Brief Report

Cephalalgia
An International Journal of Headache

International Headache Society

Impact of obesity and binge eating disorder on patients with idiopathic intracranial hypertension

Cephalalgia
2017, Vol. 37(3) 278–283

DOI: 10.1177/0333102416640514
journals.sagepub.com/home/cep

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Abstract

Background: Idiopathic intracranial hypertension (IIH) is associated with obesity, and obesity is associated with binge eating disorder (BED). The aim of this paper is to address the presence and impact of BED in patients undergoing an IIH diagnostic protocol.

Methods: This was a cross-sectional study. Consecutive patients suspected of IIH underwent neurological, neuro-ophthalmologic and psychological examinations, neuroimaging studies and intracranial pressure (ICP) measurements through lumbar puncture in the recumbent position. IIH diagnosis was based on International Classification of Headache Disorders, 2nd Edition criteria; BED diagnosis was based on Diagnostic and Statistical Manual of Mental Disorders, 5th Edition criteria. The presence of oligoclonal bands (OCBs) in the cerebrospinal fluid was also assessed.

Results: Forty-five patients were enrolled: 33 were diagnosed with IIH and five of them (15%) were obese with BED. Compared to non-obese patients, those who were obese, and particularly those who were obese with BED, were more likely to have an IIH diagnosis ($\chi^2 = 14.3$; $p = 0.001$), ICP > 200 mmH_2O ($\chi^2 = 12.7$; $p = 0.002$) and history of abuse or neglect ($\chi^2 = 11.2$; $p = 0.004$). No association with OCBs was found.

Conclusions: We reported for the first time the presence of BED among patients with IIH and showed that BED is associated to IIH, ICP and history of abuse or neglect.

Keywords

Idiopathic intracranial hypertension, obesity, binge eating disorder

Date received: 18 December 2015; revised: 15 February 2016; accepted: 29 February 2016

Introduction

Idiopathic intracranial hypertension (IIH) is a clinical condition associated with increased intracranial pressure (ICP) with no space-occupying lesions, such as brain tumours. As shown in recent literature reviews, IIH mostly occurs in young women and is associated with obesity (1,2). The incidence of IIH varies between 0.28 and 2.2/100,000 in general populations and between 11.9 and 21.4/100,000 among obese women (2): in consideration of the increasing obesity prevalence, the prevalence of IIH is expected to rise as well. In a recent study (3), oligoclonal bands (OCBs) in serum and cerebrospinal fluid (CSF) were found in 31% of IIH patients. The authors discussed whether there might be some kind of association between

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obesity and OCB positivity, and whether obesity might lead to OCB positivity and IIH through an inflammatory process.

A frequent comorbidity of obesity is binge eating disorder (BED), a psychiatric disorder characterized by recurrent episodes of binge eating episodes that occur in the absence of compensatory behaviours (i.e. purge or vomiting) (4). The 12-month prevalence of BED was recently found to be 0.8%, peaking at 41.7% among obese subjects: obese subjects with comorbidity for BED have higher body mass index (BMI) scores, comorbidity with other mental health problems and are more likely to develop chronic headaches (odds ratio: 2.3; 95% confidence interval: 1.7–3.3) (5).

To our knowledge, the association between BED and IIH has never been addressed. The aim of this paper is to demonstrate the presence and impact of BED in patients undergoing an IIH diagnostic protocol. We hypothesized that the presence of BED and obesity is positively associated with ICP > 200 mmH_2O and diagnosis of IIH, and we tested the association with the presence of depression, papilledema, optic neuropathy and chronic headache.

Methods

In this observational, cross-sectional study, patients with signs and symptoms suggesting possible IIH were enrolled between April 2013 and December 2015 on occasion of their participation in an inpatient structured diagnostic program. The program included general medical, neurological, neuro-ophthalmologic and psychological examinations, neuroimaging studies (including brain magnetic resonance imaging (MRI), magnetic resonance venography (MRV) in order to exclude possible cerebral venous thrombosis and MRI angiography of intracranial vessels) and lumbar puncture with ICP assessment in the recumbent position. Serum and CSF diagnostics were also performed, including a search for OCBs. Patients received the diagnosis of IIH according to the guidelines of the International Classification of Headache Disorders, 2nd Edition (ICHD-2), released in 2004 (6). The study was approved by the Besta Institute ethics committee (protocol number: 194/2013). Written informed consent was obtained from all participants.

