Journal of Affective Disorders 170 (2015) 255–265

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research report

Pharmacological treatment of depression with and without headache disorders: An appraisal of cost effectiveness and cost utility of antidepressants

Yi-Ju Pan [a,b,c,*], Kuei-Hong Kuo [c,d], Shuu-Jiun Wang [c,e]

[a] Department of Psychiatry, Far Eastern Memorial Hospital, No.21, Sec. 2, Nanya S. Road., Banciao District, New Taipei City 220, Taiwan
[b] Centre for the Economics of Mental and Physical Health, Health Service and Population Research Department, Institute of Psychiatry, King's College London, United Kingdom
[c] School of Medicine, National Yang-Ming University, Taiwan
[d] Division of Medical Imaging, Far Eastern Memorial Hospital, Taiwan
[e] Neurological Institute, Taipei Veterans General Hospital, Taiwan

ARTICLE INFO

Article history:
Received 14 May 2014
Received in revised form
28 July 2014
Accepted 25 August 2014
Available online 2 September 2014

Keywords:
Depression
Headache
Antidepressant
Cost-effectiveness
Cost-utility

ABSTRACT

Background: Depression and headache are highly prevalent in clinical settings. The co-occurrence of headache may impact choice of antidepressants, healthcare utilisation, and outcomes in patients with depression. The current study aims to examine the cost-effectiveness and cost-utility of different antidepressants for treating patients with depression and comorbid headache disorders.
Methods: Adult patients prescribed with antidepressants for depression (n=96,501) were identified from the National Health Insurance Research Database in Taiwan. A cost-effectiveness and cost-utility analysis was conducted comparing selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants (TCAs), and by the presence of comorbid headache disorders and other pain conditions.
Results: In this study, SSRIs dominated SNRIs in both cost-effectiveness and cost-utility. As revealed in the cost-effectiveness acceptability curves, TCAs were likely to have a cost-utility advantage compared to SSRIs and SNRIs in improving quality-adjusted life years (QALYs) for patients with comorbid headache; SSRIs remained as the most cost-effective option for patients with other pain conditions.
Limitations: Limitations include the use of proxy definition of remission as effectiveness measure and the adoption of utility values from previous studies.
Conclusions: Given a pre-determined willingness-to-pay level, TCAs can be considered as a cost-effective option to improve QALYs for depressed patients with headache disorders. Future research is needed to further clarify factors influencing the cost-effectiveness and cost-utility of pharmacological treatments in depressed patients with specific pain conditions.

1. Introduction

Compared to other painful physical conditions, persons with headache were associated with higher likelihoods of experiencing nearly all depressive symptoms including suicide thoughts (Ohayon and Schatzberg, 2003). In primary care settings, around one-fourth of patients with a chief complaint of headache were found to have major depressive disorder (MDD) (Maeno et al., 2007). A strong positive association was reported between prescription of migraine (a type of headache) and antidepressant medications (Oedegaard et al., 2011). Apart from the cross-sectional findings, the child's report of headache at age 8 predicted antidepressant use by age 24 with a dose–response relationship in a nationwide birth cohort study (Luntamo et al., 2012). Indeed, previous studies suggested a bi-directional relationship between depression and specific types of headache disorders with a potentially overlapping pathophysiology (Breslau et al., 2003).

In light of these complex interrelationships, the disease course and treatment outcome may differ in patients with comorbid depression and headache. For instance, although controversial, medications for headache e.g., propranolol might worsen depressive symptoms (Steffensmeier et al., 2006). On the other hand, certain antidepressants were associated with new-onset or exacerbation of headache (Koch and Jurgens, 2009; Sir et al., 2005). In addition, migrainous headache was an independent factor to

* Corresponding author at: Department of Psychiatry, Far Eastern Memorial Hospital, No.21, Sec. 2, Nanya S. Road., Banciao District, New Taipei City 220, Taiwan. Tel.: +886 2 7728 2169; fax: +886 2 7728 2168.
E-mail addresses: panyiju0211@gmail.com, yi-ju.pan@kcl.ac.uk (Y.-J. Pan).

http://dx.doi.org/10.1016/j.jad.2014.08.034
0165-0327/

predict health-related quality of life (Hung et al., 2008) and somatic symptoms (Hung et al., 2009) in patients with MDD, which could contribute to more severe depression and poorer treatment outcome. In Taiwanese patients with depression, the presence of headache was associated with higher direct costs and greater odds of using psychiatric emergency and inpatient services (Pan et al., 2013c). Therefore, the co-occurrence of headache might influence choice of antidepressants, healthcare utilisation, and patient's quality of life, with potential impacts on the cost-effectiveness and cost-utility of antidepressants.

