Avens Publishing Group
J Neurol Psychol
February 2018 Vol.:6, Issue:1

Open Access **Review Article**

Journal of Neurology and Psychology

The Role of Celecoxib in Treatment of Psychiatric Disorders: A Review Article

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Submission: 01 February, 2018
Accepted: 19 February, 2018
Published: 26 February, 2018

Keywords: Obsession; Depression; Celecoxib; COX-2 inhibitors; Treatment; Schizophrenia; Psychiatry

Abstract

Purpose: Celecoxib is a Nonsteroidal Anti-Inflammatory Drug (NSAID) and a sulfonamide pain killer that is mainly used for treatment of Osteoarthritis, Rheumatoid Arthritis, acute pain and some other purposes such as prevention and treatment of gastrointestinal benign neoplasia. Due to the possibility of inflammatory etiologies in many psychiatric disorders, this medication has been studied for the treatment of some of the psychiatric disorders. In this paper we reviewed recent studies done on the use of Celecoxib as adjunctive medication for psychiatric treatments and discussed.

Methods: We searched some related words such as "celecoxib", "COX-2 inhibitors", "psychiatry", "treatment", "depression", "obsession" and "schizophrenia" in PUBMED indexing and collected the required data.

Results: Among all the presented articles on the influence of Celecoxib on psychiatric disorders, the effect of this drug on schizophrenia and depression has been studies more widely and the majority of these studies have confirmed the effectiveness of this drug as a successful adjuvant therapy. Moreover, two Randomized Control Trials (RCT) studies have reported a significant improvement in the treatment of Obsessive Compulsive Disorder (OCD), using celecoxib as an adjuvant medication to fluoxetine and fluvoxamine, compared to placebo. In addition to schizophrenia, depression and OCD, Celecoxib has been reported to work effectively, once applied as adjunctive therapy in bipolar disorders.

Conclusion: Celecoxib has been reported to be an effective medication as an adjunctive therapy in some of the psychiatric disorders such as depression, schizophrenia and OCD. Although evidences are less robust for OCD, results for bipolar disorder are variable and inconclusive.

Introduction

Celecoxib is a Nonsteroidal Anti-Inflammatory Drug (NSAID) which is used as a pain killer and an anti-inflammatory through Cyclooxygenase-2 (COX-2) inhibition [1]. Being a selective inhibitor of COX-2 that does not affect COX-1, Celecoxib reduces the sever gastrointestinal side effects more effectively as compared to traditional NSAIDs and therefore it is suggested as an acceptable drug [2,3]. Moreover, among all NSAIDs, Celecoxib has reported to have lower risk of toxicity [4].

This medication has been approved for treatment of Osteoarthritis (OA), Rheumatoid Arthritis (RA), Juvenile Rheumatoid Arthritis (JRA), Ankylosing Spondylitis (AS), Acute Pain (AP) and Primary Dysmenorrhea (PD) and its effectiveness has been confirmed conclusively in these conditions [5-13].

Nowadays, pro-inflammatory process is considered to be an important etiology for several psychiatric conditions, such as Depression, Schizophrenia, OCD and Bipolar Disorder [14-25]. Some articles suggest that glutamate and its subtypes, particular N-methyl-D-aspartate (NMDA), could mediate this process [26-31]. In addition, some studies have investigated the pro-inflammatory cytokines level in groups of psychiatric patients [32-37].

Therefore, anti-inflammatory drugs specially celecoxib, have been investigated as monotherapy or adjuvant therapy for treatment of psychiatric conditions in preliminary or randomized double-blind trials. The aim of this manuscript is to review studies that were conducted to investigate the role of celecoxib in psychiatric conditions.

Methods

Certain keywords such as "celecoxib", "COX-2 inhibitors", "psychiatry", "treatment", "depression", "obsession" and "schizophrenia" were searched in PUBMED indexing at 01/05/2018 and the required data were collected. The unrelated, non-English and withdrawn articles were excluded, as well as the animal studies. These data were then categorized in groups of various psychiatric disorders to be reviewed in this article.

