Journal of Psychiatric Research 63 (2015) 123–131

Contents lists available at ScienceDirect

Journal of Psychiatric Research

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

Depression and pain: An appraisal of cost effectiveness and cost utility of antidepressants

Yi-Ju Pan [a, b, *], Chun-Hao Pan [c, d], Hung-Yu Chan [e], Kuei-Hong Kuo [b, f]

[a] Department of Psychiatry, Far Eastern Memorial Hospital, New Taipei City, Taiwan
[b] School of Medicine, National Yang-Ming University, Taipei, Taiwan
[c] Department of Plastic and Reconstructive Surgery, Chang Gung Memorial Hospital, Keelung, Taiwan
[d] College of Medicine, Chang Gung University, Taoyuan, Taiwan
[e] Department of General Psychiatry, Taoyuan Psychiatric Center, Taoyuan, Taiwan
[f] Division of Medical Imaging, Far Eastern Memorial Hospital, New Taipei City, Taiwan

ARTICLE INFO

Article history:
Received 12 August 2014
Received in revised form
10 January 2015
Accepted 31 January 2015

Keywords:
Depression
Pain
Antidepressant
Cost-effectiveness
Cost-utility

ABSTRACT

Background: Although depression and chronic pain frequently co-occur, there is a lack of clarity in the literature regarding the cost-effectiveness and cost-utility of antidepressants in the presence of these two conditions. From the perspective of healthcare provider, the current study aims to compare the cost-effectiveness and cost-utility of antidepressants in a national cohort of depressed patients with and without comorbid pain conditions.

Methods: Adult patients prescribed with antidepressants for depression were identified from the National Health Insurance Research Database in Taiwan (n = 96,501). By using remission as effectiveness measure and quality-adjusted life years (QALYs) as utility measure, the cost-effectiveness and cost-utility were compared across selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants (TCAs), as well as by the presence of comorbid painful physical symptoms (PPS).

Results: SSRIs dominated SNRIs in both the cost-effectiveness and cost-utility regardless of comorbid PPS. In comparison with TCAs, SSRIs were likely to be the cost-effective option for patients without PPS. In patients with PPS, the cost-utility advantage for SSRIs over TCAs varied with threshold willingness-to-pay levels. Comorbid PPS may be considered an effect modifier of the cost-utility comparisons between SSRIs and TCAs.

Conclusions: For depressed patients without PPS, SSRIs are likely to be cost-effective in improving remission rates and QALYs compared to TCAs and SNRIs. However, to improve cost-utility in those with comorbid PPS, people need to choose between SSRIs and TCAs according to threshold willingness-to-pay levels. Future research is warranted to clarify the impacts of different pain conditions on the economic evaluations of pharmacological treatments in patients with depression.

1. Introduction

Painful physical symptoms (PPS) have been shown to precede the onset of a new depressive episode (Barry et al., 2013), and to contribute to prolongation of the duration of depressive mood (Ohayon and Schatzberg, 2003). In a community survey, the severity of PPS, including headache, pain in the abdomen, back pain and other musculoskeletal pains, has been found to correlate with the severity of depressive symptoms. Presence of PPS deteriorates physical, occupational and socio-professional activities in patients with depression (Ohayon and Schatzberg, 2010). With the evidence that comorbid PPS may be associated with a poor response to antidepressants (Bair et al., 2004; Carter et al., 2012; Kroenke et al., 2008; Leuchter et al., 2010), and with increased healthcare costs (Gameroff and Olfson, 2006; Greenberg et al., 2003; Pan et al., 2013a), the results of cost effectiveness analysis (CEA) comparing antidepressant treatments may be influenced in the presence of comorbid PPS.

Depression and pain have been reported to be among the most burdensome diseases globally (Vos et al., 2012). These two

* Corresponding author. No.21, Sec. 2, Nanya S. Rd., Banciao Dist., New Taipei City 220, Taiwan. Tel.: +886 02 7728 2169; fax: +886 02 7728 2168.
E-mail addresses: panyiju0211@gmail.com, yi-ju.pan@kcl.ac.uk (Y.-J. Pan).

http://dx.doi.org/10.1016/j.jpsychires.2015.01.019
0022-3956/

conditions contribute to the highest loss of quality-adjusted life years (QALYs) (Subramaniam et al., 2013). In patients with depression, the severity of PPS has been shown to be associated with disability (Ohayon and Schatzberg, 2010) and considered a strong predictor of impaired quality of life (Bair et al., 2004). Given the impacts of PPS on quality of life of depressed patients, a cost utility analysis (CUA) comparing antidepressants is wanted when presence of PPS is taken into consideration. In CEA, costs are considered alongside disease-specific outcomes, e.g., treatment response to antidepressants. This kind of economic evaluation is limited by the narrow focus on a single measure of effectiveness outcome. There can be difficulties in evaluating treatments that impact on more than one outcome, e.g., social functioning and quality of life. A CUA is similar to a CEA but it considers costs alongside a utility based outcome measure, usually QALYs. The advantage of CUA is that the results can be compared across different disease areas.

