Erwin A. Douwes

New Data on Lerivon (Mianserin)

Streszczenie
Praca omawia porównanie mianseryny, moklobemidu, fluoksetyny, fluwoksaminy i amitryptyliny pod względem uzyskanego stopnia poprawy oraz wyniki leczenia mianseryną stanów przewlekłego bólu i migren (red.).

Introduction

Mianserin (Lerivon, Organon) first became available in 1974 in Switzerland. Also in Poland mianserin has been available for many years. As one of the first antidepressants of a new generation mianserin offers an improved acceptability and safety profile in comparison with the conventional tricyclic antidepressants. In the passed twenty years many studies have been published about mianserin. Some recently published data on interesting subjects regarding mianserin will be summarized in this article.

Comparison of mianserin with moclobemide

In a double-blind clinical trial mianserin was compared to the reversible MAO-A inhibitor moclobemide (Aurorix, Roche) in the treatment of 20 elderly patients with major depression (Tiller 1990). Dosage regimen: initial dose of moclobemide was 150 mg with increase up to 600 mg per day divided over three doses (mean 412 mg/day); mianserin was started at 30 mg and was increased up to 90 mg per day also divided over three doses (mean 85 mg/day). The severity of depression was assessed with the HAMD and a self-rating scale: the Carroll Depression Rating Scale (CDRS) at baseline, and after 4 and 8 weeks. After 8 weeks of treatment there was a significant reduction of both the HAMD and the CDRS score for both groups. The efficacy of mianserin however, tended to be better than that of moclobemide. This difference reached statistical significance when scored with the CDRS. In addition, the effect of both drugs on the level of anxiety was assessed with the Spielberger State-Trait Anxiety Inventories (STAI-X1 and STAI-X2). Both drugs exhibited a significant decrease in anxiety scores. The anxiolytic effect of mianserin however seems stronger (see fig. 1).

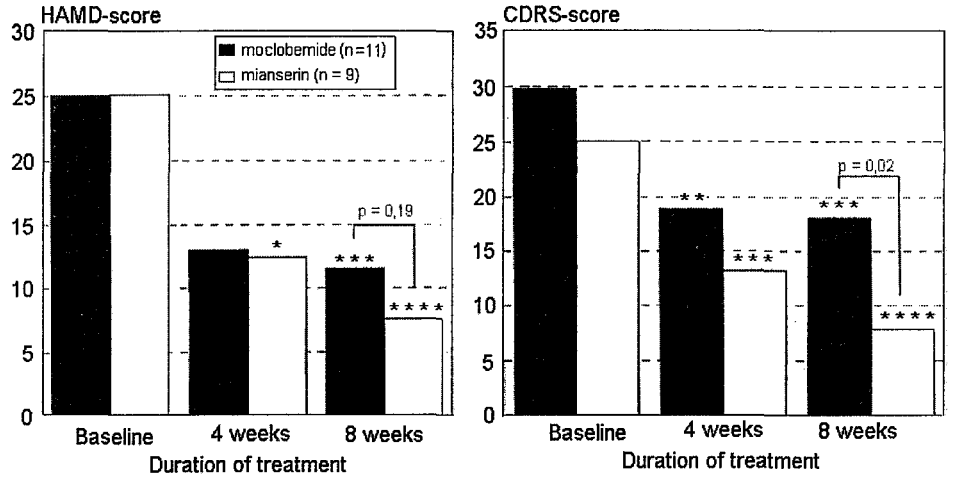

Fig. 1. Double-blind comparison of mianserin and moclobemide in the treatment of elderly depressed patients (n = 20)

Comparison of mianserin with fluoxetine

In a double-blind study mianserin was compared with fluoxetine in 65 depressed outpatients (Besançon 1993). Patients were started on 60 mg of mianserin or 20 mg of fluoxetine at night. After two weeks the dose could be increased in the event of inadequate clinical response with an additional morning dose of 30 mg mianserin or 20 mg fluoxetine. The severity of the depressive symptoms was assessed using the Montgomery Åsberg Depression Rating Scale (MADRS). Both drugs were shown to be effective as demonstrated by the statistically significant score reduction in comparison with baseline values. The score reduction was more marked in the mianserin group but the difference did not reach statistical significance. In addition,

