IDIOPATHIC INTRACRANIAL HYPERTENSION

ASSESSMENT OF VISUAL FUNCTION

AND

PROGNOSIS FOR VISUAL OUTCOME

Doctor of Philosophy thesis

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Abstract

Idiopathic intracranial hypertension (IIH) is an uncommon condition where loss of vision is the predominant morbid factor. The primary objectives of this research have been to study the population aspects of the disease, to make original observations on associated ocular motility abnormalities, to present new data on visual field survival in a cohort of patients followed prospectively and to present data on the clinical outcomes on the same cohort of patients. This constitutes the first in-depth and largest prospective study of visual function and epidemiology for the condition of IIH in the UK.

Thirty-four patients have been followed over a four year period with comprehensive documentation of presentation, associated factors and conditions, assessment of visual function, ocular motility and neurological status. Risk factors for poor visual outcome have been determined for the patients in this study.

The incidence figures for occurrence of IIH exist only for the USA and Libya. Only hospital based recruitment figures exist for UK studies and one of the objectives of this research has been to provide original epidemiological data for IIH in a defined UK population. The incidence of IIH in this UK population has been calculated as 0.70 per 100,000 persons and 1.38 for females. An age standardised adjustment to the national UK population provides an estimated incidence of 0.71 per 100,000 for the overall population and 1.39 for females. The incidence rates were also adjusted for the population of obese individuals and rose significantly to 12.25 per 100,000 for adult females with a body mass index of 30 or more. The diagnosis of a number of asymptomatic cases raised concerns regarding incidence calculations generally with lack of complete ascertainment of cases.

This is the first study to prospectively assess overweight and obesity in a population of IIH. Obesity has been confirmed as a common association with this condition and has been identified as having a high relative risk factor in this study particularly those with a body mass index of 40 or more. Analysis of serial weight measurements demonstrate no correlation between weight change and visual outcome. When reviewing the aetiology of this condition, the association of obesity should be taken into consideration as this may play a role in the disruption of the cerebrospinal fluid absorption mechanism and development of cerebral oedema.

Ocular motility disturbances have not been assessed in a prospective study and this study aims to cast light on the types of ocular motility disturbances that occur in association with the condition and those that are directly caused by the raised intracranial pressure. Ocular motility assessment was normal in 23 patients. Eleven patients, however, had an ocular motility defect and

not all were due to the classic non localising sixth cranial nerve palsy associated with raised intracranial pressure. Two patients had long-standing strabismus, two had transient ocular motility restrictions following optic nerve sheath fenestration procedures, one developed a secondary exotropia following visual loss and optic atrophy, and six patients had acquired cranial nerve palsies including third and sixth nerves. The level of intracranial pressure was not significantly associated with the development of acquired ocular motility disorders.

The prognosis for visual outcome is generally good with a favourable outcome achieved in most cases (82%). A significant improvement was found from initial to last assessment of visual function and the pattern of improvement was also significant over the period of follow up. It was noted that patients treated surgically responded more quickly, with improvement in visual status, than those patients treated medically. However, there was no difference in the final outcome or level of visual function between these two treatment groups.

Serious loss of visual function occurs in a minority of cases and appears to relate to poor visual function prior to presentation, a high degree of obesity and features of long-standing optic nerve pathology including optic atrophy. However, in general, patients who are appropriately evaluated at regular intervals and those who are treated promptly and effectively have a favourable outcome.

The recommendation for visual assessment in this study includes documentation of visual acuity, visual field assessment with automated or Goldmann perimetry with sensitive testing strategies, full Orthoptic investigation as indicated and fundus examination, and close liaison with the neurology and neurosurgery departments. The use of this regime enabled the detection of insidious and asymptomatic visual loss and therefore was of considerable prognostic value. The Humphrey 24-2 programme and a new testing strategy for Goldmann perimetry were employed for the first time in this prospective study as was the Pelli-Robson contrast sensitivity assessment. Visual field assessments using the above methods were identified as suitable and reliable testing techniques.

This thesis, in addition to the clinical study, provides a review of the literature relating to papilloedema and IIH, and the pathogenesis of visual loss in IIH. Observations are made regarding the clinical data of this study and the proposed mechanisms involved in the condition and its associated visual dysfunction.

Conclusions

The aim of this research was to prospectively assess visual performance in IIH. The objectives were to study the epidemiology of the condition, to determine the prevalence of ocular motility abnormalities in the condition, to present new data on visual field survival and clinical outcomes in a cohort of patients followed prospectively. The study commenced in May 1993 and thirty-four patients were examined.

9.1   The incidence figures for IIH have been calculated in American and Libyan populations. Two studies in the USA give an annual incidence for the condition as 0.9 per 100,000 for the total population. This rises to 1.6 to 3.5 per 100,000 for females and 3.3 to 3.5 per 100,000 for an age adjusted female population. In Libya, the total population incidence is 2.2 per 100,000 rising to 4.3 for females and 12 per 100,000 for an age adjusted female population. The paediatric incidence is also similar to that of the adult general population.

