to treatment and the zuclopenthixol serum level. 32 patients (67%) were included at least during 28 days and 19 (40%) during 80 days. Mean doses of ASP was 220 mg/injection, of AP/14 days at D 28 = 669 mg and at D 80: 555 mg. At D 28, 25 patients (78%) have been improved and 17 (89%) at D 80. The mean CF used by the improved patients was 3 at D 28 and 2.7 at D 80. It seems justified to use a CF of 3 to determine the maintenance AP dose injected each 14 days, from the mean ASP dose used during the acute phase of psychotic symptoms.

P01.62

EFFICACY OF VENLAFAXINE ER IN GAD PATIENTS WITH PREDOMINANTLY SOMATIC SYMPTOMATOLOGY

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Venlafaxine extended-release (ER) is a selective serotonin and noradrenaline reuptake inhibitor, which has been recently approved for the treatment of generalized anxiety disorder (GAD). In order to validate the efficacy of venlafaxine ER for the somatic symptoms of GAD, we examined venlafaxine efficacy on the somatic and psychic factors of the HAM-A scale[1] in patients with mainly somatic symptoms at baseline. The relative importance of somatic and psychic HAM-A factors was examined in 1841 patients from 5 double-blind, multicentre, placebo-controlled studies of venlafaxine ER efficacy in GAD, two of which had long-term extensions. At baseline, 83.6% of the 1841 patients had a ratio between the somatic and psychic factor scores lower or equal to 1. Patients with mainly somatic symptoms (somatic/psychic factors > 1; "somatizers") did not show any difference in response rates (50% decrease or greater from baseline values) to venlafaxine ER on the somatic or psychic factors after 8 weeks of treatment (54% and 63% somatic factor responders and 58% and 58% psychic factor responders for non-somatizers and somatizers respectively). Analysis of patients (767) that took part in the two 6-month study extensions revealed a trend towards an increase in both somatic and psychic response rates to venlafaxine ER in patients with mainly somatic symptoms (65% and 77% somatic factor responders and 64% and 75% psychic factor responders for non-somatizers and somatizers respectively). Venlafaxine ER induced a significantly higher percentage of somatic and psychic factors responders versus placebo at both time points.

The present study supports the efficacy of venlafaxine ER in patients with GAD, including the minority with predominantly somatic symptomatology.

(1) Hamilton, M. (1959) Br. J. Med. Psychol. 32, 50–55.

P01.63

VENLAFAXINE ER ACTION ON GENERALIZED ANXIETY DISORDER (GAD)-SPECIFIC ANXIETY SYMPTOMS

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In the DSM-IV definition[1], GAD is defined by the presence of excessive worry for a period of at least six months and the presence of 3 out of a list of six symptoms including restlessness, being easily fatigued, difficulty concentrating, irritability, muscle tension and disturbed sleep. Changes in the Hamilton anxiety rating scale (HAM-A) score are commonly used as an indicator of the efficacy of therapeutic interventions in GAD. Venlafaxine extended-release (ER) was proven effective on this scale in patients with GAD[2]. Using effect size (ES)[3] analysis we examined venlafaxine ER efficacy on HAM-A items most closely corresponding to DSM-IV diagnostic symptoms for GAD (1, 2, 4, 5, 7 and 14). ES was evaluated from data obtained from 5 double-blind, 8-week placebo-controlled studies of similar design, comparing venlafaxine ER (n = 1297) with placebo (n = 544). Two of these studies had long-term (6-month) extensions. An ES cut-off of 1 (difference between pre- and post-treatment greater or equal to the standard deviation of that difference) was used to characterize items with the largest changes. After 8 weeks of treatment, venlafaxine ER produced an ES $\geq$ 1 in item 1 (anxious mood, including worry), 2 (tension) and 14 (behavior at interview). By the end of long-term treatment, an ES $\geq$ 1 was observed in items 1, 2, 5 (intellectual), 7 (somatic muscular) and 14. After both short and long-term treatment with venlafaxine ER, the largest effect sizes were observed on HAM-A items 1 and 2.

Venlafaxine ER induced large effect sizes on 5 out of the 6 HAM-A items related to GAD diagnostic symptoms. In GAD patients, venlafaxine ER appeared to be acting on the specific symptoms of this disorder.

(1) American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, (A.P.A., Washington D.C., 1994).
(2) Hackett D et al. *Eur. Psychopharm.* 9 (Suppl. 5), S315. 1999.
(3) Leon, A.C., et al. *Psychopharmacol. Bull.* **29**, 163–167 (1993).

P01.64

QUALITY OF RESPONSE IN GAD: IS RESPONSE TO PLACEBO THE SAME AS RESPONSE TO ACTIVE TREATMENT?

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Response (defined as a 50% or greater decrease from baseline severity) is often used in anxiety and depression studies as a clinically relevant criterion to determine the proportion of patients benefiting from pharmacological treatment. However, studies designed to test the efficacy of active treatments are frequently compromised by a high placebo response. The present analysis will examine the response characteristics in patients from a pool of two 6-month double-blind multicentre studies in patients suffering from generalized anxiety disorder (GAD). The response shown by GAD patients after placebo or the specific noradrenaline and serotonin reuptake inhibitor venlafaxine ER (extended release) treatment will be characterized in terms of sustainability, loss of response, fluctuations between response and non-response and relapse to baseline severity.

After 6 months of treatment, venlafaxine ER induced response in 66% of patients ($p < 0.001$ versus 39% in placebo group). More responders in the venlafaxine ER group were shown to sustain their response until the end of the study than responders in the placebo group ($p < 0.001$, 43% versus 22% of responders respectively). This difference was paralleled by a lower percentage of loss of response and fluctuations in venlafaxine ER responders. Responders in the venlafaxine ER group also showed a lower occurrence of relapse (6% and 15% in venlafaxine ER and placebo group respectively, $p = 0.003$).

Results from this study suggest that response to venlafaxine ER is qualitatively different from the response observed in the placebo-treated population. Response to venlafaxine ER is characterised by a higher stability. The superior stability of response observed in patients responding to venlafaxine ER is probably related to the lower intensity of residual symptoms in this population, and further supports the efficacy of venlafaxine ER in GAD.

https://doi.org/10.1016/S0924-9338(00)94469-9 Published online by Cambridge University Press