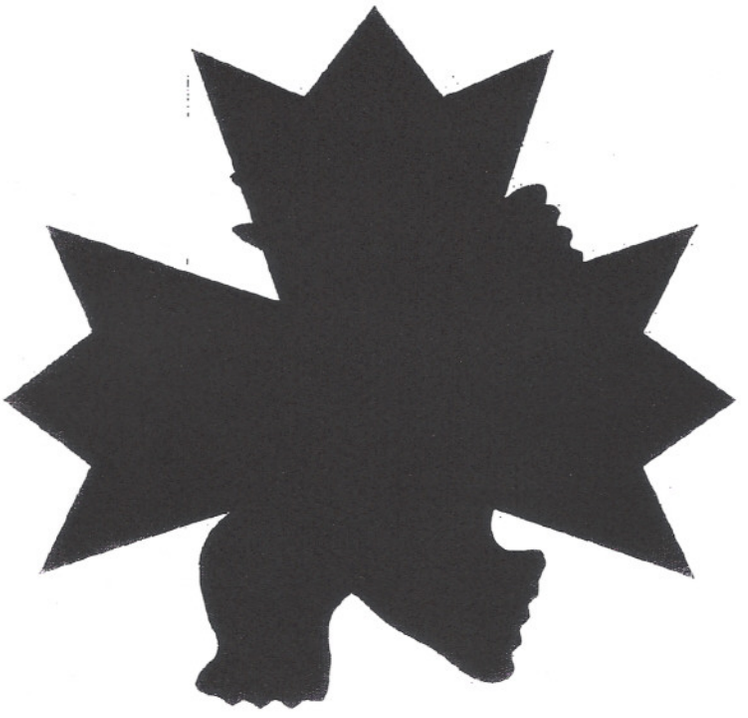
NEW RESEARCH

...SEARCH
...M & ABSTRACTS

PRESENTED AT THE 151ST ANNUAL MEETING



A DANCING BEAR SYMBOLIZES RENEWAL AND STRENGTH TO MANY NATIVE AMERICAN CULTURES

American Psychiatric Association
Annual Meeting • May 30 - June 4, 1998
Toronto, Ontario, Canada

2. Understand that a structured depression management program based in primary care can significantly enhance clinical outcomes vs. usual care in HMOs.

Summary:

The CARE study is a 12-month randomized evaluation of the Depression Management Program (DMP) compared with Usual Care (UC). We identified patients with depression by administering the SCID, via telephone interview, to high utilizers of ambulatory services in three large HMOs. Patients screening positive for major depression or depression in partial remission received a HAMD assessment two weeks later. Patients meeting study eligibility criteria, including a HAMD score of 15 or higher, were asked to complete four follow-up telephone interviews over the next year. We randomized 407 consenting patients, 218 to the DMP and 189 to UC. DMP patients initiated treatment with their primary care physicians and nonresponders received increasing levels of psychiatric care. DMP patients received the Rhythms patient education program at the first visit. DMP follow-up visits and prescription refills were also tracked to improve compliance. UC patients received the care available without the DMP. The data are from unblinding the first six months of clinical data and are based upon intent to treat. Baseline HAMDs were 19.1 for DMP and 19.2 for UC. Improvements in HAMD scores were significantly greater in the DMP group at six weeks and all later assessments ($p < 0.05$) by ANOVA. Six-month HAMD scores were 11.8 for DMP vs. 15.2 for usual care. At six months DMP patients reported better physical functioning and mental health and general health perceptions than UC on the SF-20 ($p < 0.05$). At least three antidepressant prescriptions were filled in the first six months by 68.4% of DMP patients vs. 18.5% in UC ($p < 0.05$). There were three or more specialty mental health visits in the first six months by 13.3% of DMP patients vs. 9.5% in UC ($p < 0.05$). Data on indirect costs and 12-month data will soon be available and presented.

Sponsor: Pfizer Pharmaceuticals

References:

1. Katzelnick, DJ, Kobak, KA, Greist, JH, Jefferson, JW, Henk, HJ: Effect of primary care treatment of depression on service use by patients with high medical expenditures. Psychiatric Services 1997;48:59–64.

