Migraine and bipolar disorder as comorbid disorders

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Abstract

There are several reports suggesting that patients with bipolar spectrum disorders experience migraines more frequently than the general population or those with other mood disorders. This could have implications for the treatment of bipolar disorders; untreated migraine could exacerbate their affective states. A previous study of comorbidity of these conditions in a regional hospital psychiatric outpatient department found a much lower comorbidity than expected. It was suggested this might have been attributable to under-diagnosis or under-recognition of the two conditions. Here we re-analyse data from the same outpatient department and find that with greater recognition of this comorbidity the reported prevalence has increased markedly to 33.3% of new referrals in the past year and 8.5% overall. We conclude that there may be considerable under-recognition of the co-existence of migraine and bipolar disorders.

Key words: migraine, bipolar disorder, prevalence, headache, depressive disorders.

Introduction

Identification of comorbid disorders – where multiple conditions exist in the same individual – is useful with respect to treatment as well as suggesting possible common aetiological factors. It is important to be aware of what other conditions are likely to exist in a patient with a given diagnosis; left unrecognised, a comorbid disorder may make treatment more difficult and lead to a lower overall quality of life. Bipolar affective disorders and migraine are two such conditions. Although estimates of comorbidity vary, for example, the rate of migraine found in people with bipolar disorder varies between 24.8% (1) and 39.8% (2), this rate is generally higher than the population prevalence of migraine, which ranges between 10% (1) and 25% (3).

A previous analysis of a UK regional hospital outpatient department found a much lower comorbidity of migraine in people with bipolar disorder, namely 4.7% (4). One possibility for this was under-recognition. Over the past year, new and continuing bipolar spectrum patients were assessed to determine whether they also suffered from migraine disorders.

Methods

A patient database recording age, gender, main diagnosis, other diagnoses and ethnicity of patients seen in the Bedford East Community Mental Health Team based at Weller Wing, Bedford Hospital, UK, in the previous 5 years was examined for patients with diagnoses of bipolar spectrum disorders and migraine. 1137 patients had recorded diagnoses and were suitable for analysis. Deceased patients were excluded. The 55 patients seen in the last year as new referrals were next studied for comorbidity using the same criteria; 3 had unclear diagnosis or no mental illness and were excluded. The new patients were assessed in a specific clinic known as ASPA, standing for 'Assessment and Single Point of Access'.

Results

A total of 217 patients with bipolar disorder were found, 213 excluding 4 patients whose diagnosis included 'query' bipolar disorder. These 213 represented 18.7% of the total sample of 1137 patients. 58/1137 (5.1%) of the patients were recorded as having migraine, with 18/213 (8.5%) having both bipolar disorder and migraine.

Of the 52 new referrals, there were 15 individuals with bipolar spectrum disorder (28.9%) and 5 with migraine (9.62%). All the 5 patients with migraine had a primary diagnosis of bipolar disorder, giving a comorbidity of 33.3% (5/15) in this group.
The gender of the patients and bipolar subtype were also examined, as some previous studies have suggested increased comorbidity amongst female patients (1-2) as well as with bipolar II disorder as opposed to bipolar I (5).

Table 1: Analysis of 1137 patient database from 5 years prior to September 2012.

Diagnoses	Number	Prevalence
Bipolar Disorder	213	18.7% of total (213/1137)
Migraine	58	5.1% of total (58/1137)
Bipolar Disorder + Migraine	18	8.5% of bipolar disorder (18/213)
Migraine ♀	40	69.0% of migraine (40/69)
Migraine ♂	18	31.0% of migraine (18/69)
Bipolar Disorder + Migraine ♀	11	61.1% of comorbid patients (11/18)
Bipolar Disorder + Migraine ♂	7	38.9% of comorbid patients (7/18)
Bipolar I + Migraine	7	38.9% of comorbid patients (7/18)
Bipolar II + Migraine	11	61.1% of comorbid patients (11/18)

