore not surprising that many retrospective studies have cast doubts on the effectiveness of routine non-mammographic investigations or clinical follow up, or both, for breast cancer. Despite these doubts routine follow up continues to be the norm, with many physicians assuming that patients are reassured by frequent contact with their oncologist. This view is not universal, however, as evidenced by wide disparities in follow up practice on both sides of the Atlantic, dis- parities that have been attributed to defensive perceptions by physicians unsure as to the efficacy of treatment and monitoring.

In this pilot study we compared the experience of a cohort who received conventional follow up with that of a similar cohort in whom review, in the
absence of symptoms, was restricted to the time of mammography.

Patients and methods

Participants—All eligible patients seen at the Chelsea and Westminster combined breast clinic over a 24 month period were offered randomisation. Eligibility criteria were a history of breast cancer proved by biopsy; lack of known recurrence of cancer; current lack of symptoms consistent with recurrence; no active management apart from adjuvant tamoxifen; home telephone; fluency in English; and informed consent. Details of disease stage for patients who declined participation were recorded anonymously to provide an internal control for recruitment bias. Primary treatment and staging details were obtained from information in medical records, the Charing Cross CTS computer system, correspondence with patients, and archives. Median follow up for the present analysis was 16 months.

Follow up and mammography scheduling—Table 1 presents the schedule for visits. No restrictions were placed on attendance at other hospital or local clinics.

Table 1 Scheduling of clinic visits

<table>
<thead>
<tr>
<th>Interval since diagnosis (years)</th>
<th>Conventional</th>
<th>Lumpectomy</th>
<th>Mastectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 3 months</td>
<td>1 year</td>
<td>1 year</td>
<td></td>
</tr>
<tr>
<td>1-2 4 months</td>
<td>1 year</td>
<td>2 years</td>
<td></td>
</tr>
<tr>
<td>2-5 6 months</td>
<td>1 year</td>
<td>2 years</td>
<td>2 years</td>
</tr>
<tr>
<td>&gt;5 1 year</td>
<td>2 years</td>
<td>2 years</td>
<td>2 years</td>
</tr>
</tbody>
</table>

Table 2 Characteristics of patients in each randomisation group. Figures are numbers (percentages) of patients

<table>
<thead>
<tr>
<th>Age at diagnosis (years):</th>
<th>Conventional</th>
<th>Mammogram only</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of subjects*</td>
<td>96</td>
<td>97</td>
</tr>
<tr>
<td>≤49</td>
<td>27 (28)</td>
<td>29 (30)</td>
</tr>
<tr>
<td>50-65</td>
<td>47 (49)</td>
<td>49 (51)</td>
</tr>
<tr>
<td>&gt;65</td>
<td>22 (23)</td>
<td>19 (20)</td>
</tr>
</tbody>
</table>

| Surgery:                  |              |               |
| No of subjects*           | 85           | 90            |
| Lumpectomy                | 61 (72)      | 58 (64)       |
| Mastectomy                | 24 (28)      | 32 (36)       |

| Adjuvant treatments:      |              |               |
| Irradiation after lumpectomy | 56 (89)   | 52 (84)       |
| Tamoxifen                 | 67 (50)      | 72 (57)       |

| Tumour stage:             |              |               |
| No of subjects*           | 63           | 64            |
| T1 (<2 cm)                | 36 (57)      | 33 (52)       |
| T2 (>2 cm)                | 22 (35)      | 26 (40)       |
| T3/4                      | 5 (8)        | 5 (8)         |

| Nodal stage:              |              |               |
| No of subjects*           | 74           | 82            |
| N0                        | 24 (32)      | 28 (34)       |
| N1                        | 34 (46)      | 33 (45)       |

| Years since diagnosis:    |              |               |
| No of subjects*           | 95           | 96            |
| ≤2                       | 18 (19)      | 18 (19)       |
| 2-5                      | 17 (18)      | 23 (24)       |
| >5                       | 60 (63)      | 56 (57)       |

| Numbers of subjects differ because of inability to confirm precise information—for example, date of diagnosis, date of birth, etc. |

Patients older than 70 years and for whom over five years had passed since diagnosis were not routinely scheduled for mammography but continued outpatient review according to the same schedule shown in table 1. All patients were advised to examine their breasts each month and to request an immediate appointment if they felt a lump or developed any other symptom.