2. Henk, HJ, Katzelnick, DJ, Kobak, KA, Greist, JH, Jefferson, JW: Medical costs attributed to depression among patients with history of high medical expenses in a health maintenance organization. Arch Gen Psychiatry 1996;53:899–904.

NR206 Tuesday, June 2, 9:00 a.m.-10:30 a.m.

Paroxetine and Imipramine in the Treatment of Adolescent Depression

Martin B. Keller, M.D., Department of Psychiatry, Butler Hospital/Brown Univ., 345 Blackstone Boulevard, Providence RI 02906; Neal D. Ryan, M.D., Boris Birmaher, M.D., Rachel G. Klein, Ph.D., Michael Strober, Ph.D., Karen D. Wagner, M.D., Elizabeth B. Weller, M.D.

Educational Objectives:

This presentation will provide information on the efficacy of paroxetine and imipramine in the treatment of major depression in adolescent outpatients.

Summary:

The efficacy of paroxetine and imipramine in adolescents meeting DSM-IV criteria for major depression was assessed in a double-blind, placebo-controlled trial in 275 outpatients between the ages of 12 and 19. Patients were treated for eight weeks with doses of 20 mg of paroxetine and 200 mg of imipramine. Titration to 40 mg of paroxetine and 300 mg of imipramine was undertaken for patients judged to be nonresponders. Patients were seen weekly and assessments included the 17-item Hamilton Depression Scale (HAM-D), the 7-point Clinical Global Impression of Improvement (CGI), and the 9-item depression section of the Kiddie SADS (K-SADS). Remission was defined as a score of 8 or less on the HAM-D. Among the imipramine patients, 32% withdrew for an adverse event. This compares with 10% and 7% for the paroxetine and placebo patients, respectively.

Patients treated with paroxetine demonstrated significant improvement over placebo on measures of affect, global improvement, and remission of depressive symptoms. In contrast, there was no separation from placebo on any clinical measures in patients treated with imipramine. These results support that paroxetine is an effective treatment for major depression in an adolescent outpatient population.

References:

1. Strober M: Pharmacotherapy of depressive illness in adolescents: III diagnostic and conceptual issues in studies of tricyclic antidepressants. J Child & Adol Psychopharmacology 1292;2(1):23–29.

2. Jensen PS, Ryan ND, Prien R: Psychopharmacology of child and adolescent major depression: present status and future directions. J Child & Adol Psychopharmacology 1992;2(1):31–45.

NR207 Tuesday, June 2, 9:00 a.m.-10:30 a.m.

Depressive Symptoms: A Risk for Mortality in Elderly

Junji Takeshita, M.D., Department of Psychiatry, University of Hawaii, 45-710 Keaahala Road, Kaneohe HI 96744; Kamal Masaki, M.D., Iqbal Ahmed, M.D., Daniel Foley, M.S., Yuan Qing Li, M.S.C., Daryl Fujii, Ph.D., G. Webster Ross, M.D., Helen Petrovitch, M.D., Lon White, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe how the presence of depressive symptomatology is a significant predictor of mortality in elderly men; and describe how appropriate treatment of depression may result in decreased mortality and improved quality of life.

Summary:

Objective: To evaluate the predictive value of depressive symptomatology as a risk factor for mortality in elderly men.

Methods: At the fourth examination (1991–1993) of the Honolulu Heart Program longitudinal cohort, the presence of depressive symptoms was assessed using an 11-question version of the CES-D (Center for Epidemiology Surveys-Depression) Scale, hereafter called CESD-11. A total of 3741 men aged 71 to 93 were examined and followed prospectively for an average of five years for all-cause mortality. Presence of depressive symptomatology was defined as a score of ≥ 9 points on the CESD-11.

Results: A total of 3263 subjects completed the CESD-11 and 321 (10%) had depressive symptomatology. Of those without depressive symptoms, 20% (584/2942) died during the five year follow-up period compared with 25% (81/321) of those with these symptoms. Five-year, age-adjusted mortality rates in those with and without depressive symptoms were 56.4 and 43.6 per 1000 person-years, respectively. Using Cox proportional hazards models, after adjusting for age, the relative risk for mortality with depressive symptoms was 1.30 ($p = 0.026$).

