Prevalence of probable idiopathic normal pressure hydrocephalus in a Norwegian population

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Objective – The clinical condition normal pressure hydrocephalus (NPH) is one of the few conditions with dementia that can be successfully treated. Even though NPH was described more than 40 years ago, information on prevalence and incidence of this disease is scarce. The objective of this study was to obtain information about prevalence of iNPH in a Norwegian population. Methods – In a stable population of 220,000 inhabitants, structured and intensive efforts were directed towards the public via local newspapers, radio and television channels, and directed towards the healthcare professionals via personal letters and lectures, to recruit patients with idiopathic NPH (iNPH) investigation during a 12-month period. This population is served by only one neurological department and one neurosurgical department, thus avoiding any leakage of patients during the investigation period. We determined those patients fulfilling the diagnostic criteria of probable iNPH. Results – Eighty-six patients were referred, of whom 48 patients fulfilled the diagnostic criteria of probable iNPH. This equals a minimum prevalence of iNPH in our population of 21.9/100,000. Most importantly, the prevalence was increasing with age. When excluding patients who had symptoms for more than 1 year, we found an incidence of 5.5/100,000/year. Conclusions – In this Norwegian population of 220,000 inhabitants, we found a prevalence of probable iNPH of 21.9/100,000 and an incidence of 5.5/100,000. The numbers should be regarded as minimum estimates.

Introduction

Normal pressure hydrocephalus (NPH) was first described in 1965 (1) as a clinical triad of gait disturbance, mental deterioration and urinary incontinence, combined with enlarged cerebral ventricles and a normal lumbar cerebrospinal fluid (CSF) pressure. While the cause of idiopathic NPH (iNPH) is unknown, secondary NPH can be caused by conditions such as intracranial haemorrhage, meningitis or trauma (2). There is still controversy on the pathophysiology of iNPH and on assessment of these patients, although consensus exists that the clinical symptoms can effectively be treated by insertion of a shunt draining CSF (3). This condition thus remains one of the few treatable dementias. A recent progress was the publication of evidence-based guidelines for the diagnosis and treatment of iNPH, recommending classification of suspected iNPH patients into the categories probable, possible and unlikely iNPH (4). Nevertheless, little is known about the prevalence and incidence of iNPH.

The present study was conducted to provide information on the prevalence and incidence of iNPH in a Norwegian population of 220,000 inhabitants. Various efforts were made to recruit as many patients with iNPH as possible. A
structured approach for identifying available studies on the prevalence of iNPH was performed.

Materials and methods

Study population

The Norwegian county of Vestfold is a geographically small county of 220,000 inhabitants. This county is served by only one neurological department that admits patients to a single neurosurgical department (Department of Neurosurgery, The National Hospital, Oslo). There is no leakage of patients to other neurological or neurosurgical department.

The study was approved by the regional human research committee (15 January 2004), as well as the Norwegian social science data services (26 November 2003). All patients gave their written informed consent before the start of the study, except for those patients who were found not capable of giving informed consent, in which case the written informed consent was given by their proxies. The study was performed according to the Declaration of Helsinki.

Study protocol

Patient recruitment – Patients were included during a 12-month period, starting from 31 January 2004. We recruited patients on a low-threshold basis to include as many patients as possible, using the present approach.

(a) Information letters, lectures. From December 2003, we actively and systematically issued information about iNPH to all the county’s general practitioners, municipal dementia care teams, geriatric and general hospital wards, day care centres for the elderly as well as nursing homes. The information was given by information letters, and lectures about the condition at selected sites. We included information about the project, asking for referral of any patient, irrespective of age, meeting the following wide criteria: a history of at least 3 months of gradually increasing gait and balance problems with concomitant subjective impairment in cognition and/or urinary symptoms.

(b) Media. At the same time, we aimed to inform the public by cooperating with local newspapers and local radio and television channels, which wrote articles, respectively, broadcasted programs about iNPH, and about the project. During the subsequent months, we achieved major articles about iNPH in the biggest local newspapers, as well as entries in local radio shows and news broadcasts, and emissions about iNPH in the county’s only local television channel.

