Antidepressants versus interpersonal psychotherapy in treating depression in HIV-positive patients

M Y H Moosa, FCPsych, MMed Psych, MB ChB
F Y Jeenah, FCPsych, MMed Psych, MB ChB
Division of Psychiatry, Faculty of Health Sciences, University of the Witwatersrand

Aim. Despite the prevalence of HIV and AIDS in South Africa reaching pandemic proportions, very few studies have been published on co-morbid depression. This study at Chris Hani Baragwanath Hospital was conducted on a group of HIV-positive patients with depression who were receiving antiretroviral treatment. The aim of the study was to describe their response to treatment with either an antidepressant or psychotherapy.

Method. The study was prospective, randomised and controlled. The sampling was a convenience sampling, as it included patients attending the HIV clinic. At entry to the study, a clinical diagnostic evaluation and the Hamilton Depression Rating Scale (HAMD) were performed on all subjects by the investigator. The depressed patients were randomly assigned to receive either an antidepressant (citalopram) or psychotherapy (interpersonal psychotherapy, IPT). The HAMD was repeated at the study endpoint of 8 weeks.

Results. Sixty-two HIV-positive persons receiving antiretrovirals participated in this study. Thirty of them were not depressed and served as controls, and 32 were depressed. There were no significant differences between the controls and the patients (either receiving pharmacotherapy or psychotherapy) in respect of any of the socio-demographic characteristics evaluated ($p>0.05$). Approximately 60% (n=19) of the depressed patients were, randomised to receive pharmacotherapy, while 40.6% (n=13) received IPT. The mean HAMD scores of the patients on pharmacotherapy decreased from 25.7 to 6.2 from entry to completion of the study, and those for patients receiving psychotherapy decreased from 22.5 to 8.2. The decreases in HAMD scores in patient groups receiving either pharmacotherapy or psychotherapy were not significantly associated with any socio-demographic variables ($p>0.05$).

Conclusion. Both pharmacotherapy and psychotherapy may be equally effective in the treatment of depression in HIV-positive patients. The choice of treatment will be influenced by factors such as adverse effects of antidepressants and adding another medication to an already complex antiretroviral regimen. In such cases, IPT may be particularly beneficial.

S Afr J Psych 2012;18(2):47-52.

In 2001, a meta-analysis of previously published studies found the frequency of depression among HIV-positive individuals to be almost twice that of HIV-negative individuals.[1] In 2005, Yun *et al.* reported a lifetime prevalence rate of depression of 22 - 45% compared with 15% for the general population.[2] Similiarly, other studies also reported prevalence rates ranging from 2% to 50% in HIV-positive patients.[3-5] It is evident that depression is a common co-morbid psychiatric diagnosis among HIV-positive individuals. The varying prevalence rates reported are probably explained by variations in study population and design, with differences in age, sex, education, ethnicity, stages of HIV/AIDS and diagnosis of depression.

Clinical research had documented a relationship between depression and cell-mediated immunity resulting in alterations in key parameters of cellular immunity, thereby accelerating the course of HIV and AIDS.[6] Although the exact neurobiological mechanisms remain unknown, there is a considerable body of knowledge implicating alterations in CD4, CD8 and NK cells.[7-9] Other potential immune mechanisms include an effect on C-reactive protein, interleukin-2, interleukin-6 and tumour necrosis factor-alpha. Depression is also a risk factor for non-adherence to highly active antiretroviral therapy.[10-13]

On the positive side, there are data showing that currently available treatments (pharmacotherapy and psychotherapy) are effective in the treatment of co-morbid depression and prevent the abovementioned negative sequelae. With regard to pharmacotherapy, tricyclic antidepressants (imipramine and amitriptyline) have been associated with 74 - 89% response rates in HIV patients.[14-16] However, 30% of responders discontinued use after 6 months' follow-up owing to side-effects such as constipation, hypotension, headache, weight gain and sexual dysfunction.[17] Selective serotonin reuptake inhibitors (SSRIs), although not more efficacious (64 - 100% response rates), are

tolerated better than tricyclics.[18-20] Emerging data suggest that the newer antidepressants such as escitalopram,[21,22] reboxetine,[23,24] nefazodone,[25] venlafaxine,[26] mirtazapine[27-29] and buproprion[30-32] are promising alternatives. Two recent meta-analyses of clinical trial results concluded that antidepressant medications are statistically superior to placebo in their overall effect.[33,34]