Results

Schizophrenia

Several clinical trials have investigated the effectiveness of celecoxib in the treatment procedure of Schizophrenia [38-43]. In Ref [38], the authors studied the effect of celecoxib (400 mg) plus amisulpride (200-1000 mg) in comparison with amisulpride (200-1000 mg) plus placebo. The study was performed on 49 schizophrenic patients who were diagnosed within two years of the study date, for duration of six weeks. The results show a significant difference

ISSN: 2332-3469

between celecoxib group and placebo group in Global Clinical Impression Scale (CGI) and Negative, Global and Total subscales of Positive and Negative Symptom Scale (PANSS) [38].

In Ref [39], the authors compared 60 schizophrenic patients who were randomized in risperidone 6 mg/day plus celecoxib 400 mg/day and risperidone 6 mg/day plus placebo arms for 8 weeks. It was found that celecoxib arm had superiority in Positive, General and Total scores of PANSS [39].

Similarly, Muller and his colleagues conducted a research on 50 schizophrenic patients who were randomized to risperidone plus celecoxib and risperidone plus placebo group for 5-weeks after wash-out period. They showed that patients who were in celecoxib group had better outcome in comparison to placebo group in the PANSS total score [40].

In addition a research evaluated cytokine levels in 28 schizophrenic patients who are stable on olanzapine or risperidone after 8 weeks treatment with celecoxib or placebo as adjuvant therapy. This article reported that none of the measured cytokines altered after 8 weeks [41].

There was another study that compared 38 symptomatic outpatient schizophrenic patients who were on treatment with atypical antipsychotics in 2 arms, celecoxib and placebo, as adjunctive therapy. Researchers reported there was no significant difference between two arms after 8 weeks in clinical symptoms or measures of disability [42].

Finally, a Meta-analyzes was published recently and compared 326 schizophrenic patients, 316 patients in celecoxib groups and 310 subjects in placebo groups. The authors concluded that celecoxib could be an effective and safe choice as adjunctive therapy for psychotic symptoms of schizophrenia, particularly in first episode of illness [43].

Depression

Similar to Schizophrenia, Depression has been widely studied to evaluate the effects adding celecoxib to the treatment procedure.

In a six-week study [44], 40 patients who have been diagnosed as Major Depressive Disorder (MDD) were randomized into two arms, celecoxib (200 mg twice daily) or placebo plus sertraline (200 mg/day). Researchers showed that celecoxib group had better improvement in Hamilton Depression Rating Scale (HDRS) items and further reduction of Inerlukine-6 (IL-6) [44].

In Ref [45], the authors compared two groups of 15 depressed female drug naive patients who were treated with celecoxib (100 mg/twice per day) or placebo in addition with sertraline for eight weeks. The authors reported significant improvement in depression symptoms through celecoxib group in comparison with placebo group in fourth week, whereas difference between two arms was not significant in eighth week [45].

Similarly, a six-week study conducted to compare the effects of celecoxib (200 mg/two times per day) or placebo in added to fluoxetine 20 to 40 mg per day in 40 adult patients of MDD. Researchers showed greater improvement in depressive symptoms in celecoxib arm with no difference in side effects [46].

Another study also evaluated the effectiveness of celecoxib 400mg/d against placebo plus reboxetine for six weeks in 40 depressed patients who began treating after a wash-out period. It has been reported that celecoxib plus reboxetine had greater improvement in comparison to reboxetine alone [47].

Finally, a Meta-analyses included 6262 subjects and its authors showed that anti-inflammatory agents, particularly celecoxib decrease depressive symptoms without increasing the risk of side effects [48].

Depression in particular populations

Several researches were conducted to evaluate the effectiveness of celecoxib in subjects other than adults medically healthy depressed patients.

Interestingly, two of these studies targeted depressed patients with a previously diagnosed cancer. Alamdarsaravi et al. investigated the effect of celecoxib (400 mg/d) in comparison to placebo in 40 patients with colorectal cancer and mild to moderate depression for six weeks. The authors reported a better improvement in celecoxib group [49].