Clinical assessment – All patients were referred to the neurological outpatient clinic by their doctors, and underwent clinical assessment by one neurologist (AB). In all patients, the clinical history was taken, and the length and presence of symptoms were corroborated by members of the patient’s family or relevant healthcare workers. Previous medical history was noted, with special emphasis on conditions predisposing for secondary hydrocephalus, as well as co-morbid conditions disposing for problems with gait/balance, cognition and urinary continence. A detailed neurological examination was performed. With respect to gait and balance, this included a simple standardized walking test, measuring time in seconds and number of steps during a 10-m walk, as well as evaluation of walking and standing balance, and the presence of spontaneous or provoked retropulsion. Those fulfilling the following wide clinical criteria were included in the study: a history of at least 3 months, not entirely attributable to other conditions, of gradually increasing disturbance in gait and balance with concomitant urinary incontinence or urgency and/or subjective cognitive impairment as experienced by patient and/or family.

Neuropsychology – Patients meeting the clinical criteria were examined with the following standardized neuropsychological test battery: Mini Mental Status Examination (MMSE), Dementia Rating Scale (DRS), Stroop Color Word Interference Test and California Verbal Learning Test, Short Form (CVLT-SF).

Radiology – Radiological assessment of ventricular enlargement was performed with cerebral computed tomography (CT) or magnetic resonance image (MRI) scanning. The presence of ventricular enlargement was assessed by calculating the Evan’s index (5) in the following way: maximum bifrontal distance and maximum inner diameter of the skull was measured in millimetres at the same level in transverse views of the brain, and the maximum bifrontal distance was divided by the maximum inner diameter of the skull. The shape and size of the ventricular system was subjectively evaluated, as well as the presence of macroscopic obstruction of CSF flow, and the presence of periventricular signal changes.

Lumbar puncture – The lumbar puncture was performed in the supine position in level L3/L4 using a 19-G needle, and the opening pressure was
measured using the Truwave PX-600F Pressure Monitoring Set (Edwards Lifesciences, Irvine, CA, USA). Lumbar tap test was not performed, as there is no tradition for this procedure in our departments.

Classification – The iNPH patients were retrospectively classified into the categories probable, possible and unlikely iNPH, using the recently published Guidelines for the diagnosis and management of iNPH (4). The diagnostic criteria fulfilled by our patients with probable and/or possible iNPH are detailed in Table 1.

Follow-up – On the basis of the data collected, we treated some of the included patients with a ventriculo-peritoneal (VP) shunt, and followed the patients for 12 subsequent months. These results will be reported later, and are not the subject of this paper.

Statistics
We calculated the prevalence and incidence rates with the use of population figures for Vestfold and Norway from Statistics Norway’s StatBank (6).

Systematic literature review
We searched MEDLINE for papers published in English between 1966 and February 2007 with the term ‘normal pressure hydrocephalus’, combined with the terms ‘epidemiology’, ‘prevalence’ and ‘incidence’. We also searched EMBASE from 1980 to week 11 of 2007 with the subject heading ‘normotensive hydrocephalus’ and the subheading ‘epidemiology’. The references of relevant studies (7–10) were examined for additional relevant studies.

Results
Study population
The mean figures of Vestfold county’s population does not differ significantly from that of the Norwegian with respect to percentage of elderly persons, number of hospital beds, number of nursing home beds, expectation of lifetime, man-years for physicians, median gross income and expectation of life (6) (Table 2).

Patient recruitment and categorization
During the 12-month period, 31 January 2004 to 30 January 2005, a total of 86 patients were admitted (44 women, 42 men, mean age 73.5 years). Five were not included in the study (one was wrongly admitted, four rejected participation).

Of the resulting 81 patients, nine had no urinary or cognitive symptoms, and eight had other conditions entirely explaining the symptoms (two of these had vascular dementia, one patient had Parkinson’s disease, two patients were multimorbid with advanced cardiovascular disease, and spontaneously recovered from intercurrent gait problems between the time of admission and inclusion, two patients had an established Alzheimer’s disease and one patient had stable symptoms from bilateral coxarthrosis). Thus, 64 patients met the clinical inclusion criteria. In one patient, lumbar puncture was not technically possible, and 63 underwent neuropsychological and radiological assessment and lumbar puncture (Table 3).