There are a number of different psychotherapies for depression, which may be provided to individuals or to groups. Research suggests that cognitive behavioural therapy (CBT) can perform as well as antidepressants in treating patients with moderate to severe depression.[35] However, interpersonal psychotherapy (IPT) was developed as a focused, time-limited treatment for its most common target syndrome, depression, and its efficacy has been established in a number of empirical studies.[36-39]

Despite the prevalence of HIV and AIDS in South Africa reaching pandemic proportions, very few studies have been published on co-morbid depression. Much of the work has mainly been done in the West, hence the need for this study. This study was conducted at the Perinatal HIV Research Unit, a research unit of the University of the Witwatersrand based in Soweto at Chris Hani Baragwanath Hospital, on a group of HIV-positive patients with depression who were receiving antiretroviral treatment. The source of the participants may introduce a bias, and the results therefore cannot be generalised. The objectives of this report (part of a larger study) were to describe the socio-demographic characteristics of the patients, and their response to treatment with either an antidepressant or psychotherapy.

Methods
This was a prospective, randomised, controlled and open-labelled study. The sampling was a convenience sampling as it included patients attending the HIV clinic. Volunteers included in the study were 18 years and older and had a *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV) diagnosis of a major depressive disorder (no specifiers). All patients were stable and on antiretroviral therapy to reduce any confounding effects of the antiretroviral therapy on the mood and immunity. Subjects were excluded if they met DSM-IV criteria for any other psychotic, mood or substance abuse disorder, were pregnant or breastfeeding, or were medically ill (HIV wasting syndrome, onset of a new opportunistic infection within the past 6 weeks).

After completion of screening, written informed consent was obtained from the eligible patients. At entry to the study, socio-demographic data were obtained from all the subjects. A clinical diagnostic interview (Structured Clinical Interview for DSM-IV Axis I Disorders: SCID-I) and the Hamilton Depression Rating Scale (HAMD) were performed on all subjects by the investigator. The depressed patients were randomly assigned (by the throw of a dice) to receive either an antidepressant (citalopram) or psychotherapy (IPT). The dose schedule of citalopram was fixed at 20 mg/day

for the first 2 weeks, and increased by 10 - 20 mg in the absence of clear-cut clinical improvement and significant side-effects. A minimum of 5 and up to 12 sessions of IPT were administered by the investigator during the study period (baseline and weeks 2, 4, 6 and 8). The therapy was conducted according to a comprehensive guideline on IPT published by Weissman *et al.*[40]

This clinical guideline is clear, easily digested, highly informative, and provides a conceptual model and illustrates its application in the treatment of major depression. While the investigator was not trained or experienced in conducting IPT, it is our opinion that the therapy was correctly administered according to the above guidelines. However, there were no objective measures to ensure that the IPT had been performed properly, and this is a limitation to this study. The HAMD was repeated at the study endpoint.

Descriptive statistics were computed as means and frequencies (counts and percentages). The two-sample *t*-test was used to compare the continuous characteristics (age) between the groups. The outcome variable was a response to treatment (as measured by either a 50% reduction in HAMD scores or a HAMD score reduced to below 14). Comparisons of response to treatment between the two treatment groups (antidepressant and psychotherapy) with regard to socio-demographic variables were examined by the use of contingency tables (chi-square test with Yates correction and Fischer's exact test, odds ratios). All analyses were done using the Statistical Package for Social Sciences 10.0 for Windows (SPSS Inc., Chicago, IL). A value of $p<0.05$ was considered significant.

All subjects gave written informed consent to participate in the study, which was approved by the Committee for Research on Human Subjects, University of the Witwatersrand. In addition to their regular follow-up visits, patients were required to make two other visits for which they received assistance with travelling costs. Antiretrovirals and antidepressants were supplied by the district mental health clinics.

Results
Sixty-two HIV-positive persons on antiretrovirals participated in this study. Thirty of them were not depressed and served as controls, and 32 were depressed.

Socio-demographic characteristics
The ages of the control group ranged from 27 to 51 years, with a mean of 37.7 years (standard error (SE) 1.2) (95% lower confidence limit (LCL) 34.0; 95% upper confidence limit (UCL) 39.6). Eighty per cent of the control group were females. The majority were single, i.e. not married, divorced or widowed (70%), unemployed despite being able and willing to work (70%), and had a level of education of grades 8 - 12 (83.3%) (Table 1).

