

medication we used benzodiazepines (anxiolytics and hypnotics). The group's average at the HDRS was 46 points.

After 30 days there was an improvement on 9 patients (82%), with a HDRS average score of 30 points. After 90 days there was an improvement on 10 patients (91%), and the HRDS average score was 14. After 120 days the HRDS average score of those 10 patients was 8 points.

One of the patients had no response and the treatment had to be reinforced. Only two of them had side-effects, like nausea, constipation, tremulousness and restlessness. We believe that duloxetine is one of the first choices as a treatment for melancholy.

P0031

Pooled analysis of the safety and tolerability of desvenlafaxine Succinate compared with placebo in the treatment of major depressive disorder

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Objective: To characterize the safety and tolerability of desvenlafaxine succinate (DVS) in patients with major depressive disorder (MDD).

Methods: Pooled data from 7 double-blind, placebo-controlled studies were analyzed. Adult outpatients with DSM-IV MDD received DVS or placebo for 8 weeks. Four studies employed flexible dosing of DVS (100-200mg/d [1 study]; 200-400mg/d [3 studies]); 3 studies evaluated fixed doses (100/200/400mg/d [1 study]; 200/400mg/d [2 studies]). Vital signs and treatment-emergent adverse events (TEAEs) were evaluated. In the fixed-dose subset of studies, dose-related effects were analyzed.

Results: The overall safety population consisted of 2014 patients (DVS: n=1211; placebo: n=803); 60% were women. Adverse events were responsible for discontinuations in 4% of placebo-treated patients and 15% of DVS-treated patients. Discontinuation rates increased with dose (10% with 100mg/d to 17% with 400mg/d) in the subset of fixed-dose studies. TEAEs were consistent with the serotonin-norepinephrine reuptake inhibitor (SNRI) class. Nausea was generally mild to moderate with a median duration less than or = to 6 days; the incidence decreased to placebo-like rates after week 1. With all doses of DVS, small but statistically significant changes in mean blood pressure were observed. Mean changes in pulse rate and the proportion of potentially clinically important increases in sustained elevations in supine diastolic blood pressure were higher for patients receiving 200/400mg/d than among placebo-treated subjects; values for these parameters with the 100mg/d dose did not differ from placebo.

Conclusions: DVS treatment exhibited a safety and tolerability profile that was generally consistent with the SNRI class.

P0032

Effects of Escitalopram on the processing of emotional faces

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Background and Aims: The aim of this study was to verify the effects of the selective serotonin reuptake inhibitor escitalopram on the recognition of facial emotional expressions.

Method: Twelve healthy males completed two experimental sessions each, separated by at least 2 weeks, in a randomized, balanced order, double-blind design. An oral dose of escitalopram (10 mg) or placebo was given 3 hours before the task. Face recognition task: Subjects were presented with pictures of faces from the Pictures of Facial Affect Series (Ekman and Friesen, 1976). Faces with six basic emotions (anger, disgust, fear, happiness, sadness and surprise) had been morphed between neutral (0%) and each standard emotion (100%), in 10% steps. Accuracy was analyzed through MANOVA with repeated measures. Values of $p < 0.05$ were considered significant.

Results: Volunteers recognized more accurately negative emotions in female faces than in male faces, whereas happiness was identified more easily in male faces. In general, the acute administration of a single dose of escitalopram increased the accuracy of the recognition of angry and sad faces. When the gender of the faces was analyzed, escitalopram facilitated the recognition of sad expressions and impaired the recognition of happy faces in male, but not in female faces. A global order effect has also been found; the administration of escitalopram in the second experimental session facilitated the recognition of emotional expressions.

Conclusions: These results indicate that serotonin modulates the recognition of emotional faces. Previous experience and gender of the emotional face interact with this modulation.

P0033

The impact of treatment on quality of life in major depressive disorder (MDD) and generalized anxiety disorder (GAD)

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Objective: To compare the quality of life using the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) in patients with MDD or GAD, before and after treatment and to compare remission based on symptoms versus functioning.

Methods: Q-LES-Q and symptom-specific MADRS and HAMA data from 8 published randomised, 8-week, double-blind, placebo-controlled clinical trials with escitalopram were used. The short form of the patient-rated Q-LES-Q was used to assess patients' perceived quality of life and satisfaction at baseline and at last assessment. ANCOVA was used, adjusting for study, centre, baseline value, and treatment. MADRS and HAMA total scores were equated to Q-LES-Q using the method of equipercentile linking.

Results: MDD or GAD patients report a substantial degree of impairment in their quality of life (64% and 76% of community norm, respectively). Treatment with escitalopram resulted in statistically and clinically significant improvement in patient quality of life. The improvement was greater in remitters (MADRS \leq 12 or HAMA \leq 7) than in non-remitters and greater in patients treated with escitalopram than in patients treated with placebo. There was a strong correlation between each symptom scale (MADRS, HAMA) and the Q-LES-Q. The present analyses suggest that scores as low as 3-8 on the MADRS and 5-10 on the HAMA (complete remission) correspond to a Q-LES-Q score of 58 (+/- 10%), found in community comparison subjects.