Prevalence and incidence of probable and possible iNPH
The county of Vestfold had 219,478 inhabitants as of January 2004 (6).

Probable iNPH – Of the 64 patients meeting the clinical inclusion criteria, 48 patients (25 men and 23 women) fulfilled the diagnostic criteria of probable iNPH (Table 3). This equals a prevalence of probable iNPH in our study population of 21.9/100,000. Twelve of the 48 had had their symptoms for 12 months or less at the time of inclusion, making the incidence 5.5/100,000/year in the study population (Table 4).

Possible iNPH – All 63 patients fulfilled the diagnostic criteria of possible iNPH. This equals a prevalence of possible iNPH in our study population of 28.7/100,000. Sixteen of the 63 had had their symptoms for 12 months or less at the time of inclusion, making the incidence 7.3/100,000/year (Table 4).

Clinical inclusion criteria – Sixty-four patients fulfilled our original clinical inclusion criteria, making the prevalence 29.2/100,000 and the incidence 7.3/100,000 when using these criteria alone. An intriguing observation is that the prevalence of iNPH in our material was highly dependent on age (Table 4).

Systematic literature review
We found a total of four original studies exploring the prevalence and incidence of NPH. These studies are summarized in Table 5.
Prevalence of idiopathic normal pressure hydrocephalus

Table 1  Summary of diagnostic criteria for ‘probable iNPH’ and ‘possible iNPH’ according to the iNPH guidelines (4)

Probable iNPH

1 History
   a. Insidious onset
   b. Origin after age 40 years
   c. Minimum duration of 3–6 months
   d. No evidence of antecedent known causes of secondary hydrocephalus Progression over time
   e. No other conditions that are sufficient to explain the presenting symptoms

2 Brain imaging (CT or MRI)
   a. Ventricular enlargement not attributable to cerebral atrophy or congenital enlargement (Evan’s index >0.3 or comparable measure)
   b. No macroscopic obstruction to CSF flow
   c. At least one of the following:
      i. Enlargement of the temporal horns of the lateral ventricles not entirely attributable to hippocampus atrophy
      ii. Callosal angle of 40 degrees or more
      iii. Evidence of altered brain water content
      iv. Aqueductal or fourth ventricular flow void on MRI

3 Clinical
   Findings of gait/balance disturbance must be present, plus at least one other area of impairment in cognition, urinary symptoms, or both Gait/balance: At least two of the following, not entirely attributable to other conditions:
   d. Decreased step height
   e. Decreased step length
   f. Decreased cadence (speed of walking)
   g. Increased trunk sway during walking
   h. Widened standing base
   i. Toes turned outward on walking
   j. Retropulsion (spontaneous or provoked)
   k. En bloc turning (turning requiring three or more steps for 180 degrees)
   l. Impaired walking balance

Cognition: Documented age and educational adjusted impairment and/or decrease in performance on a cognitive screening instrument, or at least two of the following, not entirely attributable to other conditions:
   a. Psychomotor slowing
   b. Decreased fine motor speed
   c. Decreased fine motor accuracy
   d. Difficulty dividing or maintaining attention
   e. Impaired recall, especially for recent events
   f. Executive dysfunction
   g. Behavioural or personality changes

Urinary symptoms: Either one of the following:
   a. Episodic or persistent urinary incontinence
   b. Persistent urinary incontinence
   c. Urinary and faecal incontinence
   Or any two of the following:
   a. Urinary urgency (frequent perception of pressing need to void)
   b. Urinary frequency (more than six voiding episodes in an average 12-h period despite normal fluid intake)
   c. Nocturia (need to urinate more than two times in an average night)

4 Physiological
   CSF opening pressure in the range of 5–18 mm Hg as determined by a lumbar puncture or a comparable procedure

Table 1 (Continued)