All the controls had disclosed their status either to their partner or to a member of their family, and only one patient had a past history of

depression. The majority (63.3%) were receiving antiretrovirals from regimen 1a, with 23% on Triomune.

The ages of the patient group ranged from 24 to 53 years, with a mean of 36.8 years (SE 1.38) (95% LCL 34.0; 95% UCL 39.6). Approximately 90.6% of the patient group were females. The majority were single (67.75%), unemployed despite being able and willing to work (81.25%), and had a level of education of grades 8 - 12 (71.9%) (Table 1).

All the patients had disclosed their status either to their partner or to a member of their family, and only 3 had a past history of depression. The majority (50%) were receiving antiretrovirals from regimen 1a, with 15.6% on Triomune.

Table 1. Socio-demographic characteristics: comparisons between the depressed patients and the controls

Characteristics	Study population (N=62) (n (%))	Controls (N=30) (n (%))	Patients (n=32) Pharmacotherapy (n=19) (n (%))	Psychotherapy (n=13) (n (%))	Significance
Gender					
Male	9 (14.5)	6 (20)	1 (5.3)	2 (15.4)	χ^2=2.045; p=0.359
Female	53 (85.5)	24 (80)	18 (94.7)	11 (84.6)	
Marital status					
Single	43 (69.4)	21 (70)	14 (73.7)	8 (61.5)	χ^2=0.547; p=0.761
Married	19 (30.6)	9 (30)	5 (26.3)	5 (38.5)	
Employment status					
Employed	15 (24.2)	9 (30)	1 (5.3)	5 (38.5)	χ^2=5.707; p=0.058
Unemployed	47 (75.8)	21 (70)	17 (94.7)	12 (61.5)	
Level of education					
Grade 0 - 7	5 (8.1)	2 (6.7)	1 (5.2)	2 (15.4)	χ^2=2.391; p=0.664
Grade 8 - 12	48 (77.4)	25 (83.3)	14 (73.7)	9 (69.2)	
Tertiary	9 (14.5)	3 (10)	4 (21.1)	2 (15.4)	
No. of children					
0 - 1	23 (37.1)	13 (43.3)	7 (36.8)	3 (23.1)	χ^2=5.022; p=0.285
>1	39 (62.9)	17 (56.7)	12 (63.2)	10 (76.9)	
PH of depression					
Yes	4 (6.5)	1 (3.3)	3 (9.4)	0 (0)	χ^2=4.124; p=0.127
No	58 (93.5)	29 (96.7)	16 (84.2)	13 (100)	
FH of depression					
Yes	1 (1.6)	0 (0)	1 (5.3)	0 (0)	χ^2=2.301; p=0.316
No	61 (98.4)	30 (100)	18 (94.7)	13 (100)	
Antiretroviral therapy					
Regimen 1a	35 (56.5)	19 (63.3)	7 (36.8)	9 (69.2)	χ^2=15.68; p=0.047
Regimen 1b	8 (12.9)	1 (3.3)	5 (26.3)	2 (15.4)	
Triomune	12 (17.9)	7 (23.3)	4 (21.1)	1 (7.7)	
Other regimens	7 (12.7)	3 (10)	3 (15.8)	1 (7.7)	
On other medication					
Yes	54 (87.1)	26 (86.7)	17 (89.5)	11 (84.6)	χ^2=0.779; p=0.677
No	8 (12.9)	4 (113.3)	2 (10.5)	2 (15.4)	

PH = personal history; FH = family history.

There were no significant differences between the controls and the patients (either receiving pharmacotherapy or psychotherapy) with respect to demographic characteristics, namely gender (χ^2=2.045; p=0.359); marital status (χ^2=0.547; p =0.761); employment status (χ^2=5.707; p=0.058); highest level of education achieved (χ^2=2.391; p=0.664); number of children (χ^2=5.022; p=0.285); past history of depression (χ^2=4.124; p=0.127); family history of depression (χ^2=2.301; p=0.316); or being on other medication (χ^2=0.779; p=0.677) (Table 1).

Response to treatment

At entry to the study, the mean HAMD score of the control group was 2.1 (SE 0.30) (95% LCL 1.5; 95% UCL 2.7), with a range from 0 to 5. At the end of the study, the mean HAMD score was 1.62 (SE 0.49) (95% LCL 0.62; 95% UCL 2.62), with a range from 0 to 14. There was no significant difference between the HAMD scores from baseline to end of study. None of the scores was 7 or more (the lowest cut-off point), which is regarded as indicative of a diagnosis of depression.