Telephone access and questionnaires—All patients were instructed to telephone immediately if they developed symptoms or had other concerns; in these circumstances an appointment to be seen within five working days was made. Records were kept concerning the content of all telephone calls from patients in the study. Questionnaires based on the Medical Research Council quality of life questionnaire were used and included additional questions relating to frequency of follow up in hospital and general practice, satisfaction with clinic visits, and the time and expense entailed in clinic attendance; these were sent to patients annually, beginning six months after study entry.

Protocol violation and termination—Documentation of progression of disease or second malignancy automatically terminated participation in the study (10 patients) as did any decision after randomisation by any patient to pursue an alternative schedule of appointments or mammograms to that specified in the protocol (three patients).
### Results

**Patterns of patient recruitment—Age distribution, duration since diagnosis, and primary disease stage** did not differ substantially between the cohorts (table 2). Fifteen eligible patients (7%) declined participation; this group was distinguished by a trend towards a higher stage of primary disease, younger age, and more recent diagnosis; other parameters were not appreciably different (table 3). We consider that the minor degree of selection bias suggested here does not confound the broad conclusions of this study.

**Interval events**

Telephone calls and visits to general practitioners—Twenty one telephone calls from patients without symptoms were received during this phase of the study: 11 in the conventional arm and eight in the mammogram only arm. Of note, eight of the 11 calls in the conventional arm related to queries about clinic appointments compared with only one such query in the mammogram only arm (table 4). Hence, the potential problems of a heavy workload of telephone counselling in the mammogram only cohort have so far failed to materialise, consistent with the experience of other clinical groups who have successfully used telephone advice lines. Forty six visits to general practitioners were recorded in the conventional cohort compared with 53 in the mammogram only group. Seven (15%) visits in the former group, however, were related to cancer problems compared with only four (7.5%) in the latter (table 4). Although these numbers are small, this finding suggests that less frequent specialist follow up of patients without symptoms may not necessarily translate into a heavier burden of care for local practitioners.

Response to clinic visits—A similar majority of respondents in both cohorts thought that their clinic visit was reassuring, perhaps more so than similar follow up with their general practitioner alone (table 5). This is consistent with the findings of similar studies, though some have suggested community follow up to be equally popular. Similar proportions of patients in both arms admitted a preference for either more or less frequent follow up visits, though in absolute terms more than twice as many favoured the latter (table 5).

Time and expense entailed in clinic visits—With respect to the inconvenience of attending the clinic as assessed by questionnaire, no substantial differences were apparent between the two groups. A minimum of four hours from door to door was required for clinic attendance in 73 patients (median three hours); 37 needed to take time off work and 80 were accompanied by another person (a quarter of whom needed to take time off work). No personal costs in attending clinics were incurred by 67, while 49 of the remainder incurred costs in excess of £10 and eight more than £50.

### Discussion

The present study is limited by its size and duration and does not justify publication of immature data concerning recurrence and quality of life. A study of survival outcomes would require several thousand patients and many years of follow up to establish the relative incidence of uncontrolled local recurrence, particularly late stage recurrence within the breast. The early phase of such a study would also need to focus on the possibility of more local or distant recurrences, or both, being detected in the “conventional” group, thus implying a shorter lead time (and, perhaps, more effective local treatment). Interim analysis of the present results indicates that no such trend has yet emerged; indeed, of the recurrences documented to date, all have been detected at interval (as opposed to scheduled) visits. We acknowledge, however, that these unpublished observations fall short of establishing the safety of less frequent follow up.

What does seem clear from the present study is that this cohort of patients with breast cancer was highly supportive of the option to pursue less frequent follow up and seemed willing to assume responsibility for seeking medical attention in the event of symptoms. These findings are consistent with those of other groups. Moreover, the data reveal surprisingly little hesitancy from subgroups one might have expected to be reluctant—that is, the young, the recently diagnosed, and those with more aggressive primary disease—withstanding that this profile was somewhat over-represented among the patients who did not participate.