There are certain issues regarding the existing evidence comparing the cost-effectiveness and cost-utility between various antidepressants in patients with depression. Firstly, only a very limited number of studies have been conducted in real-world settings (Hosak et al., 2000; Peveler et al., 2005; Serrano-Blanco et al., 2006a, 2006b, 2009). Although economic evaluations are highly context-specific, such data from Asian countries remain wanting (Pan et al., 2012). Secondly, no existing economic studies have addressed the impacts of specific painful physical conditions. Whether individual antidepressants differ in the cost-effectiveness and cost-utility by the presence of headache disorders remains to be determined. From the perspective of healthcare providers, a cost-effectiveness and cost-utility analysis was conducted among antidepressants in the current study based on the National Health Insurance Research Database (NHIRD) records of the entire national assemblage of depressed patients in Taiwan. The specific objective was to compare the cost-effectiveness and cost-utility between categories of antidepressants and to test whether and how the presence of headache affects the economic evaluations of antidepressant treatments.

2. Methods

2.1. Participants

The study protocol was approved by Asia University Medical Research Ethics Committee, Taichung, Taiwan (No. 10202001). Participants aged 18 or older meeting the following criteria were identified from Taiwan's NHIRD and the index date was defined as the date on which the subject was first prescribed an antidepressant for treatment of depressive disorders:

(1) They had been prescribed at least one antidepressant of interest (selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants (TCAs)) for treatment of MDD or other depression in 2003.
(2) Data on each participant for a minimum of 12 months before the index date and 18 months after the index date were available.
(3) They had been prescribed at least 3 antidepressants in the first 3 months after the index date or at least 4 prescriptions during the 18-month observation period.

2.2. Effectiveness outcome

A database definition of remission – antidepressant cessation for at least 6 months (Byford et al., 2011; Sicras-Mainar et al., 2010) – was modified and adopted in the current study. To prevent confusion from actual remission defined by clinical rating scales, a more descriptive term 'treatment-free status' was used to describe the 6-month-antidepressant-free period. We defined 'sustained treatment-free status' as 'treatment success' (a proxy for remission), which required no re-start of antidepressant treatments after the 6-month-antidepressant-free period through the 18 months (Pan et al., 2013a, 2014). This treatment-success status after initial antidepressant treatments was found to be associated with cost savings in the second and third years (Pan et al., 2013b). Participants were grouped according to three treatment outcomes:

(1) Sustained treatment-free status (treatment success), defined as patients who had undergone antidepressant cessation for at least 6 months and had not restarted antidepressant use by the end of the observation period.
(2) Continuous treatment, defined as patients who had not undergone an antidepressant cessation for at least 6 months.
(3) Late recontact, defined as patients who had undergone an antidepressant cessation for at least 6 months and had restarted antidepressant use by the end of the observation period.

2.3. Observation period

For each individual, the observation period started on the index date and continued for 18 months. The additional 6 months after the first 12 months was included to ensure adequate time to assess whether a treatment-free status had been achieved. The treatment-free period could begin at any point during the 12 months after the index date, but a participant must have remained free of antidepressants for a minimum of 6 months to fulfil the criterion.

2.4. Utility weights

Health state valuations (utilities) are an essential component of cost-utility analyses. In economic evaluations 'utilities' are often used to measure outcomes and are anchored by 0 and 1, where 0 indicates death and 1 indicates full health. In this study, the baseline utility scores were from a naturalistic longitudinal study which had similar inclusion criteria (Sobocki et al., 2007). The EuroQol five-dimensions questionnaire (EQ-5D), a generic instrument for obtaining utility values, was completed at each visit by the patients in that study. In the current study, the baseline utility score for patients with MDD was set at .42 assuming a group of MDD patients comprising those with moderate (79.6%, utility=.46) and severe (20.4%, utility=.27) depression as in the aforementioned study; baseline utility scores for patients with other depression were assumed to be .60 (Sobocki et al., 2007).

The utility score for the sustained-treatment-free-status health state was set at .85 as 'responder remitters' in Sapin et al. (2004) in which clinical health states were defined by Montgomery–Asberg Depression Rating Scale and the health states were valued by the EQ-5D (Sapin et al., 2004). Besides, it is assumed in this study that people who remained off antidepressants for 6 months but resumed antidepressant use later would have the 'responder non-remitters' utility (.72) at the time when they were off antidepressants (Sapin et al., 2004). The utility score for the late-recontact health state was set to .47, the baseline mean utility score of the depressed patients referenced in Sobocki et al. (2007) assuming it was a new episode of depression. Because people who remained on continuous treatment would comprise a group of patients with heterogeneous disease severity and utility value, we adopted a utility score of .66 from those who remained on antidepressants and were followed up with a mean of 165 days (Sobocki et al., 2007). The uncertainty in the utility score of the continuous-treatment health state (95% confidence interval=.53–.75) (Sobocki et al., 2007) and other utility values were tested in the section on sensitivity analyses.