We relied on the ICHD-2 criteria as the study was launched before more recent criteria were published (Friedman criteria (7); ICHD-3-beta (8)). The main change brought about by these diagnostic criteria is that they require an opening ICP pressure > 250 mmH_2O in all cases, and not >200 mmH_2O in non-obese and >250 mm H_2O in obese patients. We note that the opening ICP threshold of 250 mmH_2O or more is not universally accepted, as many cases would be missed in consideration of large diurnal ICP fluctuations (9). Thus, in line with the inclusion criteria adopted in a recent large trial of IIH (10), we also included patients with ICP opening pressures of >200 and <250 mmH_2O, but only when associated with compelling clinical and/or MRI findings suggestive of IIH, namely: pulse-synchronous tinnitus; abducens nerve palsy; grade II papilledema; no evidence of pseudopapilledema; lateral sinus stenosis or collapse on MRV; or partially empty sella with unfolded perioptic nerve CSF spaces.

ICP was measured by lumbar puncture performed in the lateral decubitus position by experienced neuroradiologists. Complete neuro-ophthalmological evaluation including standardized automated perimetry (Humprey 30-2) and spectral domain optical coherence tomography (OptoVue) measurements were obtained in order to grade papilledema or optic nerve atrophy. Chronic headache was defined as migraine- or tension-type headache occurring on 15 or more days/month for more than 3 months (i.e. codes 1.5.1 and 2.3 of ICDH-2 (6)). Depressive symptoms were evaluated with the Beck Depression Inventory – second version (BDI-II), a 21-item inventory that addresses the cognitive and somatic–affective components of depression: the score range is 0–63, and BDI-II scores of >14 are indicative of depression (11). Diagnosis of BED was posed according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V) (4), consisting of: recurrent episodes of binge eating (i.e. eating in a discrete period of time an amount of food that is larger than what most people would eat and with a lack of control); associated behaviours or feelings such as eating much more rapidly than normal until feeling uncomfortably full when not feeling physically hungry, eating alone because of feeling embarrassed by eating or feeling disgusted with oneself, depressed or very guilty afterward; marked distress with the binge eating episodes; binge eating occurring at least once a week for 3 months; and binge eating occurring without inappropriate compensatory behaviours. Diagnoses of BED was evaluated based on the psychological examination, in which the presence of depression and a past history of physical or sexual abuse or neglect were addressed and were confirmed by a consultant psychiatrist. Current use of drugs that might suppress appetite was also recorded.

Data analysis

Descriptive statistics were used to report patients' features at the overall group level, as well as among those who were or were not diagnosed with IIH.

Patients were categorized into three groups: non-obese (i.e. with BMI < 30 kg/m^2) with or without BED;

obese without BED; and obese with BED. Pearson's χ^2 test was used in order to address the association between the presence of obesity and BED and ICP > 200 mmH_2O, the diagnosis of IIH, the presence of depression, chronic headache, papilledema, visual field defect, transient vision loss, visus impairment, current use of appetite suppressive drugs, previous traumatic events, OCBs and anaemia. Significance was set at two-tailed $p < 0.0042$ after Bonferroni correction. In order to further address the association between the presence of OCBs, BED, CSF pressure and BMI among patients with an IIH diagnosis, non-parametric Mann–Whitney U tests were used to measure the difference in ICP and BMI between obese patients with and without comorbid BED and between patients with or without OCBs. Data were analysed with PAWS 18.0.

Results

Forty-five patients were included in the present study. The mean age was 37.4 years (SD: 11.3) and 39 were female. IIH was diagnosed in 33 patients (73%), 21 (47%) were obese and six had BED (13%); among those with IIH, five patients were obese with BED comorbidity (15%). One patient with BED was not obese and did not receive an IIH diagnosis. Table 1 reports the main demographic and clinical data: no patients suffered from obstructive sleep apnoea, 14 patients had anaemia and, on average, each patient had two comorbidities, irrespectively of the presence of IIH; transient visual loss and visual field defects were more common in IIH patients than in non-IIH ones.

Table 2 reports the χ^2 analysis aimed at addressing the impact of obesity and obesity with comorbid BED. Compared to non-obese patients, those who were obese, and particularly those who were obese with BED, were more likely to have an IIH diagnosis and ICP > 200 mmH_2O. An association was also found with previous abuse or neglect: this was reported in six patients, all with IIH, and was much more common among obese patients with BED (60%) than among non-obese or obese patients without BED (7.5%).

Finally, among patients with an IIH diagnosis, those who were obese with BED had higher ICPs compared to those obese without BED (350.0 ± 52.0 vs. 266.2 ± 57.1; $p = 0.012$), while no differences in BMI were found (36.5 ± 6.0 vs. 35.7 ± 3.1; $p = 0.90$); in addition, no differences were found between patients with and without OCBs for ICP (256.7 ± 51.3 vs. 301.0 ± 62.0; $p = 0.24$) and BMI (37.1 ± 3.1 vs. 32.1 ± 5.6; $p = 0.10$).