The potential benefits of less intensive monitoring are clear. Clinicians are able to rationalise their practices and thus improve the efficiency of patient care; anxiety and inconvenience for patients without symptoms is minimised; outpatient clinic waiting time

## Table 5  Patients’ responses to clinic visits and desired future frequency. Figures are numbers (percentages) of patients

<table>
<thead>
<tr>
<th>Feeling about clinic visits</th>
<th>Conventional</th>
<th>Mammogram only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychological effect:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reassuring</td>
<td>73 (94)</td>
<td>69 (88)</td>
</tr>
<tr>
<td>Wish to continue with hospital based follow up rather than with general practitioner alone</td>
<td>74 (94)</td>
<td>70 (89)</td>
</tr>
<tr>
<td>Future visit schedule:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prefer more frequent</td>
<td>7 (11)</td>
<td>10 (16)</td>
</tr>
<tr>
<td>Prefer less frequent</td>
<td>17 (23)</td>
<td>22 (35)</td>
</tr>
</tbody>
</table>

## Table 6  Response of funding agencies to requests for study support

<table>
<thead>
<tr>
<th>Funding body approached</th>
<th>Application verdict</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHS</td>
<td>Worthy study, but more appropriately funded by local audit fund</td>
</tr>
<tr>
<td>Local audit fund</td>
<td>Worthy study, but more appropriately funded by extramural Research Funding Body</td>
</tr>
<tr>
<td>Extramural Research Funding Body</td>
<td>Worthy study, but more appropriately funded by NHS</td>
</tr>
</tbody>
</table>
Funding: TG is supported by the Medical Research Council and RE by the Cancer Research Campaign.

Conflict of interest: None.

Key messages

- Although it is standard practice to advocate routine long term follow up of patients with breast cancer, the effectiveness of non-mammographic follow up has not been assessed in randomised trials
- A key concern that has delayed the implementation of such trials is whether patients would find symptom driven follow up psychologically acceptable
- In this study most patients agreed to undergo randomisation to less frequent follow up, though all continued with routine mammographic review
- After randomisation more patients expressed a desire to reduce further, rather than increase, the frequency of follow up
- Patients undergoing less frequent review did not increase their use of general practitioner or telephone (hotline) services

is reduced, increasing evaluation time for sick patients; nursing and reception staff are able to provide higher quality outpatient service by having fewer arrivals and room changes to deal with; the efficiency of general practitioner referral to hospital specialists improves; and healthcare purchasers reap the rewards of greater cost-effectiveness. Given this potentially attractive harvest, financial support for this pilot study was been surprisingly hard to find (table 6). None the less, we submit that these preliminary findings establish both the feasibility and desirability of a larger and more randomised study.

We thank E Woods for assistance with randomisation, C Coombes for support, and our patients for their kind and spirited cooperation.

Opening my mind

I was a young consultant gynaecologist in 1975 when I saw a 25 year old woman with large venereal warts. I advised ablating them with cryoacautery, but she was not happy with this advice, as she wanted to avoid surgery as far as possible. She went away and when she came back after six weeks I found to my surprise that the warts had disappeared. I asked her if she had had the surgery done elsewhere, but she told me that they had “melted away” after she had taken a homoeopathic medicine called Thuja.

This was my first introduction to homoeopathy and I was impressed by how well it had worked for her. As a doctor trained in Western medicine I was sceptical about alternative medicine, but I kept an open mind and bought all the textbooks on homoeopathy that I could find to learn more about this system of treatment. Since I could find quite amusing and hard to decipher as well, I also had to start thinking of doses in terms of the potencies rather than in terms of milligrams.

I suspended my initial disbelief and decided to try homoeopathy. Much to my surprise, it often worked, and this was a valuable learning experience for me. I may not subscribe to the “small is better” philosophy of homoeopathy, and neither do I pretend to understand why it works. But the fact that it sometimes does in indisputable. As a clinician I am happy to use whatever works for my patients, and the system of medicine that I use is unimportant. Historically, especially in the West, there has been a conflict between allopathic medicine and other systems but this was a political struggle for the “power to practise medicine.” Today, we should look for a balanced middle ground.

I agree that we need to be sceptical, especially when unsubstantiated claims are made for alternative medicine’s ability to cure all ills from AIDS to cancer. But there is the danger of throwing out the baby with the bathwater, and we must learn to keep an open mind. This will allow us to serve our patients better. I still use homoeopathy, especially when Western medicine does not have a better alternative to offer. Thanks to this experience I am now able to offer my patients treatment which works for them—“integrated medicine”—and the best of all possible worlds.

Chandrakala Malpani is a consultant gynaecologist in Bombay.

We welcome filler articles of up to 600 words on topics such as A memorable patient, A paper that changed my practice, My most unfortunate mistake, or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk.
Weight loss among older people, often due to conditions such as cancer and heart disease, has been associated with increased risks of disability and mortality. Alzheimer’s disease may be a more important source of weight loss than previously recognised, and we examined this issue in a community sample of older adults from a population based, longitudinal study.

