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.

tolerated better than tricyclics. Emerging data suggest that the newer antidepressants such as escitalopram, reboxetine, nefazodone, venlafaxine, mirtazapine and bupropion are promising alternatives. Two recent meta-analyses of clinical trial results concluded that antidepressant medications are statistically superior to placebo in their overall effect.

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. 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.

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 of mental health clinics.

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.

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 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

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Study population</th>
<th>Controls</th>
<th>Pharmacotherapy</th>
<th>Psychotherapy</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=62) (n (%))</td>
<td>(N=30) (n (%))</td>
<td>(n=19) (n (%))</td>
<td>(n=13) (n (%))</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9 (14.5)</td>
<td>6 (20)</td>
<td>1 (5.3)</td>
<td>2 (15.4)</td>
<td>χ²=2.045; p=0.359</td>
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<tr>
<td>Female</td>
<td>53 (85.5)</td>
<td>24 (80)</td>
<td>18 (94.7)</td>
<td>11 (84.6)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Single</td>
<td>43 (69.4)</td>
<td>21 (70)</td>
<td>14 (73.7)</td>
<td>8 (61.5)</td>
<td>χ²=0.547; p=0.761</td>
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<tr>
<td>Married</td>
<td>19 (30.6)</td>
<td>9 (30)</td>
<td>5 (26.3)</td>
<td>5 (38.5)</td>
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<tr>
<td>Employment status</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>15 (24.2)</td>
<td>9 (30)</td>
<td>1 (5.3)</td>
<td>5 (38.5)</td>
<td>χ²=5.707; p=0.058</td>
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<tr>
<td>Unemployed</td>
<td>47 (75.8)</td>
<td>21 (70)</td>
<td>17 (94.7)</td>
<td>12 (61.5)</td>
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<tr>
<td>Level of education</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Grade 0 - 7</td>
<td>5 (8.1)</td>
<td>2 (6.7)</td>
<td>1 (5.2)</td>
<td>2 (15.4)</td>
<td>χ²=2.391; p=0.664</td>
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<tr>
<td>Grade 8 - 12</td>
<td>48 (77.4)</td>
<td>25 (83.3)</td>
<td>14 (73.7)</td>
<td>9 (69.2)</td>
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<tr>
<td>Tertiary</td>
<td>9 (14.5)</td>
<td>3 (10)</td>
<td>4 (21.1)</td>
<td>2 (15.4)</td>
<td></td>
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<tr>
<td>No. of children</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 – 1</td>
<td>23 (37.1)</td>
<td>13 (43.3)</td>
<td>7 (36.8)</td>
<td>3 (23.1)</td>
<td>χ²=5.022; p=0.285</td>
</tr>
<tr>
<td>&gt;1</td>
<td>39 (62.9)</td>
<td>17 (56.7)</td>
<td>12 (63.2)</td>
<td>10 (76.9)</td>
<td></td>
</tr>
<tr>
<td>PH of depression</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4 (6.5)</td>
<td>1 (3.3)</td>
<td>3 (9.4)</td>
<td>0 (0)</td>
<td>χ²=4.124; p=0.127</td>
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<tr>
<td>No</td>
<td>58 (93.5)</td>
<td>29 (96.7)</td>
<td>16 (48.2)</td>
<td>13 (100)</td>
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<td>FH of depression</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1 (1.6)</td>
<td>0 (0)</td>
<td>1 (5.3)</td>
<td>0 (0)</td>
<td>χ²=2.301; p=0.316</td>
</tr>
<tr>
<td>No</td>
<td>61 (98.4)</td>
<td>30 (100)</td>
<td>18 (94.7)</td>
<td>13 (100)</td>
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<tr>
<td>Antiretroviral therapy</td>
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<td>Regimen 1a</td>
<td>35 (56.5)</td>
<td>19 (63.3)</td>
<td>7 (36.8)</td>
<td>9 (69.2)</td>
<td>χ²=15.68; p=0.047</td>
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<tr>
<td>Regimen 1b</td>
<td>8 (12.9)</td>
<td>1 (3.3)</td>
<td>5 (26.3)</td>
<td>2 (15.4)</td>
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<td>Triomune</td>
<td>12 (17.9)</td>
<td>7 (23.3)</td>
<td>4 (21.1)</td>
<td>1 (7.7)</td>
<td></td>
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<tr>
<td>Other regimens</td>
<td>7 (12.7)</td>
<td>3 (10)</td>
<td>3 (15.8)</td>
<td>1 (7.7)</td>
<td></td>
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<td>On other medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>54 (87.1)</td>
<td>26 (86.7)</td>
<td>17 (89.5)</td>
<td>11 (84.6)</td>
<td>χ²=0.779; p=0.677</td>
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<tr>
<td>No</td>
<td>8 (12.9)</td>
<td>4 (13.3)</td>
<td>2 (10.5)</td>
<td>2 (15.4)</td>
<td></td>
</tr>
</tbody>
</table>

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 ($\chi^2=2.045; p=0.359$); marital status ($\chi^2=0.547; p=0.761$); employment status ($\chi^2=5.707; p=0.058$); highest level of education achieved ($\chi^2=2.391; p=0.664$); number of children ($\chi^2=5.022; p=0.285$); past history of depression ($\chi^2=4.124; p=0.127$); family history of depression ($\chi^2=2.301; p=0.316$); or being on other medication ($\chi^2=0.779; p=0.677$) (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 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.

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. 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.

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. The efficacy of IPT to treat depression has been established in a number of empirical studies. 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. DiMascio et al. also found that either medication or IPT led to equal overall symptom reduction in patients with depression. 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. 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). 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.\textsuperscript{9,10} 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.\textsuperscript{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.\textsuperscript{51} 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.\textsuperscript{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%.\textsuperscript{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.\textsuperscript{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.\textsuperscript{58} Alternatively, the patients may have been unable to access appropriate mental health services for treatment of their symptoms.\textsuperscript{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


