PM05051 DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF ONCE DAILY VENLAFAXINE XR AND BUSPIRONE IN OUTPATIENTS WITH GENERALIZED ANXIETY DISORDER (GAD)

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Objective: This randomized, double-blind, placebo-controlled, 8-week study compared the safety and the anxiolytic efficacy of once daily venlafaxine XR 75 mg and 150 mg with placebo and buspirone 30 mg in outpatients with GAD.

Method: Patients (n = 405) who met the DSM-IV criteria for GAD, but not for major depressive disorder, and who did not improve significantly during a 4 to 10 day prestudy washout period were randomized to double-blind treatment with venlafaxine XR 75 mg or 150 mg, buspirone 30 mg, or placebo. The venlafaxine XR 150 mg and buspirone groups had their doses titrated during the first week of therapy. Improvement was evaluated at 1, 2, 3, 4, 6, and 8 weeks using the HAM-A total score, the HAM-A psychic anxiety factor, and the Clinical Global Impressions (CGI) scale as primary outcome measures. The anxiety subscale from the Hospital Anxiety and Depression Scale (HAD) was a secondary outcome measure and the HAM-A anxious mood item was another key outcome measure. Final on-therapy was the primary time point. Significant ($p < 0.05$) results are shown for the Last Observation Carried Forward (LOCF) analysis in the intent-to-treat population (n = 369).

Results: For the HAM-A psychic anxiety, factor, venlafaxine XR 75 and 150 mg were better than placebo at week 8. For CGI severity, venlafaxine XR 75 was better than placebo at weeks 3, 4, 6, and 8. For the HAD anxiety subscale, venlafaxine XR 75 mg was better than placebo and buspirone at weeks 1 through 8; venlafaxine XR 150 mg was better than placebo at weeks 1, 3, 4, 6, and 8 and better than buspirone at weeks 3, 4, 6, and 8. For HAM-A anxious mood item, venlafaxine XR 75 and 150 mg were better than placebo at weeks 2, 4, 6, and 8. The safety profile was consistent with Effexor and venlafaxine use in depressed patients.

Conclusion: This study showed significant advantages for venlafaxine XR (75 or 150 mg/day) vs placebo to treat outpatients with GAD who do not have comorbid major depressive disorder, and suggested that venlafaxine XR has significant advantages compared with buspirone.

PM05052 EFFICACY OF NEFAZODONE IN SEXUAL DYSFUNCTION AND BODY WEIGHT INCREASE INDUCED BY OTHER ANTIDEPRESSANTS: A CASE REPORT

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Introduction: Sexual dysfunction is a well known side effect of most antidepressants which seems to be specially frequent when using selective serotonin (5-HT) reuptake inhibitors. Body weight increase is also an adverse reaction associated to many antidepressants as tricyclic compounds, mianserin and mirtazapine. Nefazodone, an antidepressant which blocks 5-HT_2 receptors and inhibits 5-HT uptake, has been claimed to be free of adverse effects on sexual function and body weight. We present two cases in which switching from previous antidepressant treatment to nefazodone was able to reverse both kinds of side effects.

Case Reports: Case 1: A 43 years old female who experienced a depressive episode with obssessive ideation. She was treated with fluvoxamine, 300 mg daily, and the symptomatology completely subdued in the course of five weeks. However, she experienced severe anorgasmia which seriously interfered her marital relations. Fluvoxamine dosage was reduced to 150 mg/day but anorgasmia persisted with the same intensity; nevertheless the patient, fearing the relapse of depression and in agreement with her partner, decided to continue on fluvoxamine. Later, when nefazodone became marketed, it was proposed as an optional agent. Accordingly fluvoxamine was discontinued and nefazodone introduced gradually; less than one month after fluvoxamine withdrawal the patient quickly recovered her sexual function. After 6 months of treatment with nefazodone 400 mg daily, she remains euthymic and with a normal sexual function.

Case 2: A 32 years old female diagnosed of major depressive disorder. Having been treated with 20 mg/day of paroxetine she complained of anorgasmia. For this reason antidepressant treatment was changed to mirtazapine 45 mg/day. Under this drug the patient continued stabilized and her sexual funtion was soon normalized; however, she gained 7 kg of body weight in a period of four months, feeling so uncomfortable that she asked to be switched again to paroxetine even considering the possibility of anorgasmia. Nefazodone was then considered as a possible alternative drug which the subject accepted to try. After 6 months of treatment with 400 mg/day of nefazodone she remains well, her sexual function is still normal and she has lost 5 kg of weight to the date.

