20mg transdermal selegiline daily may be effective and well tolerated in adults with major depression


QUESTION: Is transdermal selegiline safe and effective for adult outpatients with major depressive disorder?

Participants

Participants were 177 outpatients who met the DSM-IV criteria for major depressive disorder (single episode or recurrent) and had no other primary psychiatric diagnosis. Mean age 42 years (range 20–65); 53% women; 95% white. All participants were free of any psychoactive drug within 6 months; exposure to ECT within 90 days; pregnant or breastfeeding women; women of childbearing age not using adequate birth control, or failure to respond to more than one approved antidepressant for the current episode of depression.

Intervention

Following assessment using the DSM-IV Structured Clinical Interview and a week-long placebo lead-in, participants received either 6 weeks of 20 mg per day selegiline (delivered via 20 cm² transdermal patch) or placebo. All participants followed a tyramine-restricted diet during treatment and for two weeks afterwards.

Main outcome measures

Treatment response was measured using the 17 and 28-item versions of the Hamilton Depression Rating Scale, the Montgomery-Asberg Depression Rating Scale and the Clinical Global Impression severity and improvement measures.

Main results

The transdermal selegiline group showed greater improvement on all measures of depression compared with placebo. The selegiline group had 46% greater improvement on the 17-item Hamilton Depression Scale, 52% greater improvement on the 28-item Hamilton Depression Scale and 79% greater improvement on the Montgomery-Asberg Depression Rating Scale. Differences were observed as early as the first week of treatment. There were no differences in adverse events between groups, apart from site reactions which were more common with selegiline (number needed to harm one person 5, 95% CI 3 to 16, absolute risk increase 19%, 95% CI 6% to 32%). No orthostatic hypotensive or hypertensive reactions were reported (table).

Conclusions

6-week treatment with transdermal selegiline appears to be safe and well tolerated for adults with major depression. No adverse effects associated with traditional monoamine oxidase inhibitor antidepressants were reported.

COMMENTS

Over the past five decades we have learnt that monoamine oxidase inhibitors (MAOIs) are broadly effective and useful for depressive disorders, including atypical, chronic and double depressions.1 MAO-A is the predominant isoenzyme in the digestive tract. Inhibiting MAO-A may cause hypertension following the ingestion of tyramine (the “cheese reaction”). Although at low doses selegiline is a selective inhibitor of MAO-B, the high doses usually necessary to achieve antidepressant efficacy present the familiar dietary tyramine interaction.2 Transdermal selegiline has much less effect on gut wall MAO-A, thus minimising the risk of interaction with dietary tyramine.

Bodkin et al describe the first reported clinical trial of transdermal selegiline for major depression. Transdermal selegiline was superior to placebo on all measures of efficacy. Site reactions were more common with selegiline, however, only 3 out of 89 participants discontinued treatment due to local reactions.

The participants followed a tyramine-restricted diet so the risk of a “cheese reaction” could not be assessed. A previous study found that doses of 200 mg or more of oral tyramine were required to produce a pressor response in people receiving selegiline. This far exceeds the usual content of a tyramine-rich meal, which may contain up to 40 mg.3

Several drugs are currently available for transdermal delivery, including estradiol, testosterone, nicotine and clonidine. Besides avoiding first-pass metabolism, the transdermal route offers more constant blood levels and improved compliance.4 If future trials confirm the characteristics of this new antidepressant, transdermal selegiline may be an effective alternative for people with depression.

Eliana Benedictis, MD 
Paradise International
São Paulo, Brazil

1 Robinson DS. Monoamine oxidase inhibitors: a new generation. Psychopharm Bull 2002; 36; 124–8.2


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