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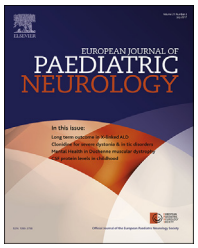

Original article

Clonidine adhesive patch for the treatment of tic disorders: A systematic review and meta-analysis

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ABSTRACT

Objective: The aim of this study was to evaluate the efficacy and safety of clonidine adhesive patch for tic disorders (TDs).

Methods: Medline, Embase, Cochrane central register of controlled trials and Chinese databases of CBM, CNKI were searched from inception to 08.2016 for randomized controlled studies (RCTs), open-label control studies of clonidine adhesive patch versus other medications or/and placebo for TDs. The cochrane Handbook for Systematic Reviews of Interventions was used to guide our study.

Results: Six studies involving 1145 participants were included in this study. Among these studies, two study ($N = 513$ patients) used placebo as a control and four studies ($N = 632$ patients) used positive drug controls. The results of meta-analysis suggested that clonidine adhesive patch may be as effective as haloperidol or tiapride for TDs. Adverse events (AEs) were reported in all studies, and the most common AEs of clonidine adhesive patch were rash (8.9%), lightheadedness (8.0%), dry mouth (4.0%). The AEs of clonidine adhesive patch were slight.

Conclusion: These data provide moderate quality evidence that clonidine adhesive patch might be an effective and safe treatment option for TDs, and results from further trials are urgently needed to extend the evidence base.

1. Introduction

Tic disorders (TDs) are common in children and adolescents, characterized by fast, sudden, non-rhythmic, repetitive and stereotyped phonic production and/or motor movements.[1–3] Tics are often associated with a diminished quality of life and functional impairment.[4,5] Currently, TDs have been managed with antipsychotics such as tiapride and haloperidol,[6–8] despite their efficacy, the side effects may limit

Abbreviations: TDs, tic disorders; RCTs, randomized controlled studies; YGTSS, Yale Global Tic Severity Scale; ICD-10, the international classification of diseases-10; DSM-IV, the diagnostic and statistical manual of mental disorders-IV; CCMD, the Chinese classification and diagnostic criteria of mental disorders; TESS, treatment emergent symptom scale.

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their clinical application,[9] so it is necessary to develop new pharmacotherapy for TDs.

Previous studies have suggested that oral and transdermal clonidine was an effective treatment for TDs in children and adolescents with a safer and better-tolerated profile.[10–12] Six RCTs of oral and the transdermal Clonidine provided a moderate degree of evidence quality that it was superior to placebo.[13] Clonidine is a 2-adrenoceptor agonist that can decrease the functional activity of the noradrenergic system, and the clonidine adhesive patch is an adhesive patch that releases clonidine at a relatively invariable rate for one week without "valley or peak" plasma concentration changes.[14,15] Because of its ease of use (self-administered patch, changed only at weekly intervals, easy disposal and a rapid onset of action), it might be an ideal medication for TDs. However, there is no systematic review and meta-analysis of the clonidine adhesive patch for TDs.

The primary aim of the systematic reviews and meta-analysis was to evaluate the efficacy of clonidine adhesive patch for TDs, and particular attention was also paid to the safety and tolerability of clonidine adhesive patch.

2. Methods

The protocol used for reviewing clonidine adhesive patch for TDs has been published online (http://www.crd.york.ac.uk/prospero/). The registration number is CRD42016048163 at the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[16]

2.1. Inclusion and exclusion criteria

According to the PICOS principles, the following selection criteria were used to conduct our study. Participants (P): patients with TDs according to these diagnostic criteria (1) the International Classification of Diseases-10 (ICD-10)[3] (2) the Diagnostic and Statistical Manual of Mental Disorders-III (DSM-III), DSM-IV, DSM-V,[1,17,18] and (3) the Chinese Classification and Diagnostic Criteria of Mental Disorders (CCMD).[20] Intervention (I): clonidine adhesive patch, placebo or/and other treatments. Comparison (C): clonidine adhesive patch versus other medications and/or placebo. Outcomes (O): efficacy and safety. The outcomes of the efficacy were assessed based on the following standard tools: Yale Global Tic Severity Scale (YGTSS), and the adverse events (AEs) was assessed by the scales including the Treatment Emergent Symptom Scale (TESS) or other scales.[19] Study design (S): RCTs and open-label control studies reporting the efficacy and safety of clonidine adhesive patch for TDs. Case series, reviews and non-original research (reviews and meta-analyses) were excluded.

2.2. Search strategy

A search of the medical literature using Embase, Medline, the Cochrane central register of controlled trials and Chinese databases of CBM, CNKI was conducted from inception to 08.2016. The terms clonidine adhesive patch or transdermal clondine patch or transcutaneous clondine patch and tic disorder [mesh] or tics or tourette syndrome were combined for searching relevant studies.

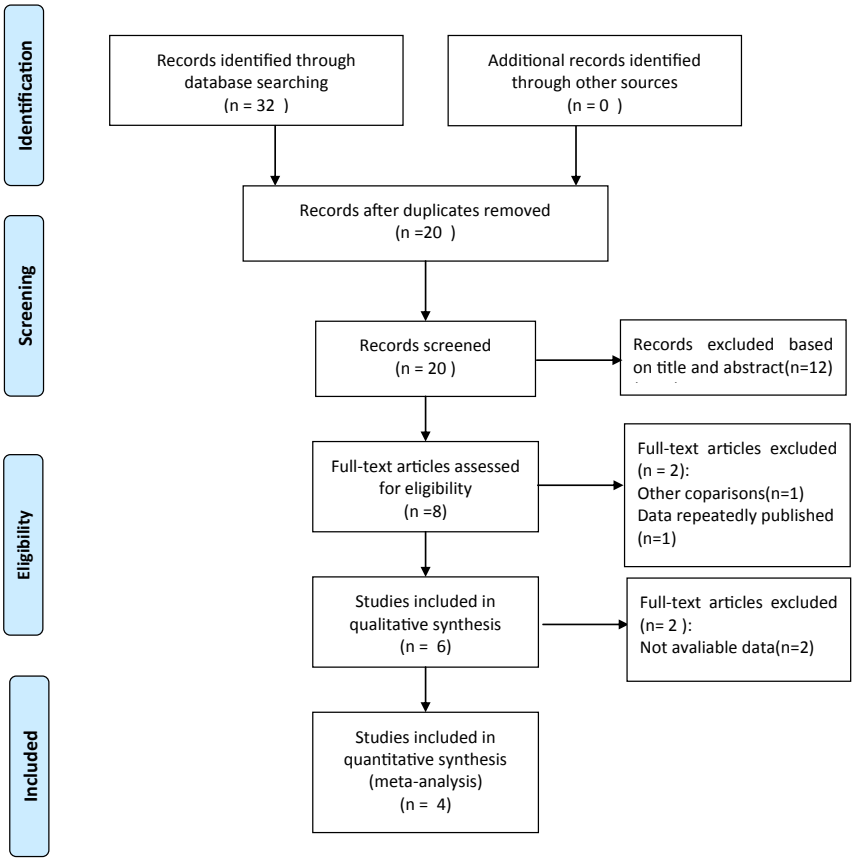

Fig. 1 – Flow chart of literature screening and the selection process.