Subjects, methods, and results

We collected data during five annual structured clinical evaluations of subjects from a stratified random sample of the population aged 65 years and older of East Boston, Massachusetts, a geographically defined community. We measured weight and height, with participants wearing light clothing, without shoes. Body mass index (weight (kg)/height (m)^2) was used to standardise weight for height. Of the 467 clinical evaluation subjects, 338 survived and underwent follow up assessments and 280 (83%) had two or more weight measurements. We diagnosed Alzheimer’s disease on the basis of structured neurological examination, neuropsychological performance testing, brief psychiatric evaluation, medical history, and review of drug treatment. We used computerised Medicare hospital discharge records to identify cancer, heart disease, and treatment. We used models to examine the relation between Alzheimer’s disease and weight loss.

Figure 1 (top) presents a plot of the mean body mass indices of the subjects with Alzheimer’s disease and those without, at the five annual assessment points. The figure overestimates the effects of the disease because people with the disease tend to be older. After adjustment for both age and sex, the body mass index in subjects without Alzheimer’s disease decreased by an average of 0.14 a year, compared with 0.52 a year in similar subjects with probable Alzheimer’s disease, a difference of 0.38 (P < 0.01). A trend in weight loss both in clinical teaching and in several studies of special groups, but the contribution of specific conditions to weight loss has not been examined carefully in population data. Several features of this study strengthen confidence in its results, including the longitudinal population based design, adequate sample size, and uniform diagnostic criteria for Alzheimer’s disease. Missing data may have led to an underestimate of the relation between Alzheimer’s disease and weight loss because the 187 of 467 participants with missing weights were generally older, thinner, and more likely to have Alzheimer’s disease.

Comment

Alzheimer’s disease is recognised as responsible for weight loss both in clinical teaching and in several studies of special groups, but the contribution of specific conditions to weight loss has not been examined carefully in population data. Several features of this study strengthen confidence in its results, including the longitudinal population based design, adequate sample size, and uniform diagnostic criteria for Alzheimer’s disease. Missing data may have led to an underestimate of the relation between Alzheimer’s disease and weight loss because the 187 of 467 participants with missing weights were generally older, thinner, and more likely to have Alzheimer’s disease.

The mechanisms linking Alzheimer’s disease and weight loss are uncertain, but in this study many people with Alzheimer’s disease had mild disease, and the magnitude of weight loss in this group did not support the idea that weight loss in Alzheimer’s disease is con-
fined to those with severe disease. This differs from the clinical perspective that weight loss occurs with advanced disease and suggests that behavioural problems—such as agitation and pacing—typically associated with more advanced disease, do not fully explain weight loss. Pathological changes in the hypothalamus have been described in Alzheimer’s disease, and this pathology may affect centres regulating food intake and metabolic processes.

We thank the residents of East Boston and the staff of the East Boston Neighborhood Health Center for their cooperation and support. This project was presented in part at the annual meeting of the Society for Epidemiologic Research, June 1995.

Funding: This work was supported in part by National Institute on Aging (grant AG-10161 and contracts N01-AG-12106 and N01-AG-02107) and the National Institute of Mental Health (award K07-MH-00953).

Conflict of interest: None.


(Accepted 2 October 1996)

Prevalence of hepatitis C antibodies among healthcare workers of two teaching hospitals. Who is at risk?

Keith R Neal, John Dornan, Will L Irving

Epidemiological evidence suggests that healthcare workers are at an increased risk of hepatitis C infection, and episodes of hepatitis C infection after needlestick incidents and transmission of the virus in hospitals in developed countries have also been reported. Studies of prevalence in healthcare workers so far published have neither supported nor repudiated the increased risk suggested by the epidemiological evidence. With increasing concern about the risks of transmission of viruses such as hepatitis and HIV between patients and healthcare workers, it is important that the real risk, if any, is measured. We report the results of a study to measure the prevalence of hepatitis C antibodies in healthcare workers whose hepatitis B status was being assessed.

Patients, methods, and results

Blood samples taken from Nottingham hospital staff for measuring hepatitis B surface antibody levels from January 1994 to October 1995 were identified from the virology computer and matched to data from the occupational health database by record linkage using surname, first name, date of birth, and date of blood test. The database included main occupational group, age, sex, and place and type of work. A unique study number was attached to the combined data set and all identifying features were removed. Microsoft Access 2.0 was used as the database and for record linkage and ssrs for Windows for the statistical analyses.