This study is the first to calculate the incidence of this condition using adjusted census records for a regional population in the UK. The incidence was calculated as 0.70 for the total population rising to 1.38 for females. The rate for an age adjusted female population was 2.85 per 100,000. The incidence rates for this study and for the American and Libyan studies were age adjusted to the UK population for further comparison. The rates for the USA and this study were comparable. The rates from the Libyan study were higher and may reflect the different population sample and prevalence of obesity in the Libyan population.

This research has confirmed a relationship between obesity and IIH. Obesity has been determined to be a high risk factor associated with this condition. 94% of patients in this study were overweight including 70.5% obese. The risk of IIH was significantly greater for obese adults than for the non-obese. Morbid obesity (BMI>40) was significantly associated with poor visual outcome. Serial obesity measures showed generally little change in weight over time and there was no correlation between weight change and visual status. Obesity may be an aetiological factor in this condition although it is unlikely to be the sole cause but more probably a precipitating factor. Weight loss is recommended although failure to lose weight is common. Any weight reduction programme must therefore be actively encouraged and monitored.

9.2   The investigation of ocular motility disturbances has not been previously documented prospectively in IIH. This study assessed the ocular motility balance of all patients with IIH and 32% of cases were found to have a disturbance in ocular movement. Two patients had long-standing strabismus which should not be unexpected when reviewing a sample population group. Long-

standing strabismus should not be confused with acquired defects of ocular motility of which nine cases were documented.

Two cases had restricted ocular movements following optic nerve sheath fenestration procedures. The only reference to such restrictive ocular motility in the literature is to the effect that this is a transient problem. These cases were also of a transient nature. The restricted movements on downgaze were attributed to vertical muscle bruising by traction sutures and all cases resolved spontaneously.

Seven cases had acquired extraocular muscle palsies of which five were typical non localising sixth nerve palsies. One patient had a combined acquired partial sixth and third nerve palsy, an unusual ocular motility disorder in association with raised ICP. These cases resolved with successful reduction of the raised ICP. One acquired case was a secondary exotropia relating to severe visual loss and optic atrophy.

Acquired cases of ocular nerve palsy were more likely to have higher levels of ICP than those patients who did not develop a nerve palsy.

Criteria for diagnosis of IIH usually state that there should be no other focal neurological signs other than a sixth nerve palsy. In view of the findings of many different types of ocular motility disturbances, it is suggested that the criteria for this diagnosis should be amended to allow inclusion of ocular motility defects in otherwise obvious cases of IIH. All cases with ocular motility disorders must however be fully investigated to exclude other pathology and the condition must remain a diagnosis of exclusion.

9.3   In assessing the visual function of cases of IIH a number of tests are employed. Loss of visual function is the only serious complication and may occur early or late in the course of the condition. An appropriate and sensitive clinical assessment regime is therefore of importance in the outpatient situation.

Visual acuity, visual field assessment, contrast sensitivity, colour vision, fundus examination and electrodiagnostic techniques have been used to assess visual function. Visual field assessment has been determined to be the most sensitive to detection of visual loss with statistically greater sensitivity and specificity in comparison to visual acuity and contrast sensitivity testing. There was no significant difference between the sensitivity and specificity of visual acuity and contrast sensitivity.

Visual acuity is usually not affected until late in the course of the condition or unless there is extension of an enlarged blind spot into the macular area. Colour vision is insensitive to mild visual

loss and colour deficit noted only where there is moderate or marked visual loss and with optic atrophy.

Electrodiagnostic techniques were used in three cases in this study. This was of use in suspected functional overlay and visual loss. One case was shown to have a delayed latency indicating a true visual defect. Electrodiagnostic techniques tend not to be of use for detecting subtle changes in visual function as the slight increases in latencies often remain within normal limits.

Visual field assessment in this study was with the Humphrey automated and Goldmann manual perimeters. The 24-2 threshold programme was used for Humphrey perimetry and has been demonstrated as suitable for detection of visual field defects associated with optic nerve pathology. It is also advantageous because of its shorter test time compared to automated strategies that test additional points more peripherally in the visual field. A new technique was designed for use with Goldmann perimetry. A modified Armaly-Drance strategy has been used in one other study (Wall and George 1991) which was found to be a sensitive technique for detection of visual field defects. This technique was found however to be time consuming and not appropriate to a standard clinical setting. In this study, the Goldmann strategy tested the kinetic boundaries of the visual field followed by static testing concentrated in the central 30 degrees corresponding to points tested by automated central field perimetry. This technique was found to be sensitive to detection of visual field defects and when compared to the detection rate of automated perimetry, was equally comparable.

The resulting clinical assessment regime designated for assessment of patients with IIH includes visual acuity, visual field assessment with either automated perimetry or Goldmann manual perimetry using disease specific strategies, fundus examination and full Orthoptic assessment where indicated.

The incidence of visual loss has been reported at between 11 to 96% and the incidence of permanent serious visual loss has been put in the range of 4 to 25%. Few prospective studies have addressed visual prognosis. Those studies using less well defined manual testing strategies do not determine the full extent of visual loss and patient outcome, and although the incidence of visual symptoms and the state of visual function with visual field assessment at the initial and final visits has been well studied in two studies, these do not document any change of visual function during the intermediary period of follow up.