Possible iNPH

1 History
   Reported symptoms may
   a. Have a subacute or indeterminate mode of onset
   b. Begin at any age after childhood
   c. Have less than 3 months or indeterminate duration
   d. Follow events such as mild head trauma, etc. that in the judgement of the clinician are not likely to be causally related
   e. Coexist with other disorders but not be entirely attributable to these
   f. Be non-progressive or not clearly progressive

2 Brain imaging
   Ventricular enlargement consistent with hydrocephalus but associated with any of
   a. Evidence of cerebral atrophy
   b. Structural lesions that may influence ventricular size

3 Clinical
   Symptoms of either
   a. Incontinence and/or cognitive impairment in the absence of an observable gait or balance disturbance
   b. Gait disturbance or dementia alone

4 Physiological
   Opening pressure measurement not available or pressure outside the range required for probable iNPH

Table 2  The Vestfold County compared with Norway (mean figures as per 2005) (6)

| Parameter | Vestfold | Norway |
|-----------|----------|--------|
| Percentage of population >67 years | 13.98 | 13.11 |
| Percentage of population >80 years | 4.86 | 4.63 |
| Hospital beds per 1000 inhabitants | 3.8 | 3.6 |
| Nursing home beds per 1000 inhabitants >80 years | 132.5 | 160.6 |
| Life expectancy when alive at age 65 (men/women) | 16.5/20.0 | 16.6/20.1 |
| Man-years for physicians per 1000 inhabitants | 0.91 | 0.82 |
| Median gross income for residents >16 years (Euro) | 27,450 | 28,187 |

Table 3  Number of patients fulfilling the diagnostic criteria of probable iNPH

| Criterion | Number of patients (n = 81) |
|-----------|----------------------------|
| History | 61 |
| Brain imaging | 50 |
| Clinical | 81 |
| Gait/balance | 60 |
| Urinary symptoms | 54 |
| Cognition | 59 |
| Physiological | 48 |
| All criteria | 48 |

Table 4  Prevalence of probable and possible iNPH

| Prevalence | Incidence |
|------------|-----------|
| Probable iNPH | |
| All individuals >65 years | 117.9/100,000 (41) |
| 50–59 years | 3.3/100,000 (1) |
| 60–69 years | 49.3/100,000 (10) |
| 70–79 years | 181.7/100,000 (27) |
| ≥80 years | 92.3/100,000 (16) |
| Total | 21.3/100,000 (48) |
| Possible iNPH | |
| Total | 28.7/100,000 |

Discussion

The fact that there is only one neurological department and one neurosurgical department serving the Vestfold County makes it highly possible that there has been no leakage of patients...
to other hospitals. The Vestfold County does not differ from the rest of Norway on a few major parameters (Table 2). Norway is ethnically relatively homogenous, and the geographical mobility in Norway is quite high, reflected by the fact that although all our included patients were registered as inhabitants of Vestfold County, many of them originated from other parts of Norway. We therefore believe that our figures can be extrapolated to the whole of Norway. As the cause of iNPH is unknown, both genetic and environmental aspects might be involved. We therefore believe that extrapolating the figures to populations in other parts of the world must be performed with care.

Most of the studies in this field originate from neurosurgical materials. By contrast, this study is population based, accepting patients on wide inclusion criteria directly from homes and nursing homes. Furthermore, the syndrome of iNPH is generally not well known to the general public, and because problems with gait, urinary continence and cognition are abundant in the elderly, few think of NPH as a probable cause in the individual elderly person. There is therefore reason to believe that the prevalence of the syndrome generally is underestimated. Our media-based recruitment strategy might have made this problem less important, and may contribute to explaining why our prevalence estimates are higher than most of those previously reported.

We took a systematic approach to define the total population, but identified the cases from this population from referrals obtained from others. Our methodology differs from a strict population-based methodology as the total population was not examined systematically. Moreover, there is an inherent referral bias in the subjects identified. This places limitations upon the interpretations of the results. However, to systematically examine such a large population for iNPH poses major practical and ethical difficulties, and would probably not be feasible.

