P01.09

Mega-analysis of sertraline vs. fluoxetine in major depression

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Objective: To increase the power to detect efficacy in clinically relevant subgroups, a mega-analysis of pooled data was conducted.

Method: Data were pooled from 8 double-blind, head-to-head studies comparing sertraline and fluoxetine. A "mega-analysis" (Thase et al, Arch Gen Psych, 1997) was conducted on the anxious depression subgroup (defined by a HAM-D-anxiety-somatization factor score > 7), and a high severity subgroup (defined by a 17-item HAM-D total score > 26).

Results: A total of 1,706 patients (65% female; mean age, 49 yrs; baseline HAM-D, 22.7) were randomized to receive at least 6 weeks of double-blind treatment. In the anxious depression subgroup, HAM-D responders (> 50% reduction) for sertraline vs. fluoxetine were 72% vs. 64% ($p < 0.05$). In the severe depression subgroup, HAM-D responder rates were 72% vs. 56% ($p < 0.02$). Treatment with sertraline was associated with significantly earlier onset of both clinical response and remission

Conclusion: Mega-analysis represents a promising new method for identifying meaningful clinical differences in the efficacy and tolerability of various antidepressants.

P01.10

Moclobemide in early poststroke depression: an open study

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Objective: Depression is a common problem in rehabilitation and functional recovery after stroke. We have performed an open study of the effect of the RIMA, moclobemide in early poststroke depression.

Method: 157 consecutive admissions to neurological unit were screened for depression and 32 patients were admitted to the study having a HDRS score > or = 15. The patients received 450–600 mg of moclobemide and underwent a neurological and psychiatric examination at 3, 6 weeks and 3, 6 months after the stroke. The antidepressive therapy was finished when a good and stabile remission has been achieved.

Results: 450–600 mg of moclobemide were well tolerated and led to > or = 50 % reduction of the HDRS score in 46 % of patients following 6 weeks of treatment and in 70 % of patients following 3 months of treatment. In 6 months observation, moclobemid must have been changed to another antidepressant in 30 % patients.

Conclusions: According to our observation RIMA, moclobemide, is an effective and well-tolerated therapy of depression after stroke and its effectiveness improves during prolonged therapy.

P01.11

Placebo-controlled efficacy comparison of escitalopram and citalopram

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Escitalopram is the single isomer responsible for the inhibition of serotonin reuptake produced by the racemic SSRI antidepressant citalopram. Recently, three placebo-controlled, randomized, 8-week double-blind trials were completed that employed parallel fixed- or flexible-dose arms of escitalopram (10–20 mg/day), citalopram (20–40 mg/day), or placebo in patients with moderately severe to severe major depressive disorder (MADRS*f*r22). The MADRS and CGI scales were endpoints in all trials. Both escitalopram and citalopram were effective in reducing depressive symptoms in both scales, and in the percentage of MADRS responders. Analysis of the comprehensive safety database shows that escitalopram was well-tolerated, with only one adverse event (nausea) occurring in more than 10% of patients at a rate greater than placebo, and with a low overall rate of discontinuations due to adverse events.

P01.12

Escitalopram prevents relapse of depressive episodes

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The efficacy of escitalopram in the treatment of MDD was established in several 8-week trials. However, continued antidepressant treatment is necessary to prevent relapse of depression; this was evaluated here with escitalopram.

The trial was an extension study in depressed outpatients who had completed 8 weeks of escitalopram, citalopram, or placebo treatment. It consisted of an 8-week open-label escitalopram (10¡V20mg/day) treatment period followed by a randomized, double-blind period. At the end of the open-label period, patients classified as responders (MADRS „T12) were assigned to escitalopram (N=181) or placebo (N=93) for 36 weeks of treatment. The primary efficacy variable was time to depression relapse from the start of the double-blind treatment. Additional efficacy variables included MADRS, HAMD, and HAMA.

Time to depression relapse was significantly longer in escitalopram-treated patients; the risk of relapse was 44% lower in escitalopram- than in placebo-treated patients. Escitalopram-treated patients continued to exhibit low mean ratings of anxiety and depression symptoms during the double-blind period, which were significantly lower than those of placebo-treated patients.

Thus, continuation treatment with escitalopram is effective in preventing relapse of depression.

P01.13

Age specificity in the psychopharmacotherapy of endogenous depressions in adolescence

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Objective: the detection of specific reactions to psychopharmacotherapy in patients with endogenous depressions in adolescence (age group 15–21 years).

Methods: the efficacy of treatment, side effects and complications during psychopharmacotherapy by antidepressive drugs of different classes (TCA, SSRI, NASSA) were studied in 220 adolescent patients with affective disorders (F31–34), compared to that of adults with similar psychotropic therapy and the use of rating scales (CGI, MIDRS, UKU).

Results: it was established that the reactions of adolescents to psychotropic drugs differs from those of adults. Along with the obvious preference of the new generation of antidepressive drugs compared to that of TCA, it also demonstrates a higher frequency and more pronounced adverse reaction, as well as the appearance of complications, which practically are not encountered in adult patients.

https://doi.org/10.1016/S0924-9338(02)80443-6 Published online by Cambridge University Press

Conclusions: the achieved results point to the specific therapeutical response to different groups of antidepressive drugs in adolescence, which may be explained by psychobiological and age factors, and especially to the incomplete morphofunctional brain maturation, and with the hormone and immunological disbalance in puberty. This confirms the necessity to single out adolescent psychopharmacotherapy into a special area and to study it on different levels.