Approximately 60% (n=19) of the depressed patients were randomised to receive pharmacotherapy, while 40.6% (n=13) received IPT. Only 1 patient was lost to follow-up. At entry to the study, the mean HAMD score of the depressed patients as a group was 24.4 (SE 0.88) (95% LCL 22.60; 95% UCL 26.21), with a range from 16 to 34. At the end of the study, the mean HAMD score was 7.03 (SE 0.58) (95% LCL 5.83; 95% UCL 8.23), with a range from 0 to 16.

There were no significant differences in baseline severity of depression in either treatment group. As shown in Fig. 1, the mean HAMD scores of the patients on pharmacotherapy decreased from 25.7 to 6.2, and the scores for those receiving psychotherapy from 22.5 to 8.2, from entry to completion of study. In addition, both
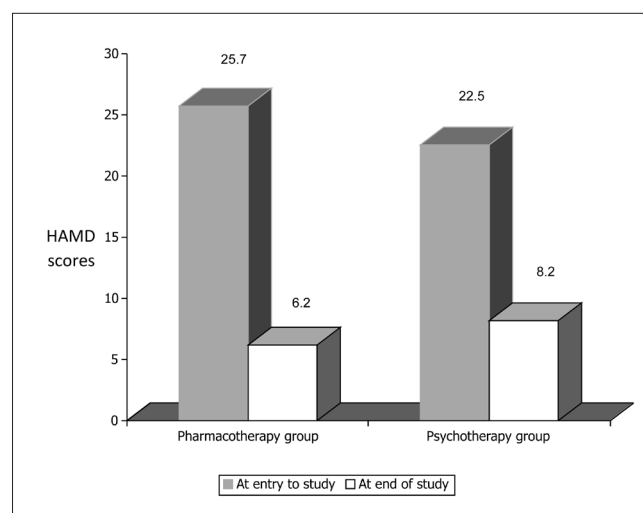

Fig. 1. Changes in HAMD scores in the two treatment groups from baseline to end of study.

treatment groups showed a similar (>50%) decline in HAMD scores. The decreases in HAMD scores in patient groups receiving either pharmacotherapy or psychotherapy were not significantly associated with any socio-demographic variables (p>0.05).

Discussion

Our analysis of patients who completed the study showed a statistically and clinically significant response rate, as evidenced by a reduction of the mean HAMD scores to below 7. Further, there was no difference associated with the type of treatment received, as the mean HAMD scores of the patients on pharmacotherapy (citalopram) decreased to 6.2 and scores for those receiving psychotherapy (IPT) decreased to 8.2. Our results are comparable to those reported in other double-blind antidepressant studies with HIV-positive patients.[15,17,19,41,42]

SSRIs are the most widely used drugs for treatment of depression in the general population because of their favourable safety profile and convenient once-a-day dosing. In addition to the absence of anticholinergic side-effects, SSRIs in general have the potential advantage of greater safety in overdose in patients at risk for suicidal ideation.[43,44] Furthermore, because SSRIs have a relatively long half-life, missed doses are less problematic during unscheduled hospitalisations for HIV-related infections. The choice of antidepressants in HIV-infected patients is still not guided by evidence, as controlled trials comparing SSRIs are lacking. Safety concerns have been raised regarding potential interactions of antidepressants and antiretroviral medications because they share similar metabolic pathways. The likelihood of drug interactions is greatest with the protease inhibitors, which are less widely used and are prescribed at lower doses as newer antiretrovirals in different classes become available. Where drug-drug interaction is a concern, sertraline, citalopram and escitalopram should be considered.[45]

IPT focuses on the social and interpersonal triggers that may cause depression. In IPT there is an assumption that clinical symptoms occur in an interpersonal context and that psychotherapeutic interventions directed at this interpersonal context will alleviate the symptoms.[46] The efficacy of IPT to treat depression has been established in a number of empirical studies.[47] The National Institute of Mental Health Treatment of Depression Collaborative Research Program reports that for the most severely depressed individuals, IPT was less helpful than medication but was of significantly more benefit than a placebo.[37] DiMascio *et al.* also found that either medication or IPT led to equal overall symptom reduction in patients with depression.[39] Similarly, in a study of 23 depressed HIV-positive individuals in 1992, Markowitz *et al.* reported that IPT was successful in resolving the depression of 87% patients in the sample.[48] In a subsequent paper in 1995, Markowitz *et al.* presented preliminary data for two treatment modalities in a randomised clinical trial (paralleling that of the NIMH Collaborative Research Program).[36] They found that for depressed HIV-positive patients who were not acutely ill, IPT was more successful than