Similarly, Mohammadinejad and his colleagues compared depressive symptoms between two arms who were treated with celecoxib (400 mg/d) or diclofenac (50 mg/d) in 52 outpatients with breast cancer and mild to moderate depression for 6 weeks. They also, showed that celecoxib group had better improvement in depressive symptoms, significantly [50].

In addition, another research conducted to evaluate celecoxib`s effect in comparison with placebo added to an antibiotic in patients with brucellosis on depressive symptoms. Researchers showed after eight week study on 40 subjects that celecoxib had superiority to placebo [51].

Obsessive-compulsive disorder

There are two Randomized-controlled trials which have investigated celecoxib as add-on therapy in order to treat Obsessive-Compulsive Disorder (OCD).

The first one is an eight-week study that compared celecoxib (200 mg/twice per day) plus fluoxetine (20 mg/d) with placebo plus fluoxetine in 50 patients with OCD. This study showed that celecoxib arm had more reduction in total score of Yale-Brown Obsessive-Compulsive Scale (YBOCS) over the trial [52].

Similarly, the second one was conducted to compare celecoxib (200 mg/twice per day) with placebo as an add-on to fluvoxamine in 50 patients with OCD over ten weeks. Researchers mentioned that celecoxib arm showed more rapid response and greater improvement in total score of YBOCS [53].

Bipolar disorders

Similarly, there are some studies about the effects of celecoxib in bipolar patients.

A study investigated 28 patients with acute episode of depressive or mixed Bipolar Disorder who were stable on treatment of a mood stabilizer or atypical antipsychotics. Patients randomized to celecoxib (400 mg/d) or placebo as an additional treatment for six weeks. The study showed that there was no significant difference after the

ISSN: 2332-3469

second week until the end of the trial, whereas researchers reported a significant difference between 2 arms in the first assessment at the end of first week [54].

Arabzadeh and her colleagues also conducted a six-week trial on 46 inpatient manic patients without psychotic features to compare celecoxib (400 mg/d) with placebo plus sodium valproate. They reported that there was significant improvement in symptoms of mania at final point of assessment in celecoxib arm [55].

In another study, celecoxib was compared to placebo added to lithium or risperidone in 42 adolescent manic patients for eight weeks. Researchers mentioned that there is a more improvement in manic symptoms in celecoxib arm significantly [56].

In addition, a study assessed 35 manic patients who were under Electroconvulsive Therapy (ECT) and were randomized to 2 arms, celecoxib and placebo as adjunctive therapy, in order to evaluate treatment response and Brain-Derived Neurotrophic Factor (BDNF). The authors reported no difference between two groups in assessed items [37].

Finally in another multicenter trial 240 depressed patients of Bipolar Disorders randomized to four arms, celecoxib plus placebo, Minocycline plus placebo, both of active drugs and two type of placebo in addition to Treatment As Usual (TAU) for 12 weeks. The authors concluded that both of the drugs could be effective to treat depressive symptoms in Bipolar Disorders [57].

Cocaine dependence

There is only one trial in order to evaluate the effect of celecoxib (200 mg/d) in comparison to placebo in addition to Cognitive-Behavior Therapy (CBT) in 23 cocaine dependent patients for eight weeks. Celecoxib arm didn`t show a better improvement over the period of this trial compared to placebo arm [58].

Conclusion

Celecoxib is reported to be an effective treatment for various psychiatric disorders including depression, schizophrenia and OCD. Although evidences are less robust for OCD, results for Bipolar disorder are variable and inconclusive and several confounding factors such as interaction of celecoxib and lithium, difference range of diagnosis and comorbidities have not been clearly studied and need further investigations. These ambiguities make future studies on role of celecoxib in Bipolar Disorder a challenging task.

More studies with larger sample sizes are required to evaluate the use of this safe and interesting drug in psychiatric conditions and obtain an acceptable clinical suggestion.

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