P0034

The development and psychomeric 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 multifatorial, 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 5HT2A 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, 5HT1A, 5HT2A, and 5HT2C receptors and shared some commonality with SSRIs. PET studies confirmed the properties of norquetiapine including occupancy of D2 and 5HT2A 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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