Reversible dementia in elderly patients referred to a memory clinic

Walstra, G.J.M.; Teunisse, S.; van Gool, W.A.; van Crevel, H.

Publication date
1997

Published in
Journal of neurology

Citation for published version (APA):

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Download date: 26 Mar 2024
Reversible dementia in elderly patients referred to a memory clinic

Abstract Dementia has a reversible cause in some cases, and these should be diagnosed without over-investigating the many patients with irreversible disease. We prospectively studied the prevalence of reversible dementia in a memory clinic, determined the added value of investigations compared with clinical examination and assessed the outcome of treatment of potentially reversible causes by measuring (1) cognition, (2) disability in daily functioning, (3) behavioural changes and (4) caregiver burden. Two hundred patients aged 65 years and over were examined, using the CAMDEX-N. If they were demented, the probable cause was diagnosed clinically and confirmed or excluded by a standard set of investigations, which were done in all patients. Of the patients, 170 (mean age 79.2 years) were demented; 31 were treated for potentially reversible causes. At follow-up after 6 months, no patients showed complete reversal of dementia. Five patients improved on clinical impression, but only one on clinical measurement. Thirty patients were cognitively impaired, but not demented; seven were treated. Judged clinically, three patients improved, but on assessment only one did so; she recovered completely. Blood tests often produced diagnostic results that were not expected clinically, but electroencephalography and computed tomography of the brain did not. None of the investigations had an effect on outcome of dementia after treatment. We conclude that in elderly patients referred to a memory clinic, the prevalence of reversible dementia is of the order of 1%, if outcome after treatment is assessed by a standardized measurement. We recommend blood tests in all patients, to detect not only metabolic causes of dementia but also co-morbidity possibly worsening the dementia. Other investigations can be performed on clinical indication. Clinical evaluation remains the mainstay of diagnosis in dementia.

Key words Dementia · Computed tomography · Electroencephalography · Blood tests
times with harmful consequences. Selective investigation may lead to under-diagnosis of reversible causes and mis-

Select several factors are important in resolving this dilemma. First, the prevalence of reversible dementia must be

knowledge, these have not previously been applied to assess reversibility of dementia.

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Patients and methods

Patients

Inclusion criteria were: (1) referral for suspected dementia by gen-

Clinical examination

Two neurologists used a standardized examination based on the

Investigations

All demented patients, regardless of clinical diagnosis and indica-

Treatment and outcome assessment

Potentially reversible causes of dementia (including depression, following the Dutch Consensus) were treated, asking specialist consultation if required, and advising general practitioners in the other cases. Assuming that secondary prevention of brain infarcts may slow down progression of vascular (components of demen-

2 , B 12 , folate, thyroid stimulating hormone (TSH), Venereal Disease Research Laboratory (VDRL) test and treponemal haemagglutina-
tion assay (TPHA), and urinalysis. In addition, a chest radiograph, electrocardiogram (ECG), electroencephalogram (EEG) and CT of the brain (without contrast enhancement) were performed. Further investigations could be ordered if appropriate. After the results of all investigations were known, a final diagnosis was made according to DSM-III-R criteria [2]. The added value of investigations for diagnosis was established by comparing the clinical with the fi-
nal diagnosis. Non-demented patients were investigated as seemed proper on an individual basis.

Dementia score 4 or less [15], standard neurological examination normal for age, and no clinical indications for other disease(s) that may cause dementia. Patients with isolated neurological signs without consequences for the differential diagnosis were classified as “PDD almost certain”. MIX was included in the differential di-

ory disturbance as initial symptom, duration of more than 6 months, Hachinski score 4 or less [15], standard neurological examination normal for age, and no clinical indications for other disease(s) that may cause dementia. Patients with isolated neurological signs without consequences for the differential diagnosis were classified as “PDD almost certain”. MIX was included in the differential di-

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neuropsychologist or her assistants, who did not know the diagnosis and treatment. Partial or total reversal of dementia was then ascertained per patient. In this way, the added value of investigations for treatment and outcome after 6 months was established.

The study protocol, including informed consent from patients and caregivers, was approved by the institutional medical ethics committee.

Analysis

To analyse reversibility of dementia, several variables were examined, for all nine (sub)scales:

1. Size of change-scores in individual patients: based on the literature [19] and a test-retest study at our memory clinic, we computed the standard measurement error and its 68% and 95% confidence intervals (CI) of each subscale [20]; positive change-scores exceeding the 68% CI were considered as a trend to improvement, and those exceeding the 95% CI as real improvement in functioning (see Table 2: criterion for real change in individual case).

2. Pattern of individual change-scores: real improvement on at least two subscales in the absence of (a trend toward) deterioration on other subscales was considered as (partial or total) reversibility.