Conclusion: Nefazodone has been shown to be an effective treatment in major depressive disorder. It is generally admitted that its 5-HT_2 receptors bloking activity prevent the appearance of sexual dysfuntion; on the other hand, probably due to its inhibition of the 5-HT reuptake, it does not induce weight gain as other 5-HT_2 antagonists like mianserin or mirtazapine do. The above described cases demonstrate that it can be considered as a first-line alternative in those patients in which sexual dysfunction and/or weight increase induced by other antidepressants have impaired their quality of life.

PM05053 GENDER-SPECIFIC SEXUAL DYSFUNCTION IN A COMMUNITY SAMPLE TREATED WITH ANTIDEPRESSANTS

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Introduction: Antidepressants are associated with sexual difficulties including reduced libido, inhibition of orgasm, and gender-specific problems such as erectile dysfunction and impaired lubrication. Both tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) have been implicated. While not life-threatening, these side-effects may impair patients' quality of life, imperil intimate relationships, and jeopardize compliance with needed treatment. Relatively little is known about the incidence of antidepressant - associated sexual dysfunction in the community. Spontaneous reporting rates substantially underestimate the problem, and confounding difficulty arises also from the fact the depression itself is commonly associated with sexual dysfunction in both sexes.

Method: After education and persuasion of family doctors, we sent a detailed, 4-page postal questionnaire to 800 patients prescribed antidepressants in general practice. Six-point Likert scales of sexual items (gender-specific and general) were embedded within a broad range of antidepressant side-effects.

Results: Interim analysis of 323 replies indicates a higher overall rate of sexual dysfunction with SSRIs (42%) than TCAs (27%). In women only, SSRIs were significantly more likely than TCAs to be associated with inhibited drive (45% vs. 20%, $p = 0.004$) and difficulty reaching orgasm (32% vs. 15%, $p = 0.03$). In males, by contrast, TCAs tended to cause greater impairment than SSRIs in getting (40% vs. 20%) and maintaining (46% vs. 29%) erections. Effects on compliance were uncertain, but more women than men tended to be non-compliant with SSRIs, possibly because of sexual dysfunction.

Conclusion: Antidepressant effects on sexual function are complex, with marked differences between men and women in response to TCAs and SSRIs. The impact of sexual dysfunction on quality of life and on compliance with treatment is likely to be significant.

PM05054 SLEEP AND ANTIDEPRESSANTS — THE IMPORTANCE OF HEALTHY NORMAL DATA

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An important symptom in depression is disturbed sleep, but with the advent of newer antidepressants the profile of antidepressant effects on sleep has become more varied. Data concerning the effects of antidepressants on sleep derived from patient studies is confounded by the fact that sleep is already disturbed because of the illness. Therefore to measure the potential of a drug to affect sleep, it is important that studies are done in healthy volunteers. A double blind placebo controlled comparison of the effects of moclobemide and dothiepin was carried out to clarify their effects on sleep. Sixteen male subjects were aged between 18 and 35 years, (median 25 years), participated in the study. The medications under investigation were moclobemide 450 mg *mane* & 600 mg *mane,* dothiepin 75 mg *nocte* & 150 mg *nocte* and placebo. They took each treatment for a period of 2 days with one dose at 0930 hours and one at 2130 hours. Each treatment period was separated by a 7 day washout period. Time in bed (TIB) in this study was kept constant, set at 480 mins with lights out at 2330 and awake time at 0730. Sleep period showed a significant treatment effect ($p = 0.003$) with both doses of dothiepin having a significantly longer sleep period than moclobemide and placebo. Sleep latency was significantly ($p < 0.001$) shorter with dothiepin than moclobemide. Neither dothiepin or moclobemide were significantly different from placebo in regard to total sleep time (TST). Sleep efficiency with moclobemide was significantly ($p < 0.001$) lower than with placebo and dothiepin. Dothiepin 150 mg had a significantly ($p < 0.001$)

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