Tues-P18

CORTISOL-, GROWTH HORMONE-, PROLACTIN-, AND TSH-RESPONSE TO COMBINED PITUITARY STIMULATION TEST IN DEPRESSIVE PATIENTS AND HEALTHY CONTROLS

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In this study the influence of combined i.v. application of four releasing hormones (CRH, GHRH, LHRH, and TRH) on Cortisol (COR)-, growth hormone (GH)-, prolactin (PRL)-, and TSH-secretion was investigated in depressive patients and healthy controls. 22 inpatients (8 men, 14 women) suffering from major depression according to DSM-III-R and 22 age- and sex-matched healthy controls were included in the study. Each patient and each control received an intravenous combination of GHRH (100 µg), CRH (100 µg), LHRH (100 µg), and TRH (200 µg). The test was started in the morning at 8 a.m.. The COR-, GH-, and PRL-concentrations were measured every 15 minutes during a period of 2 hours after the stimulation. The TSH concentrations were determined at time of releasing hormones application and 30 minutes after the stimulation. The AUC values were used as parameter for the COR-, GH-, and PRL response. The TSH stimulation was estimated using the delta-TSH value ($TSH_{t=30min} - TSH_{t=0min}$). For statistical evaluation the Student t-test was performed. Neither male nor female depressed patients differed considerably from their controls in COR-AUC values. In female patients a highly significant reduction in GH-AUC values could be demonstrated ($p < 0.01$); in male patients a blunted GH response could only be shown in recurrent depression (DSM-III-R: 296.3×). A diminished PRL stimulation could be shown in depressed patients compared to controls which was nearly significant ($p = 0.074$). Furthermore, there was a highly significant reduction of stimulated TSH secretion in depressive patients in comparison to healthy volunteers ($p < 0.01$). Our results demonstrate that depressive disorder is associated with multiple hormonal response abnormalities in the combined pituitary stimulation test.

Tues-P19

ANTIDEPRESSANT USE IN PRIMARY CARE IN THE UNITED KINGDOM: A LONGITUDINAL STUDY OF PRESCRIBING PATTERNS

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Objective: To investigate antidepressant prescribing patterns in primary care in the six months following initiation of treatment.

Method: Longitudinal data on antidepressant prescribing was obtained from a large primary care database (800,000 patient records) for patients with a diagnosis of depression, starting a new episode of treatment.

Results: Data were obtained on whether patients commencing treatment had their doses increased, had their treatment augmented by addition of another drug or had their treatment changed to an alternative antidepressant. Fluoxetine was the antidepressant on which patients were most likely to continue on same drug, same dose treatment. (See Table 1.)

Conclusions: Duration of antidepressant therapy correlates with clinical improvement, reduction of disabilities and restoration of function. Delay in achieving response because of the need to titrate dose upwards, augment, or switch treatment, may result in prolongation of illness, increase or adverse events and contribute to the development of chronic illness.

Initiation of treatment with fluoxetine is the approach most likely to minimise the need for treatment changes which may result in improved outcome.

Table 1. % of patients on same drug, same dose:

Overall	20.00		
Fluoxetine	26.48	Amitriptyline	18.64
Paroxetine	23.82	Dothiepin	16.94
Sertraline	15.51	Lofepramine	18.31

Tues-P20

PATTERNS OF ANTIDEPRESSANT USE AND THEIR RELATION TO CLINICAL GLOBAL IMPRESSION SCORES

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There is evidence that an adequate duration of antidepressant therapy is correlated with improvement in symptomatology, the reduction of disabilities, the restoration of work performance, and the prevention of relapse. The purpose of this study was to test in a clinical practice setting whether the pattern of antidepressant use was correlated with patients' clinical improvement as measured by the Clinical Global Impressions Scale (CGI). A Cox proportional hazard model was used to predict the likelihood of realizing a clinical improvement as measured by CGI score. A retrospective chart review was made to obtain a sample of patients who initiated therapy on fluoxetine, fluvoxamine, paroxetine, sertraline, or venlafaxine in a general practitioner setting in Spain.

After controlling for other observed baseline characteristics including initial depression disease severity, patients who remained on their initial antidepressant therapy for at least two months and who experienced no switching, augmentation, or upward dose titration were more likely than patients who had an adjustment to therapy to realize a clinical improvement as measured by CGI score. The pattern of antidepressant use appears is an important determinant of clinical improvement as measured by CGI scores among patients initiating therapy on the newer classes of antidepressants in clinical practice.

Tues-P21

SSRI ANTIDEPRESSANT DRUG USE PATTERNS IN THE NATURALISTIC SETTING: A MULTIVARIATE ANALYSIS

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Study of the duration and pattern of antidepressant use in actual clinical practice can provide important insights into how antidepressant use patterns compare to recommended depression treatment guidelines. The purpose of this study using data available from unipolar depressed outpatients in the United States was to assess the effects of initial SSRI antidepressant selection on the subsequent

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pattern and duration of antidepressant use. Multiple regression analysis of data from a large prescription and medical claims database (MarketScan®) for the years 1993 and 1994 were used to estimate the determinants of antidepressant drug use patterns for 1,034 patients with a "new" episode of antidepressant therapy who were prescribed one of three most often prescribed selective serotonin reuptake inhibitors (SSRIs) paroxetine, sertraline, or fluoxetine.

The results indicated that patients initiating therapy on sertraline or paroxetine were less likely than patients initiating therapy on fluoxetine to have at least four prescriptions of their initial antidepressant within the first six months. The findings suggest that antidepressant selection is an important determinant of antidepressant use patterns consistent with current recommended depression treatment guidelines.

