Rev Psiquiatr Salud Ment (Barc.). 2017;10(2):104–112

Revista de Psiquiatría y Salud Mental

www.elsevier.es/saludmental

REVIEW ARTICLE

Efficacy and safety of ketamine in bipolar depression: A systematic review☆

Susana Alberich[a], **Mónica Martínez-Cengotitabengoa**[a,b], **Purificación López**[a,d], **Iñaki Zorrilla**[a,d], **Nuria Núñez**[a], **Eduard Vieta**[c], **Ana González-Pinto**[a,d,*]

[a] *Servicio de Psiquiatría, Hospital Universitario Araba, Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Instituto de Investigación Sanitaria BIOARABA.OSI Araba, Vitoria, Spain*
[b] *Universidad Nacional de Educación a Distancia (UNED)-Centro Asociado de Vitoria, Vitoria, Spain*
[c] *Unidad de Trastorno Bipolar, Instituto de Neurociencias, Hospital Clínic, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Universidad de Barcelona, Barcelona, Spain*
[d] *Universidad del País Vasco, Departamento de Neurociencias, Vitoria, Spain*

Received 21 March 2016; accepted 12 May 2016
Available online 30 May 2017

KEYWORDS
Bipolar depression;
Ketamine;
Efficacy

Abstract The depression is the most prevalent state throughout the life of the bipolar patient. Ketamine has been shown to be an effective and rapid treatment for depression. The objective of the present work is to perform a systematic review on the efficacy and safety of ketamine as treatment of bipolar depression, as well as its different patterns of administration. The search found 10 relevant manuscripts that met the inclusion criteria: one clinical trial, 5 cohort studies, and 4 case reports. Intravenous infusion was used in 60% of the studies. According to data, ketamine seems to be an effective and safe treatment for bipolar depression, although the length of its effect is short. Adverse effects observed generally occurred at the time of infusion, and tended to completely disappear within 1–2 h. Therefore, more studies are necessary to explore new patterns of administration, as well as on its safety and adverse effects.

PALABRAS CLAVE
Depresión bipolar;
Ketamina;
Eficacia

Eficacia y seguridad de la ketamina en depresión bipolar: una revisión sistemática

Resumen El componente depresivo es el más prevalente del trastorno bipolar. La ketamina ha mostrado eficacia y rapidez como tratamiento de episodios depresivos. El objetivo del presente trabajo es realizar una revisión sistemática sobre la eficacia y seguridad de la ketamina como

☆ Please cite this article as: Alberich S, Martínez-Cengotitabengoa M, López P, Zorrilla I, Núñez N, Vieta E, et al. Eficacia y seguridad de la ketamina en depresión bipolar: una revisión sistemática. Rev Psiquiatr Salud Ment (Barc). 2017;10:104–112

* Corresponding author.
E-mail address: anamaria.gonzalez-pintoarrillaga@osakidetza.eus (A. González-Pinto).

tratamiento de la depresión bipolar, y sus tipos de administración. Se obtuvieron 10 artículos relevantes que cumplían con los criterios del estudio: un ensayo clínico, 5 estudios de cohorte y 4 series de casos. La forma de administración utilizada en el 60% de los trabajos fue la infusión intravenosa. La ketamina parece ser un tratamiento seguro y eficaz para la depresión bipolar, aunque la duración de la acción es breve. Los efectos adversos que se observaron se produjeron generalmente en el momento de la infusión y tendieron a desaparecer completamente al cabo de 1-2 h. Por tanto, es necesario realizar más estudios para explorar nuevas vías de administración, así como su seguridad y efectos adversos.

Introduction

Bipolar disorder (BD) is one of the most incapacitating medical diseases and it is also one of the most costly for the healthcare system.[1] Depression, dysthimia and mixed states as a whole are the most prevalent components of BD.[2] Although effective treatments for bipolar depression exist,[3–6] a significant number of cases are resistant due to lack of efficacy or intolerance of side effects. There is therefore a major need to develop new drugs with a rapid antidepressive effect, given the risk of suicide among these patients.[7]

During the last decade, several studies have shown that the glutamatergic system and most particularly the N-methyl-D-aspartate receptor (NMDA) are involved in the efficacy of antidepressive treatments, which makes it a target for the development of new treatments.[7] Ketamine is a phencyclidine derivate and NMDA receptor antagonist which has been shown to have a swift and potent effect against depressive episodes at sub-anaesthetic doses.[8,9] In the case of unipolar depression at least 8 clinical trials have been published that showed ketamine to be fast-acting and effective in this diagnostic group.[10–17]

This review has the aim of systematically analysing and summarising the scientific evidence of the most recent works on the efficacy and safety of using ketamine to treat bipolar depression, as well as its different forms of administration.

Material and methods

The PubMed and Embase databases were searched electronically. The search was restricted to prospective works, series of cases or clinical trials published in English or Spanish from January 2012 to October 2015. The following MESH terms were used: ''ketamine'', ''bipolar disorder'' and ''bipolar depression''. The strategy was restricted to studies undertaken in human beings. A manual search was subsequently performed together with a reverse search based on the works selected. The publications which included patients diagnosed BD were included. Works with samples containing patients with a different diagnosis were excluded from the study, as were those which did not evaluate the efficacy of ketamine in cases of depression.

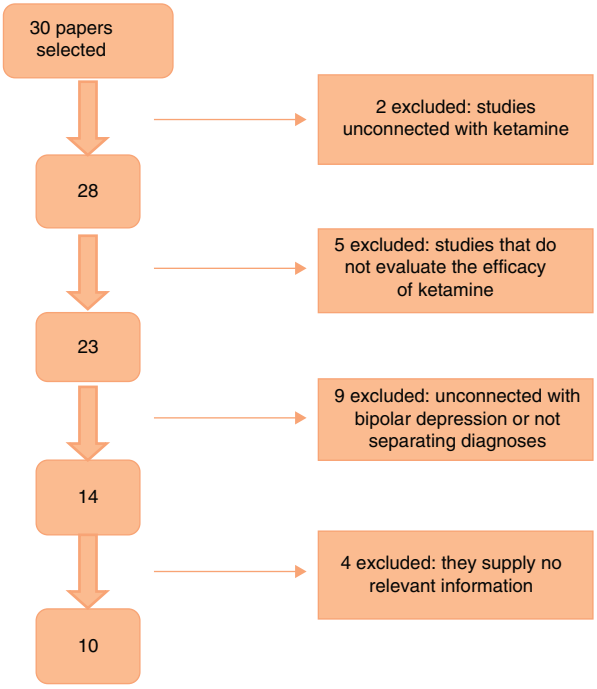

Figure 1 Paper selection flow.

The papers were summarised and evaluated using the on-line tool ''Osteba Fichas de lectura crítica''(FLC).[18] This tool makes it possible to read papers in detail and determine their methodological quality. This selection and data extraction process was undertaken by 2 reviewers, who in case of disagreement met to decide which works to include or exclude from the review, or regarding the quality of a paper.

Fig. 1 shows the paper selection flow based on PRISMA[19] methodology.

Results

The first search found a total of 30 papers, of which 10 that fulfilled inclusion criteria and contained relevant information were selected. No work selected by manual or reverse search was selected. Of the works selected, one is a clinical trial, 5 are cohort studies and 4 are case series (as shown