Conclusions: These data suggest that the presence of depressive symptomatology is a significant predictor of mortality in elderly men. Appropriate treatment of depression may result in decreased mortality and improved quality of life.

PAROXETINE IN ADOLESCENT DEPRESSION

Carlo Gagiano

Westdene Research Centre, 64 Second Avenue, Westdene, Bloemfontein 9301, South Africa

Introduction

Adolescent depression is a common problem. Most estimates of prevalence are around 5%,[1] but rates as high as 9-17% have also been reported.[2]

Depression during adolescence can disrupt normal psychosocial and educational functioning at a crucial time in development - the transition from childhood to adulthood.

Suicide is a serious risk factor with unrecognised/untreated depression in adolescents. Approximately 80% of adolescent suicide attempts are made by individuals with depression,[3] and the rate of suicidal behaviour in adolescents appears to be increasing.[4]

Despite the high prevalence and associated serious consequences, adolescent depression remains under-recognised and undertreated. This poster reviews the issues relating to recognition and management of adolescent depression and presents recent data from clinical studies with paroxetine in this patient group.

Adolescent depression: a difficult diagnosis?

Adolescents are a heterogeneous population, and depression in these subjects can be difficult to diagnose due to differences in presenting symptoms, such as antisocial or impulsive behaviour. Younger adolescents with depression often show irritable mood, persistent boredom, lack of energy, poor performance at school, long periods of time spent with a pet, and preoccupation with somatic symptoms. Older adolescents with depression most commonly show apathy, fatigue, diminished ability to concentrate, preoccupation with death/suicide, and low self-esteem.[4]

While 'adult' rating scales such as the Hamilton Depression Rating scale (HAM-D) are considered valid for assessing depression in older adolescents (age 16-18 y), they have not been exclusively studied in the whole adolescent age group. Therefore, specialised screening tests have been developed for diagnosis of depression in adolescents (and children) [Table 1].

Table 1. Screening for depression in adolescents

Validated rating scales
Clinician-rated
Diagnostic Interview Schedule for Children (DISC-2.3)
Schedule for Affective Disorders and Schizophrenia for School-Age Children and Adolescents (K-SADS)
Patient-rated
Children's Depression Inventory (CDI)
Revised Reynolds Adolescent Depression Scale (RADS)

The problem of comorbidity

Adolescent depression is often compounded by other psychiatric disorders and/or behavioural problems (Table 2). It has been suggested that over 95% of children and adolescents with depression have one other psychiatric disorder, and over 80% have two.[5]

Table 2. Common comorbidities of adolescent depression

Comorbidity
Anxiety disorders
Social anxiety disorder
Agoraphobia
Obsessive compulsive disorder
Antisocial behaviour
Conduct / oppositional disorders
Attention deficit / hyperactivity
Eating disorders
Substance abuse

The presence of comorbid conditions increases the severity and can worsen the prognosis of the depression. In these cases, the need for recognition and treatment of adolescent depression becomes even greater.

Pharmacotherapy: clinical studies of paroxetine

SSRIs have been widely investigated for treatment of depression and are generally regarded as first line therapy. Several studies have examined the antidepressant efficacy of the SSRI paroxetine in adolescent subjects [Table 3].[6-9]

Table 3. Clinical studies of paroxetine in adolescent depression

Age group	Study design	n	Dose (mg/day)	Response rate* (scale)
12 y to 18 y 11 mo	Double-blind, placebo-controlled, active comparator[a]	275	20-40	67%† [6] (HAM-D)
<14 y	Open-label[b]	45	10-25	100% [7] (CGS)
13y to 17y	Retrospective[c]	25	10-40	76% [8] (ICD-10)

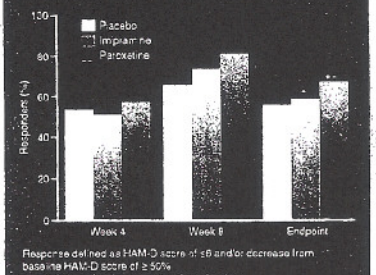
* Responders defined by:
[a] A 50% reduction in HAMD score or a HAMD score of < 8 at endpoint.
[b] Reduction in CGS on a graded scale 0-4.
[c] After 8-weeks treatment, no primary symptoms observed and ≤ 4 secondary symptoms observed, with a severity of mild to moderate.
† vs 59% imipramine, 55% placebo
CGS - Clinical Global Severity scale
ICD-10 - International Classification of Diseases 10