A total of 1949 samples were retrieved and placed into tubes with only the unique study number for identification. Hepatitis C antibody testing was performed using a second generation ELISA (enzyme linked immunosorbent assay, UBI) according to the manufacturer’s instructions. All samples showing reactivity in this assay were then tested using a third generation ELISA (Ortho). Four samples positive in both ELISAs were identified from 1949 samples, a rate of 2.05 per 1000 (95% confidence interval 0.55 to 5.2; table 1) The number of positive results was too small for subgroup analysis.

Comment

Our results show that the prevalence of hepatitis C antibodies in healthcare workers is low. The use of blood samples from staff who had already been identified as most at risk of infection by a blood borne virus emphasises this low risk; many of the staff we included in this study had been vaccinated as part of the original targeted hepatitis B vaccine programme and had had blood taken for hepatitis B surface antibody titres before their booster.

A case-control study of local blood donors showed a rate of hepatitis C infection of 1 in 1350 (0.7 per

Table 1 Staff groups, by age and sex, of health care workers tested (number positive) for hepatitis C antibodies

<table>
<thead>
<tr>
<th>Staff group</th>
<th>Age&lt; 25</th>
<th>Age 25-44</th>
<th>Age &gt; 45</th>
<th>All age groups</th>
<th>Total (both sexes)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Women</td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>Medical</td>
<td>33</td>
<td>26</td>
<td>77 (1)</td>
<td>175</td>
<td>11</td>
</tr>
<tr>
<td>Nursing</td>
<td>297</td>
<td>15</td>
<td>503 (1)</td>
<td>57</td>
<td>127</td>
</tr>
<tr>
<td>Allied professions*</td>
<td>52</td>
<td>23</td>
<td>145 (55)</td>
<td>55</td>
<td>19</td>
</tr>
<tr>
<td>Others†</td>
<td>28</td>
<td>17</td>
<td>68 (20)</td>
<td>20 (1)</td>
<td>76</td>
</tr>
<tr>
<td>Total</td>
<td>410</td>
<td>96</td>
<td>793 (2)</td>
<td>307 (1)</td>
<td>233</td>
</tr>
</tbody>
</table>

* Includes ambulance crews, laboratory workers, physiotherapists, radiographers, and theatre staff.
† Includes domestics and porters.
Severe persistent visual field constriction associated with vigabatrin

T Eke, J F Talbot, M C Lawden

We report three cases of severe, symptomatic, persistent constriction of the visual fields associated with vigabatrin treatment.

Case reports

Case 1—A 22 year old woman with longstanding complex partial epilepsy started taking vigabatrin 2000 mg/day in addition to carbamazepine 600 mg/day and sodium valproate 1400 mg/day. Thirty seven months later she complained of tunnel vision and was found to have normal acuity but severely constricted visual fields in both eyes (fig 1 (top)). Her optic discs were slightly pale, and the peripheral retina seemed somewhat atrophic. Magnetic resonance imaging showed left hippocampal atrophy. Blood tests, including mitochondrial DNA screen and measurement of phytic acid and lysosomal enzyme concentrations, gave normal results. Cone and rod electroretinography showed normal latency and amplitudes for a and b waves. Photopic and scotopic visual evoked responses were normal. Fluorescein fundus angiography gave normal results, and magnetic resonance imaging showed hippocampal asymmetry. After 38 months she noticed that she was bumping into objects, although her central vision remained normal. Visual symptoms and fields remained stable since presentation.

Case 2—A 44 year old man with longstanding temporal lobe epilepsy had vigabatrin 4000 mg/day added to a regimen of phenytoin 400 mg/day and sodium valproate 3000 mg/day. Twenty eight months later he noticed constriction of his visual fields. Detailed assessment showed normal acuity with appreciable contraction of the peripheral fields, particularly nasally (fig 1 (centre)). Ocular and neurological examinations gave normal results, and magnetic resonance scanning showed hippocampal asymmetry. Blood test results, as for case 1, were normal. Vigabatrin treatment was discontinued 36 months later after temporal lobectomy. Four years after presentation the optic discs were slightly pale. Fluorescein fundus angiography showed nothing unusual. Electro-oculography showed a low to abnormally low Arden index (185%). Electroretinography showed normal latency and amplitudes for a and b waves, but oscillatory potentials were not assessed. Visual evoked responses were normal to both pattern reversal and flash stimuli. Visual symptoms and fields remained stable since presentation.