Although tricyclic antidepressants (TCAs) and serotonin norepinephrine reuptake inhibitors (SNRIs) were shown to be probably more effective than selective serotonin reuptake inhibitors (SSRIs) in reducing PPS (Bair et al., 2004; Peveler et al., 2006), results from other clinical trials revealed similar response rate and pain relief across antidepressant groups in patients with both depression and pain (Qaseem et al., 2008). Whether and how individual antidepressants differ in the effectiveness of depression treatment and pain relief remains to be determined. According to a previous review (Pan et al., 2012), most of the existent economic evaluations of antidepressants were based on modelling and relatively few CEA and CUA studies have been conducted with patients of depressive disorders in real-world settings (Hosak et al., 2000; Peveler et al., 2005; Serrano-Blanco et al., 2006a; 2006b; 2009). Among the economic evaluations addressing individual antidepressants in patients with selective pain disorders, a systematic review showed that even for duloxetine (a SNRI), no relevant cost or cost-effectiveness data could be identified in high quality studies (Lunn et al., 2014). In patients with depression and comorbid PPS, evidence regarding the cost-effectiveness (or cost-utility) comparisons across individual antidepressants remain wanting.

Therefore, from the perspective of healthcare providers, we conducted both CEA and CUA among individual antidepressants in the current study based on the National Health Insurance Research Database (NHIRD) records of the entire national assemblage of adult depressed patients in Taiwan. Because antidepressants might differ in their effects on the management of PPS, we hypothesise that results of CEA and CUA comparing antidepressant treatments differ by the presence of comorbid PPS. The objective was to compare the cost-effectiveness and cost-utility across antidepressant categories and to test whether and how the presence of PPS could affect the economic evaluations of antidepressants in a real-world setting.

2. Materials and methods

2.1. Subjects

National Health Insurance (NHI) in Taiwan is a single-payer compulsory social insurance plan that centralises the disbursement of healthcare funds and guarantees equal access to healthcare for all citizens. The NHI system in Taiwan contains the NHIRD which consists of data characterising healthcare utilisation of insured residents, including expenditures, medical procedures/treatments, and basic characteristics of patients, providers and physicians. Subjects 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 (SSRIs, SNRIs, or TCAs) for treatment of major depressive disorder (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 three antidepressants in the first three months after the index date or at least four prescriptions during the 18-month observation period (Pan et al., 2014b).

2.2. Demographic and clinical information

Data including age, gender, diagnosis of depressive disorder, initial antidepressant, physician speciality, and clinical setting on the index date, were extracted. Baseline characteristics regarding comorbid PPS (headaches, back pains, gastrointestinal pains, and musculoskeletal pains), other mental and physical disorders, as well as baseline healthcare expenditure were traced back for all patients for the 12 months prior to the index date.

2.3. Effectiveness outcome

A database definition of remission, ie, antidepressant cessation for at least six months (Byford et al., 2011; Sicras-Mainar et al., 2010), was modified. To prevent confusion from actual remission, a more descriptive term ‘treatment-free status’ was used to describe the 6-month-antidepressant-free period. We defined ‘sustained treatment-free status’ which required no restart of antidepressants through the 18-months observation period after the treatment-free status had been attained (Pan et al., 2013b, 2014b). This sustained treatment-free status has been shown to be associated with cost savings in the second and third years (Pan et al., 2014a) and was considered as ‘treatment success’ (a proxy for sustained remission) in this study. Participants were grouped according to the following three treatment outcomes:

(1) Sustained treatment-free status (treatment success), defined as patients who had undergone antidepressant cessation for at least six 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 six months.
(3) Late recontact, defined as patients who had undergone an antidepressant cessation for at least six months and had restarted antidepressant use after the cessation of antidepressant use.

2.4. Observation period

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 six months to fulfil the criterion.