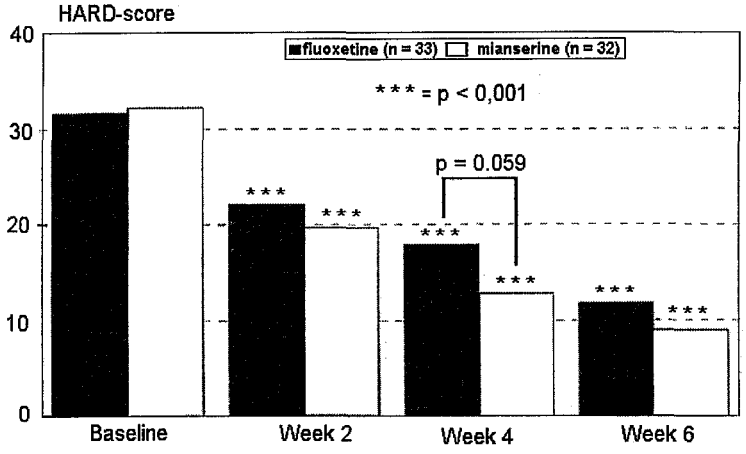

Fig. 2. Double-blind comparison of mianserin with fluoxetine (n = 65)

the drug effects were also rated with the HARD diagram. The HARD diagram is composed of four factors:

H = Mood (sadness, disinterest, appetite)
A = Anxiety (psychic anxiety, somatic anxiety, insomnia)
R = Retardation (fatigue, concentration, attitude)
D = Danger (depreciation, suicidal thoughts, delirious ideas)

With the HARD score, the effect of mianserin was again more pronounced than the effect of fluoxetine. This difference almost reached statistical significance after 4 weeks of treatment (see figure 2).

Effect of mianserin on sleep in comparison with fluoxetine

In the same study by Besançon mianserin was superior to fluoxetine with respect to various sleep parameters: total sleep time, fitful sleep, nocturnal awakening, early morning awakening, refreshing sleep. The sleep improving effect could be even more pronounced if mianserin would have been administered as a ones daily nighttime dose for all patients. This regimen has proved to improve sleep and reduce daytime drowsiness in comparison with a regimen of dose distribution over the day (Montgomery 1980).

Comparison of mianserin with fluvoxamine

The efficacy of mianserin was compared with the selective serotonin reuptake inhibitor fluvoxamine in a double-blind randomized trial (Perez 1990). The data of 63 patients (mianserin 33, fluvoxamine 30) with major depression were analyzed. Dosage regimen for mianserin was 60 mg per day starting dose and, if necessary, after one week dose increase to a maximum of 180 mg per day; for fluvoxamine the starting dose was 100 mg and dose increase up to a maximum of 300 mg. The severity of depression was assessed with the Montgomery

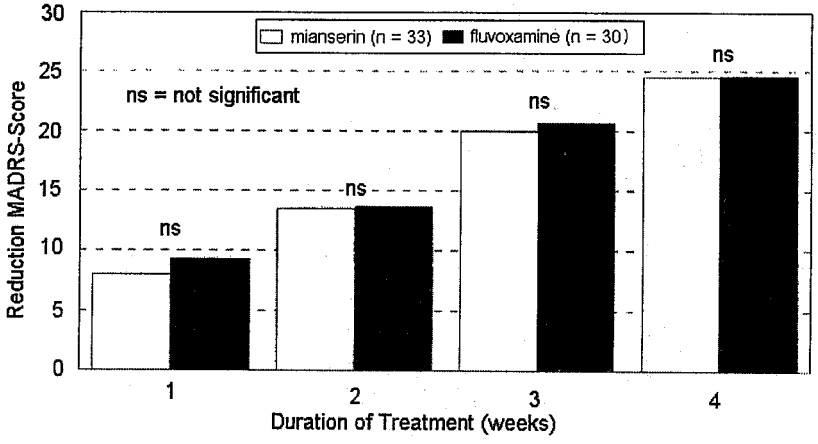

Fig. 3. Double-blind comparison of mianserin and fluvoxamine (n = 63)

Åsberg Depression Rating Scale (MADRS). In figure 3 the reduction in MADRS-score for both drugs is reflected. No significant differences were found. Therefore, it is concluded that mianserin and fluvoxamin are equally effective in the treatment of patients with major depression.

More rapid onset of action of mianserin in comparison with amitryptyline?