Table 2: Analysis of 52 new Referrals over ~1 year prior to September 2012

Diagnoses	Number	Prevalence
Bipolar Disorder	15	28.9% of total (15/52)
Migraine	5	9.6% of total (5/52)
Bipolar Disorder + Migraine	5	33.3% of bipolar disorder (5/15)
Migraine ♀	2	40.0% of migraine (2/5)
Migraine ♂	3	60.0% of migraine (3/5)
Bipolar Disorder + Migraine ♀	2	40.0% of comorbid patients (2/5)
Bipolar Disorder + Migraine ♂	3	60.0% of comorbid patients (3/5)
Bipolar I + Migraine	3	60.0% of comorbid patients (3/5)
Bipolar II + Migraine	2	40.0% of comorbid patients (2/5)

Discussion

It appears that, in contrast to the entire patient group, amongst whom comorbidity of migraine in patients with bipolar disorders was relatively lower than previously reported in the general literature at 8.5%, the new referrals with bipolar disorders, in whom active enquiry was made about migraine, had a much greater comorbidity of 33.3% which is closer to reports from previous studies.

Interestingly, although the prevalence of migraine overall amongst the new patients (9.6%, 5/52) was almost double that found over the past 5 years, it is still lower than the general population prevalence. Figure 1 compares the comorbidity prevalence together with the results of the previous analysis described in Holland et al. 2011.

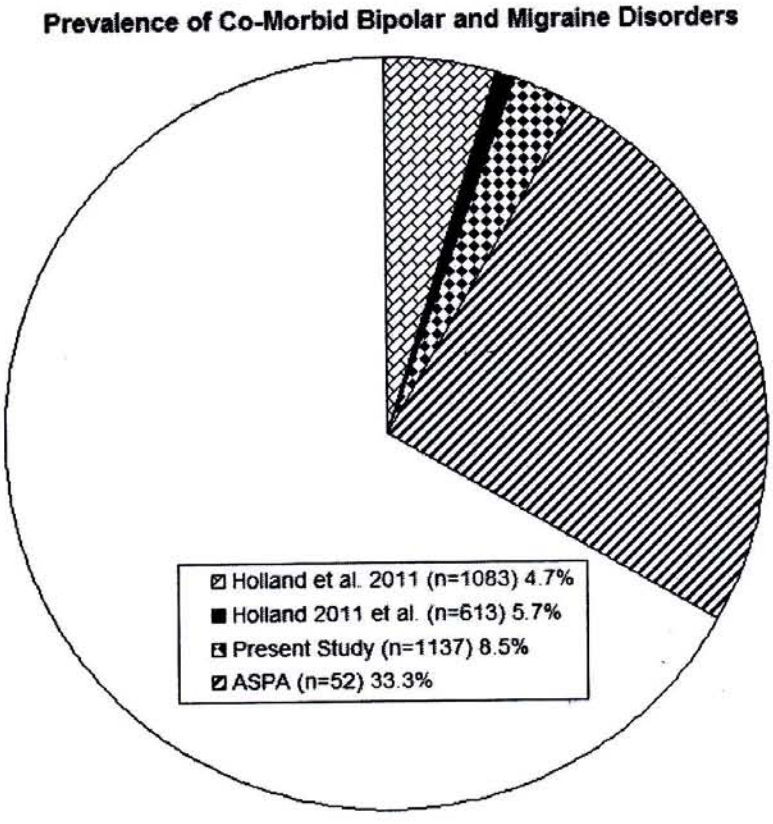

Figure 1: Comparison of analysis of present data with Holland et al. 2011. The comorbidity prevalence is shown as the percentage of patients with bipolar and migraine amongst those patients in their respective samples with bipolar disorder.

From the larger patient sample, migraine was more frequent amongst females and accordingly comorbidity was increased amongst females. Comorbidity was also greater for patients with bipolar II disorder. However, these findings were not replicated amongst the new patients seen in the ASPA Clinic, in whom there was no clear difference between gender and bipolar subtype. This is probably attributable to the much smaller sample size.