Table 1. Clinical and demographic information.

	With IIH ($n = 33$)	Without IIH ($n = 12$)	All cases ($n = 45$)
Female gender	30 (91%)	9 (75%)	39 (87%)
Age	37.2 ± 11.8	37.3 ± 9.7	37.2 ± 11.2
Number of headaches/3M	41.8 ± 35.7	48.9 ± 31.0	43.7 ± 34.3
Chronic headache	16 (48%)	6 (50%)	22 (49%)
ICP	297.0 ± 61.8	161.7 ± 21.6	260.9 ± 81.0
ICP > 200 mmH_2O	33 (100%)	1 (8%)	34 (76%)
ICP > 250 mmH_2O	24 (73%)	0 (0%)	24 (53%)
BDI-II	10.4 ± 7.2	13.7 ± 9.5	11.3 ± 7.9
Depression (BDI-II > 14)	9 (27%)	4 (33%)	13 (29%)
BMI	32.6 ± 5.6	24.4 ± 2.9	30.4 ± 6.2
Obese (BMI > 30)	21 (64%)	0 (0%)	21 (47%)
BED	5 (15%)	1 (8%)	6 (13%)
Papilledema	18 (54%)	3 (25%)	21 (47%)
Transient vision loss	14 (42%)	2 (17%)	16 (36%)
Visual field defect	11 (33%)	1 (8%)	12 (27%)
Visus impairment	8 (24%)	3 (25%)	11 (24%)
Haemoglobin (g/dL)	13.7 ± 1.3	13.5 ± 1.7	13.7 ± 1.4
Mean cell volume (fl)	85.5 ± 6.9	85.3 ± 6.2	85.4 ± 6.7
Anaemia	9 (27%)	5 (42%)	14 (31%)
Total number of comorbidities	2.1 ± 1.2	2.1 ± 1.7	2.1 ± 1.3
Hypertension	3 (9%)	2 (17%)	5 (11%)
Appetite-suppressive drugs	7 (21%)	2 (17%)	9 (20%)
Abuse/neglect	6 (18%)	0 (0%)	6 (13%)
OCBs	3 (9%)	0 (0%)	3 (7%)

Data are reported as frequencies and percentages for categorical variables and as means ± SDs for continuous variables.
Appetite suppressive drugs included: topiramate (five patients, 25–150 mg/day), levetiracetam (one patient, 1000 mg/day), pregabalin (one patient, 150 mg/day) and metformin (two patients, 1500 mg/day).
IIH: idiopathic intracranial hypertension; Number of headaches/3M: number of headaches in the previous 3 months; ICP: intracranial pressure; BDI-II: Beck Depression Inventory, 2nd edition; BMI: body mass index; BED: binge eating disorder; OCB: oligoclonal band.

Discussion

Our results suggest that a relationship exists between the presence of BED in obese patients, increased ICP pressure and diagnosis of IIH according to ICHD-2 criteria. Compared to the non-obese and obese patients without BED counterparts, patients with obesity and BED were more likely to have ICP > 200 mmH_2O and a diagnosis of IIH; moreover, obese IIH patients with BED were more likely to have a past history of physical

Table 2. Association between obesity, binge eating disorder and other clinical parameters.

	Non-obese ($n = 24$)	Obese without BED ($n = 16$)	Obese with BED ($n = 5$)	χ^2 (p-value)
Diagnosis of IIH				
No ($n = 12$)	12	0	0	χ^2: 14.32
Yes ($n = 33$)	12	16	5	$p = 0.001$
ICP > 200 mmH_2O				
No ($n = 11$)	11	0	0	χ^2: 12.74
Yes ($n = 34$)	13	16	5	$p = 0.002$
Papilledema				
No ($n = 24$)	11	10	3	χ^2: 1.17
Yes ($n = 21$)	13	6	2	$p = 0.56$
Visual field defect				
No ($n = 33$)	21	8	4	χ^2: 7.03
Yes ($n = 12$)	3	8	1	$p = 0.03$
Transient vision loss				
No ($n = 29$)	18	9	2	χ^2: 2.94
Yes ($n = 16$)	6	7	3	$p = 0.23$
Visus impairment				
No ($n = 34$)	18	12	4	χ^2: 0.06
Yes ($n = 11$)	6	4	1	$p = 0.97$
Appetite-suppressive drugs				
No ($n = 36$)	19	13	4	χ^2: 0.03
Yes ($n = 9$)	5	3	1	$p = 0.99$
Anaemia				
No ($n = 31$)	17	11	3	χ^2: 0.23
Yes ($n = 14$)	7	5	2	$p = 0.89$
Abuse/neglect				
No ($n = 39$)	23	14	2	χ^2: 11.18
Yes ($n = 6$)	1	2	3	$p = 0.004$
OCBs				
No ($n = 42$)	24	13	5	χ^2: 5.83
Yes ($n = 3$)	0	3	0	$p = 0.05$
Chronic headaches				
No ($n = 23$)	14	6	3	χ^2: 1.84
Yes ($n = 22$)	10	10	2	$p = 0.40$
Depression (BDI-II > 14)				
No ($n = 32$)	18	12	2	χ^2: 2.65
Yes ($n = 13$)	6	4	3	$p = 0.27$