3. Mean change-scores on all subscales in the group of patients treated for a potentially reversible cause of dementia.

Results

Patients

Two hundred consecutively referred patients entered the study. Of these, 170 met DSM-III-R criteria for dementia. Their mean age was 79.2 years (SD 6.3); 68 were men and 102 women. The severity of dementia according to CAMDEX-N was: 7 minimal, 140 mild, 23 moderate, 0 severe. Mean duration of symptoms was 24 months (2–190).

Clinical diagnosis

PDD was the most frequent diagnosis (Table 1). Vascular (component of) dementia was also diagnosed frequently (Table 1). The panel discussions did not result in major changes of diagnosis or indications for investigations.

Diagnosis after investigations

Complete investigations were performed in 169 demented patients (one patient with PDD refused). PDD of the Alzheimer type, now according to DSM-III-R criteria, remained the most frequent diagnosis (Table 1). There was no significant difference between the two neurologists regarding the percentage of patients with this diagnosis in whom CT was considered to be indicated. The same comparison was made between the first and last 50 patients of the neurologist who examined most patients; again, no significant difference was found.

Treatment and outcome

Twenty-six patients had serum vitamin B₁₂ levels below 200 pg/l. Two could not be treated; 24 were given cobalamin replacement; two of these died before follow-up. Two patients were treated for hyperthyroidism, one for hypothyroidism and four for depression. Two patients had small tumours with CT characteristics of meningiomas (one parasellar, one parasagittal) but these were regarded as incidental and no surgery was performed. For vascular (components of) dementia, in 16 patients treatment with aspirin and (or) anti-hypertensives was advised; in two others, a small intracerebral haematoma was found and aspirin (given before referral) was stopped. Potentially re-

<table>
<thead>
<tr>
<th>Diagnosis or differential diagnosis before AI</th>
<th>Diagnosis after AI according to DSM-III-R</th>
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<tbody>
<tr>
<td>PDD certain</td>
<td>Dementia not otherwise specified, MIX and multi-infarct dementia</td>
</tr>
<tr>
<td>PDD almost certain</td>
<td>Vitamin B₁₂ deficiency (5)</td>
</tr>
<tr>
<td>PDD/other</td>
<td>Vitamin B₁₂ deficiency (12)</td>
</tr>
<tr>
<td>PDD/MIX</td>
<td>Vitamin B₁₂ deficiency (5), hypothyroidism (1), hyperthyroidism (1), vascular factor (3), vascular factor/vitamin B₁₂ deficiency/alcohol (1), Parkinson’s disease (1), diffuse Lewy body disease (1), dementia pugilistica (1), depression/epilepsy (1)</td>
</tr>
<tr>
<td>PDD/MIX/other</td>
<td>MIX (7)</td>
</tr>
<tr>
<td>MID/MIX</td>
<td>MIX (2), MIX/hypothyroidism (1), MIX/vitamin B₁₂ deficiency (1), intracerebral haematoma (1), vitamin B₁₂ deficiency (1)</td>
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<tr>
<td>MID/MIX/other</td>
<td>MIX (2), MID (1)</td>
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<td>MIX (2), intracerebral haematoma (1), vitamin B₁₂ deficiency (1)</td>
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*Ancillary investigations were performed in 58 patients
versible non-vascular causes of dementia were therefore found in 33 patients (19%, 95% CI 14–25%); 31 of these patients were treated (Table 1, italic). Apart from potential causes of dementia, secondary pathology and non-cognitive disturbances were treated (sometimes several factors in one patient). All patients with treatable causes were seen at follow-up except the two with low vitamin B₁₂ levels who died (see above). In the group without treatable causes, eight patients died and three were lost to follow-up.

Complete reversal of dementia was seen in none of the 169 demented patients subjected to investigations. On clinical impression, partly based on patient’s functioning during the follow-up visit, five patients improved after treatment of a potentially reversible cause. Measured assessment did not confirm this. When size and pattern of individual change-scores were taken into account, consistent improvement (on 5 and 6 subscales, respectively) was seen in only two patients. As improvement in one of these might reflect recovery from a respiratory infection, it could be attributed to treatment in only one patient (woman, 66 years, treated for dementia complicated by depression and epilepsy; consistent improvement on five subscales, related to disability, behavioural changes, and burden to the caregiver). At group level, assessment showed no reversibility (Table 2); functioning of patients and caregivers at follow-up was comparable with or worse than at baseline on all subscales. When change-scores of patients treated with cobalamin were compared with those of (untreated) patients with Alzheimer’s disease, no clear indications were found of slowing of progression in treated patients [27]. Treatment of secondary pathology (e.g. cardiac failure) and non-cognitive disturbances (e.g. hallucinations) was often effective in itself, but had no effect on the severity of dementia; this will be reported in detail elsewhere.