Recent data from well-designed clinical trials suggest that there could be a more rapid onset of antidepressant activity in patients using mianserin in comparison with those using amitriptyline. In 1991 Carman published a study about the use of mianserin in moderately to severely depressed outpatients (Carman 1991). In this trial mianserin was compared to amitriptyline and placebo. Dosages of up to 150 mg/day of mianserin were used in this study (average 104 mg/day). Amitriptyline was given in doses ranging from 60–300 mg. In this study the Hamilton Rating Scale for Depression was used. Concerning the antidepressant effect, the earliest statistically significant difference vs. placebo could be observed already after one week for the patients treated with mianserin and after 3 weeks for the amitriptyline treated patients. The only side effect that occured significantly more often with mianserin than with placebo was somnolence.

Wilcox et al. performed a placebo-controlled comparative trial with mianserin and amitriptyline in 149 outpatients with major depression (Wilcox 1994). Starting dose for mianserin was 30–60 mg/day and increased up to 150 mg/day. Starting dose for amitriptyline was 60–120 mg/day and increased up to 300 mg/day. HAMD-scores were taken every week for a duration of treatment of 7 weeks in total. Statistically significant reductions in the HAMD score were recorded for both active drugs compared with placebo. There were no statistically significant differences between mianserin and amitriptyline in terms of efficacy; however, the results do suggest a more rapid therapeutic response for mianserin compared with amitriptyline, in terms of percentage of patients showing > 50% improvement at weeks 2 (30% vs 23%) and 4 (61% vs 44%). The most common adverse experiences were somnolence (amitriptyline and mianserin 60%, placebo 31%) and dry mouth (amitriptyline 76%, mianserin 30% and placebo 20%).

Mianserin in the treatment of chronic idiopathic abdominal pain

Because of its antagonistic effect on both histamine-1 and 2-receptors and being an α-2 receptor blocker, mianserin could be of particular value in somatoform gastrointestinal disorders. In double-blind placebo-controlled trial mianserin was given for 8 weeks to 47 patients with chronic idiopathic abdominal pain of more than 2 years' duration (Tanum 1994). Patients with

a diagnosis of depressive or anxiety disorders were excluded. Daily dosage was 120 mg. Other psychopharmacologic or analgesic medication was not allowed during the trial. Pain response was measured objectively by means of the Clinical Global Improvement Scale and subjectively by daily self-reporting with the Visual Analog Scale. Seventy-five percent of patients on mianserin experienced major improvement, and 60% complete remission of previous symptoms. Mianserin patients experienced significantly better response than placebo patients on all parameters with p-values less than 0.0001. At follow-up 3 months after tapering of the drug, patients still experienced the degree of improvement induced by the active drug.

Mianserin in the treatment of migraine and tension headache

As an α2-adrenoceptor antagonist, mianserin could have potential as an antimigraine drug. In a study by Denaro the efficacies of the α2-agonist clonidine and mianserin were compared in two treatment groups: common migraine patients and patients with tension headache. Forty patients entered this double-blind placebo-controlled study. Placebo, clonidine 0.150 mg, and mianserin 30 mg were each administered for a period of 90 days. Headaches were induced by intravenous doses of histamine dihydrochloride. In the migraine group mianserin decreased attack frequency significantly. Duration and intensity of the attack were decreased but this did not reach statistical significance. In the clonidine group only duration of the attack decreased significanlty but not frequency and intensity. In the tension headache group both frequency and intensity of the attack were decreased significantly by mianserin. No effect was seen in patients treated with clonidine here. The efficacy of the antidepressant mianserin in the treatment of tension headache is in line with the assumption that tension headache is a monosymptomatic form of depression or a psychosomatic illness (Bakal 1977). The results in the migraine group suggest that long-term preventive treatment of migraine could be possible with drugs that inhibit the activity of presynaptic α2-receptors like mianserin.

Conclusion

During the last 20 years mianserin (Lerivon) has gained a strong position in the treatment of depression. This is mainly due to its more beneficial acceptability and safety profile in comparison with the older tricyclic antidepressants. Also when compared with newer antidepressants like the selective serotoning reuptake inhibitors (SSRI's) fluoxetine and fluvoxamine or the reversible MAO-A inhibitor moclobemide, mianserin performs well. Clinical research has demonstrated that, apart from its established value in the treatment of depression, mianserin could also prove useful for treating other disorders like idiopathic abdominal pain, tension headache, and migraine.

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