P01.14

Glucocorticoid Receptor-mRNA levels are regulated in human blood cells by different types of antidepressants

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Beside other data, increases in glucocorticoid serum levels and disturbances of the circadian secretion of these hormones in depressive patients point to a putative glucocorticoid receptor (GR)-dysfunction in this illness.

Therefore, the aim of the present study was to investigate the regulatory effects of different types of antidepressants (desipramine, imipramine, mirtazapine and maprotiline) on GR-mRNA levels in blood cells of healthy male probands.

Total RNA was extracted from whole blood samples after 24 h of incubation with the antidepressants using Trizol® reagent and RT-PCR methods were used for the semiquantitative analysis of GR-transcripts. Our results suggest that a concentation of 10^{-7} M of mirtazapine induces a down-regulation of GR-mRNA levels in human blood cells. Interestingly, the same concentration of maprotiline lead to a significant up-regulation of GR-mRNA levels. These treatments did not induce changes in the levels of the house-keeping gene glyceraldehyde-3-phosphate dehydrogenase (GAPDH).

Therefore, antidepressants with different modes of action affect GR-mRNA-levels in human blood cells in vitro, although not in the same direction. These changes further support the assumption that this may represent a relevant mechanism of action in the course of the treatment of diseases such as major depressive disorder.

(Supported by the DFG/SFB 297)

(1) Vedder H, Bening-Abu-Shach U, Lanquillon S and Krieg JC (1999). Regulation of glucocorticoidreceptor-mRNA in human blood cells by amitriptyline and dexamethasone. Journal of Psychiatric Research 33: 303–308

P01.15

Duloxetine 60 mg QD is efficacious in the treatment of depression

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This study examined duloxetine (60 mg QD), a potent and balanced reuptake inhibitor of norepinephrine and serotonin, in the treatment of the mood and physical symptoms associated with major depressive disorder. In a multicenter, randomized, double-blind, parallel, placebo-controlled study, adult MDD patients (n=245) were randomly assigned to receive placebo or duloxetine 60 mg QD for a 9-week treatment period. The primary efficacy assessment was HAMD17 total score. Physical symptoms were measured by somatic symptom inventory and a visual analog scale for pain. Duloxetine was statistically significantly superior to placebo at weeks 2 through 9 on the reduction of HAMD17 total score and resulted in an estimated probability of remission of 44%. Duloxetine resulted in a significant reduction in severity of overall pain compared with placebo. Duloxetine was well tolerated and none of the duloxetine-treated patients reported any serious adverse events. These results indicate that duloxetine administered at 60 mg once daily is a safe and efficacious treatment of MDD. Moreover, these results also indicate that duloxetine may be an important treatment for MDD patients with physical symptoms, including pain.

P01.16

Duloxetine in the treatment of depression: a double-blind placebo-controlled comparison with paroxetine

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In this study, duloxetine (40 & 80 mg/day), a potent and balanced dual serotonin and norepinephrine reuptake inhibitor, was compared with the SSRI paroxetine (20 mg QD) and placebo in the treatment of MDD. In this 8-week, randomized, double-blind controlled study in outpatients with MDD, efficacy was evaluated using total HAMD17 (primary), MADRS, CGI-S, and PGI-I. Secondary measures included the HAMA and visual analogue scales for pain. Safety and tolerability were also assessed. Duloxetine at 80 mg/day was superior to both placebo and paroxetine on the reduction of HAMD17 total score. Duloxetine 80 mg/day was superior to placebo on most secondary efficacy measures. The remission rate for duloxetine 80 mg/day was 50%, paroxetine 37%, and placebo 30%. Duloxetine 80 mg/day significantly reduced overall pain. Insomnia was the only adverse event reported significantly more frequently for duloxetine 80 mg/day than for the SSRI paroxetine. The number of cases of hypertension observed did not differ between duloxetine and placebo groups. These results indicate that duloxetine is well-tolerated and efficacious in the treatment of the mood and physical symptoms associated with MDD.

P01.17

Olanzapine-fluoxetine combination in treatment-resistant depression

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Objective: This 8-week, double-blind study compared olanzapine-fluoxetine combination (OFC) with olanzapine (OLZ), fluoxetine (FLX), and nortriptyline (NTP) monotherapies in treatment-resistant depression (TRD). TRD was defined as historic SSRI failure and prospective nortriptyline failure.

Method: 499 subjects failing a 7-week nortriptyline lead-in phase were randomized to OFC, OLZ, FLX or NTP treatment groups, and efficacy evaluated with the MADRS.

Results: OFC subjects demonstrated significantly better total scores than the monotherapies from week 1–4, except OLZ at week 3. OFC maintained treatment effect throughout 8 weeks, however, at endpoint OFC statistically separated only from OLZ (-8.6, -6.5). Sub-analysis of subjects with >3 depressive episodes within the last two years also demonstrated the fast OFC onset of action, and statistical separation from OLZ and FLX at endpoint (-11.33, -4.57, -5.76). Subjects with SSRI failure during the current MDD episode demonstrated fast OFC onset of action, and statistical separation from component monotherapies through week 7, and from OLZ at endpoint (-9.66, -5.16). OFC's safety profile was similar to component monotherapies.

Conclusion: OFC had a rapid onset of action and was particularly efficacious in subsets of more treatment-resistant subjects.

https://doi.org/10.1016/S0924-9338(02)80443-6 Published online by Cambridge University Press