A survey among the participating general practitioners revealed that during the study period they had also referred patients to other specialists for pragmatic reasons such as travel distance, but no reversible dementia had been detected. Others had not been referred because of poor condition or refusal by patients or caregivers.

Added value of investigations

Clinical prediction of results of blood tests proved unreliable, both for potential causes of dementia (vitamin B₁₂, TSH, VDRL/TPHA) and for secondary pathology. Chest radiography and ECG, useful for secondary pathology, never contributed to diagnosis or treatment when not indicated clinically. EEG was thought to be indicated in only 12 cases, for example in the patient mentioned above. Four categories of indications for CT could be distinguished: (1) suspicion of a neurosurgical cause of dementia in 33 patients (normal pressure hydrocephalus, cerebro tumour, subdural haematoma); (2) clinical diagnosis of vascular dementia in 29 patients; (3) suspicion of other anatomical lesions and Hachinski score of 4 or less in seven patients; (4) isolated neurological signs that could not be explained in 17 patients. In the last group CT never influenced diagnosis or management. If considered not indicated, neither EEG nor CT ever had an effect on diagnosis or treatment. Overall, none of the investigations had an effect on outcome of dementia.

Non-demented patients

Thirty patients were cognitively impaired without meeting all DSM-III-R criteria for dementia. Seven were treated: one completely recovered (woman, aged 94, with severe depression) and two improved as judged clinically (one on vitamin B₁₂, who also stopped drinking alcohol; another after antidepressive treatment), but not on assessment.

Discussion

We found a very low prevalence of reversible dementia – 0.6% (95% CI 0–3%) – in this series of patients referred to a memory clinic. A recent quantitative review demonstrated that, although the prevalence of reversible demen-
ties in 16 patient series reported between 1972 and 1994 was about 11% on average, it has fallen to about 1% in the four most recent series [30]. This decrease was associated with the change from inpatient to outpatient setting and with the use of stricter diagnostic methods [30]. Both conditions apply to our study.

Measured assessment of treatment effects has not previously been employed in studies of reversible dementia [30]. Such formal measurement, rather than subjective clinical judgement, is usual nowadays in drug trials for Alzheimer’s disease. In our study, five patients improved as judged clinically, but only one (partially) on assessment. This more rigorous evaluation has contributed to the pretest probability of treatment. This was often the case for blood tests, but not for chest radiographs, ECGs, EEGs and CT. In the same way, the investigations cannot replace it. Together with personal and social evaluation, it is the basis for symptomatic treatment, practical management and counselling, which should be offered to all patients with dementia, including the vast majority with irreversible conditions [23].

We think our findings have implications for diagnostic management of elderly outpatients with dementia. First, the very low prevalence of reversible dementia – see also [30] – means that the pretest probability of finding actually reversible conditions by routine investigations is very low. False positive results are more likely. Second, routine blood tests seem warranted, as possible metabolic causes of dementia are often not diagnosed clinically. Though treatment of these was disappointing in our study, it may be effective in some cases. Moreover, routine blood tests can detect secondary pathology, which can often be alleviated [18]. However, the question whether blood tests should be performed routinely – and if so, which tests – merits further study. Third, major investigations, such as CT of the brain, can be performed selectively, based on the clinical picture. If vascular dementia is clinically possible and secondary prevention is deemed worthwhile, CT is also appropriate. However, if investigations are targeted at reversible causes of dementia, routine CT does not seem warranted by our findings. Emphatically, our message is not that patients with dementia need not be investigated.

Potentially reversible causes should be looked for with the same diligence in patients with cognitive impairment not meeting DSM-III-R criteria for dementia as in demented patients. Cognitively impaired, but not demented patients tend to have the best prognosis [11]. This is supported by our findings: in 30 non-demented patients one completely recovered after treatment versus none in 170 demented patients. This group of patients may explain part of the higher prevalence of completely reversible “dementia” in older studies.

Painstaking clinical evaluation [7], including a history from a reliable informant, mental status testing and routine application of diagnostic criteria, is the mainstay of diagnosis in dementia. It is time-consuming, but investigations cannot replace it. Together with personal and social evaluation, it is the basis for symptomatic treatment, practical management and counselling, which should be offered to all patients with dementia, including the vast majority with irreversible conditions [23].

Acknowledgements. We thank the Dementia work group in the Academic Medical Centre for critical comments and Professor J.D.F. Habbema and the Centre for Clinical Decision Sciences of the Erasmus University in Rotterdam for cooperation. This study was supported by grant OG 90-027 of the National Committee on Investigative Medicine of the Health Insurance Executive Board of the Netherlands.

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