Tues-P22

THE COST-EFFECTIVENESS OF IXEL®, A NEW SNRI, IN COMPARISON WITH A PANEL OF TCAs AND SSRIs, IN THE TREATMENT OF DEPRESSION

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A model based on the theory of clinical decision analysis was constructed in order to estimate costs and outcomes when treating patients with a major depressive episode. Ixel® (milnacipran - Pierre Fabre Médicament), a new serotonin and norepinephrine reuptake inhibitor (SNRI), was compared with a French representative panel of tricyclic antidepressant (TCA) and selective serotonin reuptake inhibitor (SSRI).

The effectiveness of the alternatives, based on the safety/efficacy ratios, was evaluated from a meta-analysis of the studies included in the NDA dossier, taken into account the compliance as observed in usual practice. The other data used in the model came mainly from the literature and from a panel of psychiatrists.

Direct medical costs included antidepressant drugs, visits, lab tests and hospitalisations. Economic appraisal was performed according to the viewpoint of the French National Sickness Fund.

The model concluded in favour of a better cost-effectiveness of Ixel®: its expected cost of treatment per depressive episode was lower than either the one of the panel of TCAs (savings: 228 FF., 1 EURO = 6.62 FF.) or SSRIs (savings: 961 FF.). Moreover, its expected length of clinical remission was slightly higher. The robustness of these findings were supported by several threshold sensitivity analyses conducted on the main parameters.

Tues-P23

CITALOPRAM TREATS MAJOR DEPRESSION IN THE ELDERLY, WITH FEWER SIDE EFFECTS THAN AMITRIPTYLINE

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Depression is more common in the elderly than in the general population. Elderly patients, however, are more sensitive to the anticholinergic side effects of tricyclic antidepressants (TCAs), making their treatment especially problematic. Citalopram is the most selective of the serotonin re-uptake inhibitors, a class that is as efficacious as the TCAs, but causes fewer side effects. This double-bind, multicentre general practice study in the UK and Ireland compared citalopram and amitriptyline with respect to safety and efficacy in 365 elderly patients (65–90 years) with major depression. Patients with a diagnosis of major depression (including a score of ≥ 22 on the Montgomery-Asberg Depression Rating Scale [MADRS]) were randomised to receive either citalopram (20 or 40 mg once daily; n = 179) or amitriptyline (50 or 100 mg/day; n = 186) for 8 weeks. Efficacy was measured at weeks 1, 2, 4, 6 and 8 using the MADRS, the Hamilton Depression (HAMD) Scale and the Clinical Global Impression (CGI) Scale. The incidence of withdrawal due to adverse events (the main reason for discontinuation) was higher in amitriptyline- than in citalopram-treated patients (25% *vs* 17%; NS). A further 5% and 7% of patients, respectively, withdrew for other reasons. Adverse events considered to be treatment-related were experienced by significantly ($p < 0.001$) fewer patients in the citalopram group (45%) than in the amitriptyline group (63%). Confusion, hallucination, anxiety and suicide attempt occurred only in patients receiving amitriptyline. Nausea was the only adverse event to be observed more frequently with citalopram than with amitriptyline. The response (MADRS $\leq$ 12) rate was 54.5% and 53.5% in the citalopram and amiptriptyline groups, respectively (intent-to-treat). Improvements in HAMD and CGI were also comparable for the two groups. Thus, citalopram is as efficacious as amitriptyline in treating major depression, but causes fewer side effects; importantly, it does not cause the anticholinergic effects observed with amitriptyline. Citalopram is therefore an excellent candidate for treating depression in the elderly.

Tues-P24

CITALOPRAM IS EFFECTIVE AND WELL TOLERATED IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER

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Citalopram is the most selective of the selective serotonin re-uptake inhibitors currently available and has a chemical structure unrelated to that of other SSRIs or other available antidepressants. This double-blind, randomised, placebo-controlled trial was designed to confirm the safety, efficacy and minimum effective dose of citalopram in patients with moderate to severe depression. In total, 650 patients were randomised to receive citalopram 10 mg (n = 131), 20 mg (n = 130), 40 mg (n = 131) or 60 mg (n = 129), or placebo (n = 129), given once daily for 6, weeks. The percentage of responders (defined as $\geq$ 50% decrease from baseline on the Montgomery-Asberg Depression Rating Scale) was significantly ($p < 0.05$) greater in each of the citalopram groups (49 to 61%) than in the placebo group (35%). The reduction in Hamilton Depression Scale total score was significantly ($p < 0.05$) greater in patients receiving citalopram 40 mg than in those receiving placebo. Increasing the dose to 60 mg appeared to offer little additional benefit. A similar number of patients withdrew from each treatment group. There were more withdrawals because of lack of efficacy, and fewer withdrawals because of adverse events in the placebo and citalopram 10 mg groups than in the higher-dose citalopram groups. The incidence of withdrawal because of adverse events was similar in the citalopram 20, 40 and 60 mg groups. The most frequent treatment-emergent events were nausea, insomnia, dry mouth, somnolence and increased sweating. The incidence of accepted SSRI-related side effects, including nausea and dry mouth, did not appear to be dose-dependent, although there was a trend towards a higher frequency of insomia, somnolence and fatigue in the citalopram 40 and 60 mg groups. In conclusion, this trial confirmed that citalopram is efficacious in moderate to severe

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