Conclusions: Treatment with escitalopram results in a statistically significant improvement of quality of life in patients with MDD or GAD.

P0034

The development and psychometric assessment of an instrument to measure adherence in patients with depression

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Background: Evidence in the literature supports the introduction of interventions to enhance adherence to antidepressant therapy, especially in patients with major depression.

Objective: The objectives of this study are; (1) to examine patient and population-based research on patient's adherence to antidepressants and (2) to develop and psychometrically assess a four-item instrument to measure adherence to antidepressants.

Method: Although causes for non-adherence are multifactorial, drug omissions could occur in one or more, of main four mechanisms; forgetting, carelessness, stopping the drug when feeling worse, or stopping the drug when feeling better. To our knowledge, no reliable valid instruments were developed to measure adherence to antidepressants. Authors modified an instrument that was developed by (Morisky 1986), to measure adherence to antihypertensive drugs. The modified instrument was distributed to experts in depression (n=12), to rate the instruments' relevancy, as a measure of patients' adherence to antidepressants, and was administered to patients (n=63), who are on antidepressants.

Results: The modified instrument has an improved reliability (Chronbachs' Alpha = 0.66), there is 90 %, overall agreement among experts, that the instrument relevant to measure adherence in outpatients with depression, supporting a strong evidence for content validity, and there is also strong evidence for convergent and criterion related validities.

Conclusion: The developed instrument is short, both reliable and valid, and could be completed in approximately 3 minutes. Although it was developed for with outpatients, it could be applied in different sittings, with wide range of psychiatric population who suffer from depression.

P0035

Preclinical mechanisms for the broad spectrum of antipsychotic, antidepressant and mood stabilizing properties of Seroquel[®]*

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Background: SEROQUEL[®] (quetiapine) is an atypical antipsychotic in the dibenzothiazepine class. Clinical studies have demonstrated consistent efficacy in the treatment of schizophrenia, bipolar mania, and bipolar depression. Further clinical results suggest robust efficacy in the long-term treatment of bipolar disorder and major depressive disorder. This broad spectrum of clinical effect has not been fully predicted based on quetiapine's preclinical pharmacology. However, norquetiapine, a recently discovered major active human metabolite of quetiapine, has unexpected properties that may explain the observed clinical antidepressant and mood-stabilizing effects.

Methods: Radioligand binding and functional assays using rat and human tissue were used to characterize receptor interactions. Positron emission tomography (PET) studies performed on cynomolgus monkeys and man explored the relationship between clinically relevant plasma exposures and occupancy at serotonin 5HT_{2A} and dopamine D₂ receptors and the norepinephrine transporter (NET).

Results: Norquetiapine had high affinity for and potently inhibited the NET, a property shared by tricyclic antidepressants and SNRIs but not other atypical antipsychotics at clinically relevant doses. In addition, norquetiapine had moderate-to-high affinity for D₂, 5HT_{1A}, 5HT_{2A}, and 5HT_{2C} receptors and shared some commonality with SSRIs. PET studies confirmed the properties of norquetiapine including occupancy of D₂ and 5HT_{2A} receptors as well as the NET at clinically relevant plasma exposures.

Conclusions: A unique combination of direct and indirect effects at noradrenergic, serotonergic, and dopaminergic receptors by quetiapine and norquetiapine provides a putative mechanism of action for the broad spectrum of clinical efficacy observed with SEROQUEL[®] in psychiatric disorders.

P0036

Early discontinuation on treatment and its consequences in patients treated with Venlafaxine or Escitalopram

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Background and Aims: Two-month head-to-head clinical trials of escitalopram and venlafaxine demonstrated similar efficacy and better tolerability for escitalopram. However, as routine practice may differ from controlled trial, it is necessary to investigate the translation of clinical trial findings into real life. This work aims at comparing treatment early discontinuation (ED) at 1 and 2 months and its economic consequences at 6 months, under venlafaxine and escitalopram.

Method: Using US denominator-based claims database PharMetrics (includes data from 86 managed care health plans covering 45 million patients), we included adult patients diagnosed with depression who started venlafaxine or escitalopram between January 1st and December 31st 2004. ED was compared at 1 and 2 months using Cox proportional hazard models and healthcare costs at 6 months, using log-linear regression. Propensity scoring was used to account for baseline differences.

Results: 13,227 patients started escitalopram; 5,922 patients started venlafaxine. ED at 2 months was 47% for venlafaxine, 45% for escitalopram. At 1 month, venlafaxine patients had 50% more risk of ED than escitalopram patients (Hazard Ratio=0.493 [95%CI 0.432-0.564]); while this difference decreased at 2 months, (Hazard Ratio=0.955 [95%CI 0.912-0.999]). Continuing treatment at 2 months doubled the chance of still being on treatment at 6 months. Moreover 1) ED at 2 months incurred more costs over 6 months (+US\$173); 2) 6-month healthcare costs were higher with venlafaxine (+US\$626, p<0.001).

Conclusion: Early discontinuation rate was higher with venlafaxine than escitalopram, possibly due to intolerance to venlafaxine. ED was shown to affect later continuation and incurred costs.

P0037

Antidepressant prescribing in outpatients and inpatients

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