This present study comprehensively studied visual function prospectively using well defined testing strategies and documented not only the final visual outcome but the state of visual function throughout the follow up period and therefore identified episodes of recurrence of the condition and any change of visual function during treatment. Visual loss was detected at presentation or during follow up in 86% of cases by Goldmann perimetry and in 82% of cases by Humphrey perimetry. The types of visual field defects documented in these patients were typical of optic nerve pathology in IIH and related to axoplasmic stasis. In addition to enlarged blind spots, arcuate defects, nasal steps, reduced nasal sensitivity, global constriction and scotomas were recorded.

66.7% of the documented visual field defects were minimal or mild. The remainder were moderate, marked or blinding visual defects. The patients with minimal or mild visual field defects were often asymptomatic and detection of asymptomatic visual loss was of note. At presentation, 47% of patients had symptoms of visual disturbance (41% with documented visual field defect) and 53% of patients were not aware of any visual deficit. However, of this latter group, 44% had a visual field defect documented on assessment. Visual field assessment by Humphrey or Goldmann perimetry had a good prognostic value for detection of asymptomatic visual loss.

9.4   The prognosis for visual outcome is generally good. Visual outcome does not appear related to the presence or duration of symptoms, age at presentation, or the presence of associated conditions. In this series of patients managed by conservative, medical and/or surgical means, a significant improvement was found from initial to last assessment of visual function and the pattern of improvement was also significant over the period of follow up. An excellent outcome was achieved in 41.2% of patients, a good outcome was achieved in 41.2% of cases, a satisfactory outcome in 11.6% and a poor outcome in 6%. Risk factors associated with a poor visual outcome included a high degree of obesity, presence of atrophic optic discs and presentation with poor visual function.

In this study, six patients did not receive treatment and their visual function did not deteriorate. Twenty-eight patients received treatment for their raised ICP and visual loss. Treatment included medical (acetazolamide and renal diuretics) and/or surgical options (CSF shunt procedures and optic nerve sheath fenestration). The response to the different types of treatment was significant with improvement of visual function occurring more quickly in surgically treated patients compared to medically treated patients. This relates to the immediate effect on CSF pressure with surgical treatment and the slower mechanism of action of diuretics on CSF formation. These patients were assessed pre and post commencement of treatment and were found to improve significantly. Patients requiring a combination of medical and surgical treatment appeared to have a more chronic

course of IIH in relation to their visual function. However, recurrence which occurred in a number of patients occurred most commonly in patients treated with shunts and related to shunt associated complications.

With prompt treatment, the visual outcome was excellent or good in 82% of patients. The prognosis for reversible visual loss is therefore considered to be very good.

Despite the active encouragement of weight loss, no patient achieved weight loss to within their normal weight for height range. It appears that a substantial weight loss is required to have a sustained effect on outcome in these patients and treatment strategies aimed at achieving such a degree of weight loss would be beneficial.

9.5   It is reasonable to assume a relationship exists between visual function and ICP. Visual function is seen to deteriorate with exacerbation of ICP which is often seen with a blocked shunt device and an accumulation of ICP. There is communication between the intracranial cavity and the optic nerve sheath and visual loss occurs with raised ICP where there is accumulation of CSF around the optic nerve. This increases pressure on the optic nerve and causes axoplasmic stasis of nerve conduction. There is an accumulation of axoplasmic fluid in the anterior optic nerve with secondary vascular changes and papilloedema is seen on fundus examination. Visual function generally improves with treatment to reduce the raised ICP.

Development of visual loss relates to the level of ICP. ICP is known to fluctuate considerably and this fluctuation may explain why patients generally retain good visual function. Fluctuation in ICP between high and normal manometric levels may allow periods of recovery for the optic nerve. The periodic falls in pressure are probably not of sufficient duration to allow the optic nerve head to recover completely but may allow intermittent improvement of local circulation in the optic nerve and improvement in axoplasmic transport. A significant relationship could be demonstrated in this study between the level of ICP and visual outcome. Higher levels of ICP correlated with poor visual outcome.

This study constitutes the largest UK prospective study to date. The incidence rates and obesity data provide original observations on the epidemiology of this condition in the UK. The study comprehensively studies the visual performance of patients with IIH with new data on the survival of visual function and clinical outcomes in this condition of raised ICP.

It is recommended that further research be considered in the study of this condition. A multi centre study of epidemiology would aid more accurate calculation of incidence rates and evaluate more extensively the effect of differing treatment strategies. A study specifically targeting weight

loss in these patients without including other treatment regimes (to exclude the bias of their effect on outcome) would demonstrate the impact of overweight and obesity, and weight loss, on the condition particularly in view of its confirmed status as a risk factor for IIH. One requirement for further research is long-term studies to more accurately assess the rate of recurrence and the stage at which this reported 'self-limiting' condition ceases. Neurological studies of ICP and ophthalmological studies involving advanced technology, including scanning laser ophthalmoscopy, will provide invaluable information of intracranial hydrodynamics and the response of the optic nerve to this.