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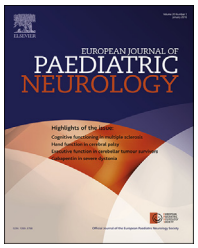

Original Article

Clinical observation on treatment of Tourette syndrome in Chinese children by clonidine adhesive patch

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ABSTRACT

Objective: To evaluate the therapeutic effectiveness and safety of clonidine adhesive patch in treating Tourette syndrome (TS).

Methods: From July 2010 to July 2014,a total of 261 children, who met the Chinese Classification of Mental Disorders (third edition) diagnostic criteria for TS, aged 5–12 years, were referred to the department of Pediatrics, Shaanxi Provincial People's Hospital. The patients were divided randomly into a treatment group (clonidine adhesive patch, n = 128) and a control group (haloperidol, n = 116), 17cases dropped out. The clinical effectiveness was assessed by the Yale Global Tic Severity Scale (YGTSS) at the end of fourth week. The short-term effectiveness and adverse reaction to the treatment were assessed at the end of treatment.

Results: The YGTSS score in both groups decreased after 4 weeks of treatment, but the clonidine adhesive patch group showed a higher reduction in the overall tic symptom scores (40.05 ± 3.44%) than that of the control group (17.88 ± 4.40%; $P < 0.05$). In the clonidine adhesive patch group, the effectiveness was 81.3% (effective in 104 patients), while it was 66.4% in the control group (effective in 77 patients). The overall effectiveness rate showed no statistical significance between the two groups ($p > 0.05$). There were no severe adverse events in both groups, but mild side effects (decrease of blood pressure and dizziness) were observed in 3 patients in the clonidine adhesive patch group. 2 had mild cervical muscle tension and 4 had mild drowsiness and fatigue in the control group.

Conclusion: In the treatment of TS in children and adolescents, the clonidine adhesive patch is superior to the standard treatment with haloperidol with a safer and better-tolerated profile.

Abbreviation: TS, Tourette syndrome; YGTSS, Yale Global Tic Severity Scale; CGI, Clinical Global Impression scale; TTS, transdermal therapeutic system.

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1. Introduction

Tourette syndrome (TS) is a neurodevelopmental disorder defined by childhood onset of motor and phonic (vocal) tics, lasting a cumulative total of at least 1 year, in the absence of a known medical cause.[1] The prevalence of TS varies widely based on study design and location; an international prevalence of 0.6–1% has been reported for mainstream school age children.[2] It is often cause of difficulties for children both at home and at school. If behavioral intervention is ineffective and unavailable, pharmacotherapy should be considered.[3] The α-2-adrenoceptor agonists guanfacine and clonidine are usually recommended as initial pharmacotherapy in the United States and Canada, primarily because of their preferable side-effect profile, compared with anti-psychotics as haloperidol.[4] Clonidine, whose main site of action is the locus ceruleus, decreases the functional activity of the noradrenergic system.[5] Several studies have demonstrated beneficial effects on tic disorders, particularly Tourette disorder.[6] The clonidine adhesive patch is a transdermal therapeutic system (TTS), an adhesive patch that releases clonidine at a relatively constant dose for 7 days without "peak or valley" plasma concentration changes.[7] A study compared clonidine adhesive patch to placebo in 437 children and adolescents and reported efficacy.[8] The aim of the study was to assess the therapeutic effectiveness and adverse effects profile of the clonidine adhesive patch comparing with oral haloperidol treatment.

2. Materials and methods

2.1. Participants

The study group was composed of children with TS who met the Chinese Classification of Mental Disorders-third edition (CCMD-3)[9] criteria for Tourette disorder, and were aged 5–12 years. This research selected 261 children in the department of Pediatrics, Shaanxi Provincial People's Hospital. Participants with an intellectual disability or drug allergy for more than two medicines including the clonidine adhesive patch were excluded from the sample studied, 17 cases dropped out. Informed consent was obtained from the parents of all patients as a condition of study enrollment, and the study was carried out with pre-approval by the local Medical Ethics Committee. We divided the patients into two groups, one treated with clonidine adhesive patch (n = 128, 97 males and 31 females, mean age 9.1 years-old) and the other treated with haloperidol (n = 116, 90males and 26 females, mean age 7.8 years-old). The subject group had a male to female ratio of 3.28:1. The average duration of symptoms was 1.9 years. Data on age of treatment, age of onset, and the course of the disease are demonstrated in Table 1.

2.2. Methods

YGTSS is a semi-structured clinician-rated instrument of motor and vocal tic severity.[10] It consists of two domains: motor and vocal tics, assessed on frequency, intensity, complexity and interference. It has robust psychometric properties as a measure of change in tic severity and has been used in a number of studies internationally.[11–13] The Clinical Global Impression scale (CGI) consists of 0–7 points. It is used to evaluate the severity of clinical symptoms and measure change in them over the course of the study.

Changes in the rating scale scores and a reduction rate indicate changing in symptoms. Affected patients who came to the hospital for the first time received an assessment by specially trained doctors, with screening for motion tics, vocalization tics, and functional impairment level, with the sum of the three scores indicating the total twitch score. After 4 weeks of treatment, the doctors carried out the YGTSS again to assess the score. The assessment index for the treatment is determined by the reduction in the value of the scores, divided by the base score.

Reduction Rate was calculated by the following formula: Reduction Rate = (total score before the treatment − total score after the treatment)/total score before the treatment*100.

The treatment was considered effective when the reduction rate was greater or equal than 50% and ineffective when the reduction rate was less than 50%.

The dosage of the clonidine adhesive patch was given to patients according to their weight in three different doses. The patients with weight between 20 and 40 kg were given 1.0 mg/film; patients with weight of 41–60 kg were given 1.5 mg/film and those with weight greater than 60 kg were given 2.0 mg/film. For maximum benefit, patches were affixed to the skin of the lower subscapular corner, and replaced once per week, for a total of four weeks. When each new patch was replaced, the patch was also switched to a new location, usually to the contralateral scapula. The haloperidol group was given a small dose of combination of Haloperidol-Antin treatment. Both doses were 0.5–0.7 mg/time, twice a day (morning and evening), applied orally. If relief of symptoms was not obvious, the dose was increased by 0.25 mg, with the maximum dose being 1 mg/time.[14] According to the date visiting the doctor, we distribute the drug.

2.3. Statistical analysis method

Count data was analyzed using a χ^2 test, and measurement data using an independent sample *t* test. SPSS13.0 was used to conduct statistical analysis.

Table 1 – Characteristics of compared group of patients.

Group	Numbers	Age (years)	Gender		Duration of Illness (years)	Age of Illness onset
			M	F		
Control (haloperidol)	116	7.8 ± 1.5	90	26	1.8 ± 0.8	6.2 ± 1.8
Treatment (clonidine)	128	8.5 ± 2.7	97	31	1.3 ± 0.2	7.5 ± 2.3