Recognition of comorbid migraine in patients with bipolar disorder is important for several reasons. First, the stress of experiencing a migraine may act as a triggering factor for a manic or depressive episode; altered sleeping patterns resulting from migraine may also be contributory. Furthermore, patients already restricted in their active participation in society due to episodes of mania or depression may suffer additional or prolonged restrictions through suffering severe migraine, which in turn, could exacerbate their affective symptoms.

Treatment should also be modified in these patients to cover both conditions. For example, sodium valproate and lamotrigine are effective in the treatment of both migraine and bipolar disorder (6). In contrast, tricyclic antidepressants are routinely used for migraine prophylaxis but can induce manic episodes in patients with bipolar disorders (7). One case report describes effective control of both conditions using lithium with topiramate (8).

A final point is in reference to the 'kindling' phenomenon, whereby risk of recurrence of bipolar episodes increases with the number of previous episodes (9). If untreated migraine were to lead to more bipolar episodes, it could indirectly worsen the primary condition. Much as we might aim to achieve a better blood lipid profile in diabetic patients, we should attempt to optimise the treatment of both conditions in patients who suffer with comorbid bipolar disorder and migraine. In addition to this, untreated migraine may evolve into a form of chronic daily headache known as 'transformed migraine' which is generally resistant to treatment (10), emphasising the importance of effective early treatment.

The underlying reasons for the apparent increased frequency of migraine in people with bipolar disorder remain unclear but there are several hypotheses relating to the underlying neurobiology that are currently under investigation.

It appears that multiple pathways may be dysfunctional in these disorders, and that their combined effects produce the phenotype characteristic of each condition. There is some overlap in these processes. It is feasible that a shared pathology could lead to each condition.

A family history of bipolar or migraine disorders increases an individual's likelihood of developing each condition, which suggests that genetic factors may be important. As high as 60% heritability in bipolar disorder and 40-65% for migraine have been reported, with attempts to find responsible genes identifying possible overlapping 'susceptibility zones' encoding various ion channels (11).

One of the more significant effects of these genetic changes may be how they affect levels of neurotrophic factors such as BDNF. There appears to be less BDNF in patients affected with bipolar disorder (12) and more in chronic migraine (13). Altered levels of neurotrophic factor support for neurons may produce altered neural network function, perhaps one manifestation of which is the abnormal EEG recordings observed in migraine and bipolar disorders. For both, decreased inhibitory alpha with increased theta band activity has been seen (14-15).

It is increasingly suggested that chronic inflammation plays a part in development of neuropsychiatric conditions. A study of migraine patients identified the presence of auto-antibodies associated with white matter hyperintensities (16). In bipolar disorder, levels of pro-inflammatory compounds in circulating monocytes have been reported, apparently as a result of environmental influence upon individuals with genetically-determined susceptibility (17). Of interest with regard to the general practice setting, the involvement of inflammation has implications for cardiovascular disease risk. Many antipsychotic agents have adverse effects on lipid profiles and, together with an inherent pro-inflammatory disease state, this could accelerate atherosclerotic plaque development. Furthermore, some groups advocate essential fatty acid supplementation as an adjunct to symptom control in bipolar disorder (18). A few studies suggest eicosapentaenoic acid supplementation may benefit headache disorders (19).

Prior to the recognition of the increased prevalence of migraine amongst patients with bipolar disorder in our community mental health team, it appears that comorbid migraine may have been under-treated. It remains to be seen whether, in the longer term, treatment of the comorbid migraine actually will lead to better quality of life outcomes for these patients.

The population analysed here is relatively small, which could account for the observed difference from our previous data. Nonetheless, we would still suggest that clinicians assessing patients with bipolar

disorder routinely enquire about symptoms of migraine. Migraine encompasses a broad range of conditions and ideally requires a neurologist diagnosis. However, in the majority of cases patient self-reporting of the characteristic symptoms is probably enough for the wise practitioner to attempt to treat comorbid migraine in conjunction with bipolar disorder.

GP Comment

What have I learned from this paper?
Migraine appears to be more common in patients with bipolar disorders. Specific enquiry for migraine should be made in these patients so that early treatment can be provided.

Dr Mayruja Santhirakumar, GP Trainee.

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