supportive psychotherapy in lessening depression. Differences were observable by the middle of treatment (8 weeks) and remained after termination of treatment. Patients receiving IPT benefited from improved functioning physically as well as emotionally. As is the case with pharmacotherapy, psychological intervention studies using large samples with sufficient statistical power have also found significant changes in the immunity of patients responding to treatment.[49-51] Our study also found IPT to be as effective as antidepressants in treating depression and supports these previous studies. Significantly more patients drop out of antidepressant treatment than psychotherapy because of the side-effects of antidepressants.[52] Successful psychotherapy appears to prevent the recurrence of depression even after it has been terminated or replaced by occasional 'booster' sessions.

The combination of psychotherapy and medication may be the most effective way to treat depression.[53] Both treatments together are even more effective, because the medication improves the vegetative symptoms and the IPT helps with mood, suicidal ideation, work and interests. A study of depressed outpatients one year after treatment with either IPT or amitriptyline, alone or in combination, found that almost all patients were functioning well.[38] However, those who had received IPT (with or without medication) did better with regard to social functioning. Choice of treatment should be based on considerations such as accessibility (e.g. the guideline manual for IPT is not freely and easily available to all clinicians), side-effect profile (e.g. citalopram, where drug-drug interaction is a concern), and past experience with effective or ineffective treatments. While its relative cost-effectiveness may give IPT the edge against CBT, in terms of therapist training costs it may be less cost-effective than antidepressant medication and group psycho-education and problem-solving treatment (both of which require considerably fewer sessions).

Almost all the subjects in the patient group denied a past history of depression. This would be unusual considering the fact that depression is extremely common in the general population, with a worldwide lifetime prevalence rate of 20%.[54] Further, many studies report that current major depression in HIV-positive patients was significantly associated (40 - 45%) with a lifetime history of major depression.[55-57] Our patients may have experienced depressive symptoms in the past but did not report them to a healthcare professional, or depressive symptoms were reported but missed or misdiagnosed by the patients' primary care clinicians.[58] Alternatively, the patients may have been unable to access appropriate mental health services for treatment of their symptoms.[59,60]

Some possible limitations of this study should be noted. The sample size was small and this was not a population-based study, so the results may be biased by the methods of recruitment and enrollment and therefore not generalisable. The subjects were overwhelmingly female and the treatment outcomes of depressed HIV-positive men, who face different psychosocial and socio-economic pressures, may be different. The HAMD, although established as a highly reliable and valid assessment tool, has many challenges: it is comparatively long to administer (30 minutes) in the outpatient setting, oversensitive to somatic symptoms (patients with physical illness may rate more severely), and relies heavily on the clinical interviewing skills and expertise of the assessment rater in eliciting the necessary information. Several strengths of the present study should also be noted. We performed depression analyses with the traditional 17-item HAMD, as well as a clinical interview (SCID-I) that eliminated physical symptoms which might overlap with symptoms of HIV disease progression. Comparisons of the demographic characteristics and behavioural characteristics of subjects did not reveal any significant differences between the groups.

Conclusion

Results of this study may have implications for the treatment of depression among people with HIV. Screening for depression is essential, and patients who are found to be depressed can be targeted for closer monitoring and treatment at all antiretroviral rollout clinics. Both pharmacotherapy and psychotherapy appear to be equally effective in the treatment of depression, although the sample size was too small to make this conclusion. However, barriers to successful treatment include refusal or non-adherence to antidepressants because of the stigma and adverse effects. Adding another medication to complex regimens of antiretrovirals may not be acceptable to the patient, and IPT may therefore be particularly beneficial and preferred. Yet, as the sole study of its kind, our results require replication in a study with a larger sample size and a more general population.

