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Journal of Affective Disorders 89 (2005) 183–188

JOURNAL OF AFFECTIVE DISORDERS

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Brief report

MAOI efficacy and safety in advanced stage treatment-resistant depression—a retrospective study

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Received 12 January 2005; accepted 20 June 2005
Available online 6 October 2005

Abstract

Objective: Evidence-based data suggest that MAOI therapy may be effective in up to 50% of patients with treatment-resistant depression (TRD). We hypothesized that MAOI therapy is similarly effective in patients with advanced stage TRD who are unresponsive to ≥ 4 prior antidepressant drug (AD) trials compared to patients with early stage TRD who are unresponsive to ≤ 3 prior AD trials.

Methods: To test this hypothesis, data were harvested from 400 patient charts. Of these, 59 patients received a total of 75 MAOI treatment trials. 50 patients had 1 MAOI trial and 9 patients had 2 or more MAOI trials. Response was assessed using the Clinical Global Impressions Change (CGI/C) scale.

Results: 56% of MAOI trials resulted in a CGI/C score of 1 ("very much better") or 2 ("much better"). Only 25% resulted in a CGI/C score of 4 or more ("no change" or "worse"). 32.5% of MAOI trials resulted in a CGI/C score of 1 in patients with early stage TRD, while only 12.1% of MAOI trials resulted in a CGI/C score of 1 in patients with advanced stage TRD ($p=0.04$). There was a significant negative correlation between the number of prior, failed AD trials and the final CGI/C score ($p=0.03$). The odds associated with attaining a CGI/C score of 1 diminished by a factor of 30% with each prior failed AD trial. We observed only 1 case of acute hypertension which responded to sublingual nifedipine therapy.

Limitations: The sample size was limited, and MAOI outcome was not compared with other AD therapy. The adequacy of prior AD trials could not always be verified.

Conclusion: These data suggest that MAOI therapy may be beneficial in patients with early stage TRD who are unresponsive to ≤ 3 prior treatments. However, the relative efficacy of MAOI therapy in advanced stage TRD remains uncertain.
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Keywords: Monoamine oxidase inhibitor; MAOI; Treatment-resistant depression; Major depression; Treatment outcome

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0165-0327/$ - see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.jad.2005.06.011

1. Introduction

Treatment-resistant depression (TRD) occurs along a continuum from early stage non-response to initial antidepressant drug (AD) therapy to advanced stage non-response to multiple prior AD trials. While much attention has been focused on developing treatment algorithms for early stage TRD (Lavori et al., 2001; Adli et al., 2002), less attention has been given to the study of advanced stage TRD (Amsterdam, 1991; Amsterdam and Chopra, 2001). Several evidence-based reports have suggested that monoamine oxidase inhibitors (MAOIs) may be effective for TRD (Anderson et al., 2000; Karasu et al., 2000; Thase et al., 1995). Most clinical trials of MAOI therapy have shown good efficacy in early stage TRD (Nolen et al., 1985, 1988a,b; Thase et al., 1992a,b, 1995; McGrath et al., 1993; Thase and Rush, 1995). Fewer studies, however, have examined MAOI therapy in advanced stage TRD. An early study of high-dose tranylcypromine in 14 patients with advanced stage TRD found a response rate of 70% and a remission rate of 50% (Amsterdam, 1991).

In the present study, we hypothesized that MAOI therapy may have similar efficacy in patients with early stage TRD (unresponsive to ≤3 prior AD trials) and advanced stage TRD (unresponsive to ≥4 prior AD trials). To test this hypothesis, we retrospectively examined the efficacy and safety of MAOI therapy in 59 patients with TRD.

2. Methods

2.1. Patient sample

The purpose and procedures of this study were reviewed and approved in accordance with the ethical standards of the Institutional Review Board of the University of Pennsylvania. Data were harvested from 400 randomly selected clinical charts of patients treated between 1983 and 2002. 59 patients (15%) with DSM III, DSM III-R, or DSM IV major depressive episode (MDE) were identified who received a total of 75 MAOI trials in the current episode: 50 patients received one MAOI trial, and 9 patients received ≥2 MAOI trials. Adequacy of prior AD therapy before receiving a MAOI was assessed for each treatment and based upon the minimum dose and treatment duration listed in Table 1.

2.2. Efficacy ratings

Efficacy was retrospectively assessed using the Clinical Global Impression Change (CGI/C) scale (Guy, 1976) which compared the index MAOI trial response to the AD treatment received just prior to MAOI therapy.

2.3. Safety

Treatment-emergent adverse events during MAOI therapy were retrospectively assessed. Particular attention was given to the type and severity of cardiovascular events. These included changes in resting systolic and/or diastolic blood pressure, hypertension, orthostatic hypotension, and symptoms such as lightheadedness, dizziness, and headaches.

2.4. Statistical methods

The primary outcome was CGI/C score of 1 ("very much better"), 2 ("much better"), 3 ("minimally better"), 4 ("no change"), 5 ("minimally worse"), and

Table 1
Adequacy of antidepressant dose and treatment duration

Drug/ECT	Minimum dose (mg/day)	Duration (weeks)
SSRIs		
Fluoxetine, paroxetine, citalopram	20	6
Sertraline	100	6
TC As		
Imipramine, amitryptyline, desipramine	150	4
Doxepin, clomipramine	150	4
Nortryptyline	100	4
Protryptyline	30	4
Bupropion	225	4
Maprotiline	150	4
Trazodone, nefazodone	300	4
Mirtazepine	30	4
MAOIs		
Tranylcypromine, isocarboxazid, selegiline	30	4
Phenelzine	45	4
ECT	6 sessions	2

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