Case 3—A 46 year old woman with longstanding complex partial epilepsy started taking vigabatrin 3500 mg/day in addition to carbamazepine 600 mg/day. After 38 months she noticed that she was bumping into objects, although her central vision remained normal. Visual fields were concentrically constricted in both eyes (fig 1 (bottom)), but funduscopy and fluorescein angiography gave normal results. Electroretinography showed reduced oscillatory potentials; electrodiagnostic test results were otherwise normal. Magnetic resonance imaging of the brain showed no abnormality. Vigabatrin was stopped, but the fields failed to improve.

Comment

These three cases have the common feature of symptomatic constriction of the visual field two to three years after starting vigabatrin treatment. Though visual complaints such as diplopia have occasionally been reported with vigabatrin use,1 visual field impair-
ment has rarely been noted. One reported case of uni-
lateral visual field constriction was ascribed to an
immune mediated anterior ischaemic optic
neuropathy. A literature search found brief details of
one other case of bilateral field constriction apparently
induced by vigabatrin. By January 1997 nine cases of
visual field defects had been reported to the
Committee on Safety of Medicines (Medicines Control
Agency, adverse drug reactions online information
tracking service), including our three cases. The manu-
facturers of vigabatrin had received 28 reports of visual
field abnormalities worldwide by January 1997 in an
estimated 140 000 patients treated (Hoechst Marion
Roussel, personal communication).

Vigabatrin causes microvacuolation in myelin
sheaths in the white matter of rats, mice, and dogs but
not in monkeys or humans. However, the low Arden
index and reduced oscillatory potentials in our cases
suggest that the outer retina rather than the optic nerve
is damaged. In albino but not pigmented rats vigabatrin
has a dose dependent effect on the outer retina, charac-
terised histologically by disruption of the outer
nuclear layer. The significance of this finding to our own
observations is unclear. A prospective evaluation of
visual fields in asymptomatic patients taking vigabatrin
is in progress, and we have identified several other
abnormalities, which will be reported in due course.

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Conflict of interest: None.

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3 Faedda MT, Giallonardo AT, Marchetti A, Manfredi M. Terapia con viga-atrin nelle epilessie parziali resistenti. G Nervenarzführmedicat


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the central nervous system and retina of Sprague Dawley and

(Accepted 29 November 1996)

MISTAKES AVOIDED
On life and death certificates

From my corner of the cramped outpatient consulting room I could
see that the crowd in the waiting room was thinning out. The clinic
had been particularly hectic. One colleague was doing a caesarean
section. Another was on vacation in neighbouring Namibia. It was a
blessing that the nurses could manage most of the minor cases.

I pressed on with the next case—a patient with Parkinson’s disease
who was nearly frozen because the country had run out of the drug
he needed. Out of the corner of my eye I noticed one of the nurses
standing in the doorway cradling an emaciated and limp child in her
arms. I could tell that she wanted my attention, yet she was not in any
hurry. Nobody hurries here—except me when I first arrived. There was
a familiar looking form dangling from her hand—a death certificate. I
hesitated, then looked at the child. Pale, shrivelled, lifeless—probably a
baby. Out of the corner of my eye I noticed one of the nurses
hesitated, then looked at the child. Pale, shrivelled, lifeless—probably a
baby. Out of the corner of my eye I noticed one of the nurses

I glanced at the nurse. “What’s up?”

In deference to the four other patients in the room waiting their
turn to see me she gave the familiar, almost imperceptible, Shona nod
and mouthed her reply: “Dead.”

Only wanting my signature, she gave the form a gentle wave. I
beckoned her over, took the form, and poised the pen to sign. I
hesitated, then looked at the child. Pale, shrivelled, lifeless—probably a
combination of malnutrition, tuberculosis, and AIDS. I returned to the
signing position with four pairs of eyes examining every move. The
advice of an acquaintance from long ago momentarily came to me:
“The only good doctor is a thorough doctor.”

I put the pen down. Reaching over the frozen man, I took the
child from the nurse. A brief but close inspection followed. Lifeless,
severely dehydrated, malnourished, but—await—a flicker of movement
and, yes, the child was breathing.

Several weeks later a mother was ushered into the consulting
room carrying a fairly healthy looking little boy of around 2 years of
age. At first I could not tell why he was there. The writing on his card
looked familiar: “Child brought in ‘dead’ for certification. Resuscitated
with intravenous fluids and admitted for high calorie milk and high
protein diet.”

This has been my only fond memory of death certificates.

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