In the largest trial with paroxetine, 275 adolescents with depression who were currently experiencing an episode of major depression (DSM-III-R criteria) diagnosed using the Schedule for Affective Disorders and Schizophrenia for School-age Children - Lifetime version (K-SADS-L), were recruited by 12 centres in the USA.[6] Subjects had to have a HAM-D score of ≥12 and a severity score of <60 on the Child Global Assessment Scale (C-GAS).

Patients were randomised (1:1:1) for 8 weeks treatment with: flexible-dose paroxetine 20-40 mg/day, flexible-dose imipramine 200-300 mg/day, or placebo.

- The demographic characteristics of the three groups were comparable.
- By week 8, there were significantly more HAM-D 'responders' in the paroxetine group compared with placebo (p=0.051) [Figure 1]. At this timepoint, the imipramine group also showed an improved response compared with placebo, but this was not statistically significant (p=0.363).

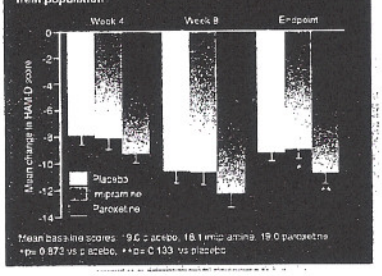
Figure 1: Percentage responders - intent-to-treat population



Response defined as HAM-D score of ≤8 and/or decrease from baseline HAM-D score of ≥ 50%
*p= 0.612 vs placebo, **p= 0.122 vs placebo

- The paroxetine group experienced a greater reduction from baseline HAM-D score at all timepoints, compared with placebo. Reductions were less marked in the imipramine group and were similar to that observed with placebo at the end of the study [Figure 2].

Figure 2: Mean change from baseline HAM-D score: intent-to-treat population



Mean baseline scores: 19.6 placebo, 18.1 imipramine, 19.0 paroxetine
*p= 0.873 vs placebo, **p= 0.133 vs placebo

- By the end of the study, the proportion of patients who experienced remission of depression (HAM-D score ≤ 8) was significantly greater with paroxetine (63%) compared with placebo (46%, p=0.019). The imipramine treatment group did not separate from placebo with respect to remission (50%, p=0.574 vs placebo).
- The large 'placebo response' observed in adolescents may be attributed to the psychosocial supportive therapy provided by the investigators.
- Paroxetine was well tolerated and had a lower incidence of withdrawals due to adverse events compared with imipramine.

Conclusions

- Adolescent depression can have serious consequences, as individuals are at a critical stage of emotional, social, and educational development.
- Paroxetine is effective in the treatment of adolescent depression and is better tolerated than imipramine.
- Paroxetine has the additional advantage of being an efficacious treatment for common psychiatric comorbidities of depression, such as social anxiety disorder and obsessive-compulsive disorder.

References

1. Kashani JH, Carlson GA, Beck NC et al. Am J Psychiatry 1987; 144: 931-934.
2. Feehan M, McGee R, Raja SN, et al. Aust NZ J Psychiatry 1994; 28: 87-99.
3. Humphries LL, Metzler EE. J Ky Med Assoc 1983; 81: 693-696.
4. Hodgman CH, McAnarney ER. Hosp Prac 1992; 27: 73-96.
5. Biederman J, Faraone S, Mick E et al. J Am Acad Child Adolesc Psychiatry 1996; 34: 579-590.
6. SmithKline Beecham. Data on file.
7. Rey-Sanchez F, Gutierrez-Casares JR. J Am Acad Child Adolesc Psychiatry 1997; 36: 1443-1447.
8. Ramos PR, de Dios Vega JL, Cabases JSS et al. Eur J Clin Res 1996; 8: 49-61.

creative design & imaging

PAR001982238

PAR001982238