References

1. Ciesla JA, Roberts JE. Meta-analysis of the relationship between HIV infection and risk for depressive disorders. Am J Psychiatry 2001;158:725-730. [http://dx.doi.org/10.1176/appi.ajp.158.5.725]
2. Yun LWH, Maravi M, Kobayashi JS, et al. Antidepressant treatment improves adherence to antiretroviral therapy among depressed HIV-infected patients. J Acquir Immune Defic Syndr 2005;38:432-438. [http://dx.doi.org/10.1097/0000147524.19122.fd]
3. Treisman G, Angelino A. Interrelation between psychiatric disorders and the prevention and treatment of HIV infection. Clin Infect Dis 2007;45(Suppl 4):S313-317. [http://dx.doi.org/10.108/522556]
4. Dubé B, Benton T, Cruess DG, et al. Neuropsychiatric manifestations of HIV infection and AIDS. J Psychiatry Neurosci 2005;30(4):237-246.
5. Judd F, Komiti A, Chua P, et al. Nature of depression in patients with HIV/AIDS. Aust N Z J Psychiatry 2005;39(9):826-832. [http://dx.doi.org/10.111/j.1440-1614.2005.01659.x]
6. Kemeny ME, Weiner H, Taylor SE, et al. Repeated bereavement, depressed mood, and immune parameters in HIV seropositive and seronegative gay men. Health Psychol 1994;13:14-24. [http://dx.doi.org/10.1037/ 0278-6133.13.1.14]
7. Levy JA. The importance of the innate immune system in controlling HIV infection and disease. Trends Immunol 2001;22:312-231. [http://dx.doi.org/10.1016/S1471-4906(01)2901925-1]
8. Ickovics JR, Hamburger ME, Vlahov D, et al. (HIV Epidemiology Research Study Group). Mortality, CD4 cell count decline, and depressive symptoms among HIV seropositive women. JAMA 2001;285:1466-1474. [http://dx.doi.org/10.1001/jama.285.11.1466]
9. Gea-Banacloche JC, Migueles SA, Martino L, et al. Maintenance of large numbers of virus-specific CD8+ T cells in HIV-infected progressors and long-term nonprogressors. J Immunol 2000;165:1082-1092.
10. Ammassari A, Antinori A, Aloisi MS, et al. Depressive symptoms, neurocognitive impairment, and adherence to highly active antiretroviral therapy among HIV-infected persons. Psychosomatics 2004;45:394-402. [http://dx.doi.org/10.1176/appi.psy.45.5.394]

11. Starace F, Ammassari A, Trotta MP, et al. Depression is a risk factor for suboptimal adherence to highly active antiretroviral therapy. J Acquir Immune Defic Syndr 2002;31(Suppl 3):S136-S139. [http://dx.doi.org/10.1097/00126334-200212153-00010]

12. Murphy DA, Wilson CM, Durako SJ, et al. Antiretroviral medication adherence among the REACH HIV-infected adolescent cohort in the USA. AIDS Care 2001;13:27-40. [http://dx.doi.org/10.1080/09540120020018161]

13. Lucas GM, Cheever LW, Chaison RE, et al. Detrimental effects of continued illicit drug use on the treatment of HIV-1 infection. J Acquir Immune Defic Syndr 2001;71:251-259. [http://dx.doi.org/10.1097/00126334-200107010-00006]

14. Anderson IM. Selective serotonin reuptake inhibitors versus tricyclic antidepressants: A meta-analysis of efficacy and tolerability. J Affect Disord 2000;58(1):19-36. [http://dx.doi.org/10.1016/S0165-0327(99)00092-0]

15. Markowitz J, Kocsis JH, Fishman B, et al. Treatment of depressive symptoms in HIV-positive patients. Arch Gen Psychiatry 1998;55:452-457.

16. Anderson IM. SSRIS versus tricyclic antidepressants in depressed inpatients: A meta-analysis of efficacy and tolerability. Depress Anxiety 1998;Vol 7:Suppl 1:11-17. [http://dx.doi.org/10.1002/(SICI)1520-6394(81998)7:1+ <11::AID-DA4>3.O. CO;2-I]

17. Ferrando SJ, Goldman J, Charness WE. Selective serotonin reuptake inhibitor treatment of depression in symptomatic HIV infection and AIDS. Gen Hosp Psychiatry 1997;19:89-97. [http://dx.doi.org/10.1016/S0163-8343(96)00172-7]

18. Penzak SR, Reddy YS, Grimsley SR. Depression in patients with HIV infection. Am J Health Syst Pharm 2000;57:376-386.

19. Rabkin JG, Rabkin R, Wagner G. Effects of fluoxetine on mood and immune status in depressed patients with HIV illness. J Clin Psychiatry 1994;55:92-97.

20. Targ EF, Karasic DH, Diefenbach PN, et al. Structured group therapy and fluoxetine to treat depression in HIV-positive persons. Psychosomatics 1994;35(2):132-137.