We applied very wide inclusion criteria, nevertheless only 86 of nearly 220,000 inhabitants were admitted. This was somehow surprising, given the fact that problems with gait, urinary continence and cognition are abundant in the elderly. This might have several explanations, one being that we asked for referral of individuals with ‘gradually increasing’ difficulties, thus a priori excluding individuals with relatively stable symptoms, which probably constitutes the majority of patients. Another explanation might be that we did not sufficiently succeed in informing the public and/or healthcare workers about the project. The fact that the majority of the referred patients (64 of 86) fulfilled our clinical criteria, however, indicates that most of those who referred patients to our project had well understood our information.

There were patients in our population who had previously been operated on for suspected NPH. When collecting data from the National Hospital concerning all patients from the Vestfold County who underwent surgery for iNPH during the previous 10 years, we found 18 patients. Ten of these were still alive at the end of the follow-up period of the patients in this study. We have not had sufficient data on these patients to tell whether they preoperatively fulfilled the criteria for probable iNPH. These patients are therefore not included in the study. There is an obvious discrepancy between the average of 1.8 patients shunted per year during the previous 10 years, and the incidence rate in our study of 12 per year in the same population. This might indicate that iNPH is under-diagnosed in our population; on the other hand, it is important to bear in mind that our incidence rate only relates to patients fulfilling the diagnostic criteria of ‘probable iNPH’, and not to the rate of successfully shunted patients. No study has so far investigated the relation between these diagnostic criteria and response to shunting.

A challenge concerning epidemiological studies of iNPH has been the lack of universally accepted diagnostic criteria. This is illustrated by the very diverse diagnostic criteria in the studies already published (Table 5). It has been proposed that the only reliable means of validating the diagnosis of iNPH is to demonstrate a favourable response to shunt treatment (11). However, this poses a problem when trying to estimate the occurrence of the condition itself. Patients lacking a favourable shunt response because of co-morbid conditions (e.g. Alzheimer’s disease and cerebrovascular disease)
can be overlooked (false negatives), and the amount of false positives because of placebo response after a shunt placement cannot be estimated reliably. The recently published ‘Guidelines for the diagnosis and management of iNPH’ tries to overcome these problems by recommending classification of iNPH into the categories probable, possible and unlikely iNPH (4). The present study was completed before the publication of the guidelines, but as patients were included on a wide basis and detailed clinical data were collected, it was possible to retrospectively categorize the patients into the categories probable and possible iNPH. It may be that knowledge of the diagnostic criteria in the guidelines before the preparation of our study protocol would have yielded different inclusion criteria, and hence different results. For instance, as the guidelines specifically states ventriculomegaly as a prerequisite for the diagnosis of probable iNPH, it might be that we would have included brain imaging as mandatory before accepting referrals to the study, thus making the threshold for referral higher and the number of referred patients lower. No studies have yet tested the usefulness of these diagnostic criteria in predicting response to shunt treatment. Our estimations of prevalence and incidence of iNPH therefore only relates to the occurrence of patients fulfilling these diagnostic categories, and the occurrence of potentially shunt responsive iNPH is not a subject of this paper.

It was previously reported that iNPH usually presents in the sixth and seventh decades (12). In our study, the prevalence was highest in the eighth decade, with more than half of the patients entering the study between 70 and 79 years of age. This might be partly due to our recruitment strategy, asking for referral of patients ‘irrespective of age’. It might therefore be that we have recruited patients that normally would not be admitted to neurosurgical treatment because of their age.

In our systematic literature review, we found very few original studies exploring the prevalence and incidence of NPH (Table 5). The huge variations in the estimates for prevalence and incidence in these studies probably reflect varying diagnostic criteria, ranging from Vale and Miranda’s lack of definition of NPH (8) to Vanneste et al.’s strict classification according to response to shunt treatment (7). This illustrates the need for more uniform diagnostic definitions in this field of study, and therefore the importance of the recently published guidelines (4). It also illustrates the need for further epidemiological studies both related to the epidemiology of the condition by itself, and to the response to shunt treatment.

Taken together, using an approach of recruiting as many patients with NPH as possible from a Norwegian population of 220,000 inhabitants, we found a prevalence of probable iNPH of 21.9/100,000 and an incidence of 5.5/100,000. As the study design is not population based according to strict criteria, the numbers should be regarded as minimum estimates.

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