Significance is set at $p < 0.0042$ after Bonferroni correction.
IIH: idiopathic intracranial hypertension; ICP: intracranial pressure; BED: binge eating disorder; OCB: oligoclonal band; BDI-II: Beck Depression Inventory, 2nd edition.

or sexual abuse and neglect. These results are completely novel and add data to the general notion that obese IIH patients have a worse disease profile (1,2) by including information on the impact of BED.

Obesity is associated with IIH and the presence and severity of visual problems is associated with higher BMI levels: in fact, weight reduction is among the treatment strategies that are aimed at reducing ICP and reversing, or at least limiting, visual symptoms (12). Presence of BED is a negative prognostic factor for weight reduction. As reported in a meta-analysis that compared 16 samples of BED and non-BED obese subjects (388 vs. 465 participants in total), obese BED individuals' average post-treatment weight loss was 2% of initial body weight, while non-BED obese individual lost 11% of their body weight on average (13). So what was the impact of BED on ICP and visual impairments?

In our sample, six patients were diagnosed with BED: one was not obese and not diagnosed with IIH and five (out of 33: a 15% ratio) were obese and diagnosed with IIH. Obese patients with BED had higher ICP, but not higher BMI than those without BED; by contrast, the presence of transient vision loss or visual field defects, which were quite common in IIH patients, was not specifically associated with obesity or BED. Therefore, it could be hypothesized that BED exerts a role in ICP independently of BMI severity and visual problems; we hypothesize that patients with BED might have experienced a recent large weight increase, which might have had an effect on CSF pressure.

It should also be noted that half of these patients had past experiences of abuse or neglect, which is likely to have had an impact on BED and obesity (14,15). We specifically targeted BED in our analysis of eating disorders and none of our patients had other eating disorders. Future studies with larger samples should confirm the prevalence of BED in IIH patients, as well as of other eating disturbances, such as bulimia nervosa or night eating syndrome, which have a relevant impact on mental health and weight.

We did not find any specific association between BMI, CFS pressure and OCBs, a commonly used biomarker of central nervous system inflammation; in a recent paper, OCBs were detected in 31% of IIH patients (3), while in our sample, only 9% of IIH patients (and none of the non-IIH patients) had OCBs. However, we did not screen for cytokine levels, and therefore we have only partial information on the inflammatory features of our patients. By contrast, we found a prevalence of iron-deficiency anaemia that was higher compared to that of a previous study (27% vs. 10.4%) (16): however, none of our patients had severe anaemia, and they had higher values for both haemoglobin (12.1 vs. 8.0 g/dL) and mean cell volume (80.5 vs. 59.9 fl).

This report has some limitations that should be taken into account, particularly the small sample size and the cross-sectional nature of the data. In particular, this study does not have the power to show an independent relationship between BED and IIH, given the small numbers of patients with BED. It has to be noted that this research is intended to be a preliminary report on a new finding, and therefore a cautious interpretation of our results is needed, as our sample is limited and does not enable us to generalize our results to the entire population of IIH patients in terms of both the prevalence and impact of BED.

In conclusion, we reported – for the first time to our knowledge – data on the presence of BED among patients with IIH and showed that BED is associated with the disease itself, with the levels of ICP and with a history of abuse or neglect. Further studies with larger samples and a longitudinal design are needed in order to confirm the impact of BED on IIH and to address the relationship between weight loss and improvements of the clinical signs of IIH.

Clinical implications

- Obesity is common in idiopathic intracranial hypertension (IIH) patients and binge eating disorder (BED) is common in obese patients.
- Among patients with IIH, 15% were obese with comorbid BED: they had higher intracranial pressure and were more likely to have a past history of abuse or neglect.
- It might be important to screen for BED in obese patients with IIH, because this might impact on patients' ability to lose weight, which is a recommendation for IIH treatment.

Acknowledgements

The authors thank the participants for taking part in the present study. Supplementary materials are available upon request to the corresponding author.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship and/or publication of this article: this paper is based on the results of Iter-IIH (Diagnostic and Therapeutic Iter for Idiopathic Intracranial Hypertension) project, sponsored by the Neurological Institute C. Besta IRCCS Foundation.

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