21. Lepola UM, Loft H, Reines EH. Escitalopram (10 - 20 mg/day) is effective and well tolerated in a placebo-controlled study in depression in primary care. Int Clin Psychopharmacol 2003;18(4):211-217. [http://dx.doi.org/10.1097/00004850-200307000-00003]

22. Wade A, Michael LO, Bang HK. Escitalopram 10 mg/day is effective and well tolerated in a placebo-controlled study in depression in primary care. Int Clin Psychopharmacol 2002;17(3):95-102. [http://dx.doi.org/10.1097/00004850-200205000-00001]

23. Montgomery SA, Schatzberg AF. Introduction. Reboxetine: a new selective antidepressant for the treatment of depression. J Clin Psychiatry 1998;59(Suppl 14):3.

24. Berzewski H, Van Moffaert M, Gagiano CA. Efficacy and tolerability of reboxetine compared with imipramine in a double-blind study in patients suffering from major depressive episodes. Eur Neuropsychopharmacol 1997;7:S37-47. [http://dx.doi.org/10.1016/S0924-977X(97)00418-5]

25. Elliott AJ, Russo J, Bergam K, et al. Antidepressant efficacy in HIV-seropositive outpatients with major depressive disorder: an open trial of nefazodone. J Clin Psychiatry 1999;60(4):226-231.

26. Klesmer J, Badescu R. Pharmacologic treatment of mood disorders in acquired immune deficiency syndrome (AIDS). Curr Psychiatry Rep 2002;4(3):222-227. [http://dx.doi.org/10.1007/s11920-002-0033-6]

27. Mayers AG, Baldwin DS. Antidepressants and their effect on sleep. Hum Psychopharmacol 2005;20(8):533-559. [http://dx.doi.org/10.1002/hup.726]

28. Winokur A, DeMartinis NA, McNally DP, et al. Comparative effects of mirtazapine and fluoxetine on sleep physiology measures in patients with major depression and insomnia. J Clin Psychiatry 2003;64(10):1224-1229. [http://dx.doi.org/10.1002/hup.726]

29. Elliott AJ, Roy-Byrne PP. Mirtazapine for depression in patients with human immunodeficiency virus. J Clin Psychopharmacol 2000;20(2):265-267. [http://dx.doi.org/10.1097/00004714-200004000-00023]

30. Zisook S, Rush AJ, Haight BR, et al. (2006). Use of bupropion in combination with serotonin reuptake inhibitors. Biol Psychiatry 2006;59(3):203-210. [http://dx.doi.org/10.1016/Fj.biopsych.2005.06.027]

31. Rush AJ, Trivedi MH, Wisniewski SR, et al. Bupropion-SR, sertraline, or venlafaxine-XR after failure of SSRIs for depression. N Engl J Med 2006;354(12):1231-1242.

32. Trivedi MH, Fava M, Wisniewski SR, et al. Medication augmentation after the failure of SSRIs for depression. N Engl J Med 2006;354(12):1243-1252.

33. Kirsch I, Deacon BJ, Huedo-Medina TB, et al. Initial severity and antidepressant benefits: A meta-analysis of data submitted to the Food and Drug Administration. PLoS Med 2008;5(2):e45.

34. Turner EH, Matthews AM, Linardatos E, et al. Selective publication of antidepressant trials and its influence on apparent efficacy. N Engl J Med 2008;358(3):252-260.

35. Roth A, Fonagy P. What Works for Whom? A Critical Review of Psychotherapy Research. 2nd ed. New York: Guilford Press, 2005:78.

36. Markowitz JC, Klerman GL, Clougherty KF, et al. Individual psychotherapies for depressed HIV-positive patients. Am J Psychiatry 1995;152:1504-1509. [http://dx.doi.org/10.1056/NEJMoa052963]

37. Elkin I, Shea MT, Watkins JT, et.al. National Institute of Mental Health Treatment of Depression Collaborative Research Program. General effectiveness of treatments. Arch Gen Psychiatry 1989;46(11):971-982. [http://dx.doi.org/10.1001/archpsyc.1989.01810110013002]

38. Weismann MM, Klerman GL, Prusoff BA, et al. Depressed outpatients: results one year after treatment with drugs and /or interpersonal psychotherapy. Arch Gen Psychiatry 1981;38:51-55. [http://dx.doi.org/10.1001 rchpsyc.1981.01780260053005]

39. Di Mascio A, Weismann MM, Prusoff BA, et al. Differential symptom reduction by drugs and psychotherapy in acute depression. Arch Gen Psychiatry 1997;36:1450-1456.

40. Weissman MM, Markowitz JC, Klerman GL. Comprehensive Guide to Interpersonal Psychotherapy. New York: Basic Books, 2000.

41. Zisook S, Peterkin J, Goggin KJ, et al. Treatment of major depression in HIV seropositive men. J Clin Psychiatry 1998;59:217-224.

42. Levine S, Anderson D, Bystritsky A. A report of eight HIV-seropositive patients with major depression responding to fluoxetine. J Acquir Immune Defic Syndr 1990;3:1074-1077.

43. Cote TR, Biggar RJ, Dannenberg A. Risk of suicide among persons with AIDS: a national assessment. JAMA 1992;268:2066-2068. [http://dx.doi.org/10.1001/jama.268.15.2066]

44. Starace F. Epidemiology of suicide among persons with AIDS. AIDS Care 1995;7:S123-S128. [http://dx.doi.org/10.108)/09540129550126100]

45. Caballero J, Nahata MC. Use of selective serotonin-reuptake inhibitors in the treatment of depression in adults with HIV. Ann Pharmacother 39:141-145. [http://dx.doi.org/10.1345/aph.1E248]

46. Klerman GL, Weissman MM, Rounsaville BJ, et al. (1984). Interpersonal Psychotherapy of Depression. New York: Basic Books, 2005.

47. Ferrando SJ, Freyberg Z. Treatment of depression in HIV-positive individuals: an evidence-based review. Int Rev Psychiatry 2008;20:61-71.

48. Markowitz JC, Klerman GL, Perry SW. Interpersonal psychotherapy of depressed HIV positive outpatients. Hosp Community Psychiatry 1992;43:885-890.

49. Goodkin K, Feaster DJ, Asthana D, et al. A bereavement support group intervention is longitudinally associated with salutary effects on the CD4 cell count and number of physician visits. Clin Diagn Lab Immunol 1998;5:382-391.

50. Gregerson MB, Roberts IM, Amiri MM. Absorption and imagery locate immune response in the body. Biofeedback and Self-Regulation 1996;21:149-165. [http://dx.doi.org/10.1007/BF02284693]

51. Hewson-Bower B and Drummond PD. Secretory immunoglobulin A increases during relaxation in children with and without recurrent upper respiratory tract infections. J Dev Behav Pediatr 1996;17:311-316. [http://dx.doi.org/10.1097/00004703-199610000-00004]

52. Cuijpers P, van Straten A, van Oppen P, et al. Are psychological and pharmacologic interventions equally effective in the treatment of adult depressive disorders? A meta-analysis of comparative studies. J Clin Psychiatry 2008;69(11):1675-1685. .

53. Van Voorhees BW, Smith S, Ewigman B. Treat depressed teens with medication and psychotherapy. J Fam Pract 2008;57(11):735-739.

54. Steffens DC, Skoog I, Norton MC, et al. Prevalence of depression and its treatment in an elderly population: The Cache County study. Arch Gen Psychiatry 2000;57:601-607. [http://dx.doi.org/10.1001/archpsyc.57.6.601]

55. Perkins DO, Stern RA, Golden RN, et al. Mood disorders in HIV infection: prevalence and risk factors in a non-epicenter of the AIDS epidemic. Am J Psychiatry 1994;151:233-236.

56. Williams JW, Rabkin JG, Remien RH, et al. Multidisciplinary baseline assessment of homosexual men with and without human immunodeficiency virus infection. Arch Gen Psychiatry 1991;48:124-130. [http://dx.doi.org/10.1001/archpsyc.1991.01810260032005]

57. Perry S, Jacobsberg LB, Fishman B, et al. Psychiatric diagnosis before serologic testing for the human immunodeficiency virus. Am J Psychiatry 1990;147:89-93.

58. World Health Organization. Johnson & McLeod. 2007. http://www.who.org.int (accessed 30 August 2009).

59. Moosa MYH, Jeenah FY. Community psychiatry: An audit of the services in Southern Gauteng. South African Journal of Psychiatry 2008;14:36-43.

60. Lund C, Flisher AJ. Norms for mental health services in South Africa. Soc Psychiatry Psychiatr Epidemiol 2006;41(7):587-594. [http://dx.doi.org/10.1007/s00127-006-0057-z]