PATTERNS OF ANTIDEPRESSANT PRESCRIPTIONS: II
CONTINUATION PHASE TREATMENTS

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ABSTRACT

In an exercise carried out to ascertain adequacy of antidepressant treatment, seventy case notes of patients of depression on continuation treatment with antidepressants were scanned. Antidepressants had been used universally. TCAs were the most commonly used drugs, although Fluoxetine had also been used quite frequently. Continuation treatment was found to be deficient in over a third (n=24; 34%) of the cases, on either of the two parameters i.e. dose of drugs or duration of treatment. The outcome was poorer in those treated inadequately. The reasons for this 'treatment gap' need to be explored. Similar studies need to be conducted in other settings. Education of all clinicians about these central issues of antidepressant treatment is essential.

Key words: Antidepressant prescriptions, continuation phase of depression

Two aspects of long term treatment with antidepressants are relapse prevention during a continuation treatment period in responders to acute treatment, and maintenance treatment for those who have remained well during the continuation phase, to prevent new episodes (Montgomery, 1994) Relapse prevention studies have shown that premature discontinuation of antidepressant treatment soon after response to treatment of the acute episode is associated with return of original symptoms in approximately half of the patients (Prien & Kupfer, 1986). The continuation phase of treatment is thus required for consolidation of apparent response to antidepressants, and prevent early relapses.

Two central issues in continuation therapy are duration of treatment and doses of the antidepressants to be used. Regarding the former the unanimous conclusion is that all episodes of depression, whether first onset or recurrent, should be treated for a further period of about six months after the patient has responded (Montgomery, 1994). Most authors also recommend that full doses of antidepressants should be used during this period (Frank et al., 1990), although some studies have suggested that lower doses might be as effective (Mindham et al., 1973). The consensus view reflected by some of the current guidelines seems to be that, continuation doses should be no less than those used for acute treatment (American Psychiatric Association Work Group on Major Depressive Disorder, 1993; Clinical Resource Audit Group, 1993).

These viewpoints though well known are often not translated into clinical practice. There are several reports of inadequate treatment with antidepressants during the acute phase (Quitkin, 1985). There are, however, very few similar investigations of continuation treatment. Case records of 4052 patients with a diagnosis of depression followed-up for 2 years were studied by Melfi et al. (1998) in a recent investigation. They demonstrated that those patients who continued treatment for longer periods fared better in terms of recurrences and relapses. In another retrospective study 102 patients who had recovered from an acute episode of depression were interviewed 18 months after discharge (Ramana et al., 1999). Assessments of adequacy of treatment and patient compliance were made.
monthly over this period. About 30% of the patients had failed to receive adequate long-term treatment. Although deficiencies in treatment were greater inpatients who had not recovered fully, further episodes of depression were not particularly associated with inadequate treatment.

A survey of adequacy of treatments in depression would be particularly useful in the Indian context where there is a marked variability in practice across different treatment settings, and a genuine need to establish minimum standards in all aspects of psychiatric care. This study was a part of larger exercise to ascertain the nature and adequacy of antidepressant treatment in a selected group of depressed patients. This paper deals with the nature of treatment in the continuation phase, focusing mainly on the type and doses of drugs used and the length of treatment.

MATERIAL AND METHOD

The study was carried out in the psychiatric unit of a large multi-speciality teaching institution (Nehru Hospital of the Postgraduate Institute of Medical Education and Research, Chandigarh). All patients attending the unit are initially screened by a psychiatrist at the ‘Walk-in’ clinic level, and drug treatment often started. Subsequently, a detailed evaluation is done by a trainee psychiatrist under supervision of a consultant. Treatment plans are charted out, and patients are then followed-up in the outpatient clinic, unless admitted, or referred elsewhere.

Case notes for the year 1996 were scanned for all cases of depression. Those, which fulfilled the selection criteria, were included for purposes of the study. The data pertaining to antidepressants was then extracted from the notes and entered onto the pre-set proforma. Selection criteria: Cases were included if they were diagnosed to have either depressive episodes of mild, moderate, or severe type, with or without somatic symptoms (ICD-10), or recurrent depressive disorder with similar current episodes. Cases were excluded if they had: bipolar depression, any comorbid diagnoses, psychotic symptoms, chronic episodes (>2 years), organic brain syndrome, substance abuse, associated physical problems judged to be interfering with antidepressant treatment & follow up period less than 6 weeks.

A deliberate attempt was thus made to include relatively ‘uncomplicated’ cases of depression by excluding secondary depression, chronic episodes, and comorbid conditions. Although this restricted the scope of the study, it was felt that proper judgements about adequacy of treatment could only be made after ruling out these confounding variables.

A total of 108 such cases of depression were identified. Seventy of these had received continuation treatment after recovering from the acute episode. Data regarding various aspects of antidepressant treatment during the continuation phase were extracted from these 70 case notes. The criteria for ‘adequacy’ of treatment during the continuation phase were derived from standard guidelines and results of original studies. These have been included in the appendix.

RESULTS

Only results pertaining to the continuation phase treatment are presented here. Demographic and clinical profile: Majority of the sample was female (n=41; 59%), most in the age range of 30 to 49 years (57%), with 17% below 30 years, and 26% above 50 years. Average age of the sample was 42.23 (s.d. 13.83) years. Fifty cases had a diagnosis of single depressive episode, 20 had recurrent depressive disorders. The commonest diagnosis for the index episode was moderate depression with or without somatic symptoms (n=40; 57%), followed by severe depression without psychotic symptoms (n=24; 34%). In summary, the sample comprised mainly of middle aged females with moderate depression. Modes of treatment: Antidepressants were used in all cases. One case received three treatments of ECT over the first two weeks of the continuation phase, in combination with
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Antidepressants were used singly in 61 cases, 9 cases received a combination of these drugs. In all cases, except one where drugs were switched (from Fluoxetine to Imipramine), antidepressant(s) used during the acute phase were continued during the continuation phase. TCAs were the most commonly used agents, 40 cases (57%) received a drug from this group either alone or in combination with others. Imipramine was the TCA most commonly used (n=26; 37%). However, Fluoxetine was used in 27 cases (39%), in eight of these an additional drug was also used (table -1).

TABLE - 1
M ODES OF CONTINUATION TREATMENT

1. Treatment with a single drug
Type of drug (n = 62)
Imipramine 24
Dothepin 7
Nor-‘triptiline 3
Amitriptyline 2
Clomipramine 1
Fluoxetine 19
Mianserin 4
Amoxapine 1

2. Treatment with a combination of drugs
Drug combination (n = 9)
Fluoxetine & Trazodone 4
Mianserin & Trazodone 1
Fluoxetine & Imipramine 2
Fluoxetine & Nor-‘triptiline 1
Fluoxetine & Amoxapine 1

Total number of cases - 70; one patient received two drugs in succession
One patient received ECT in addition to Imipramine

TABLE - 2
DOSE OF ANTIDEPRESSANTS

| Dose range                | No of Cases |
|---------------------------|-------------|
| TCAs* (n = 40)            |             |
| Less than 150 mg/day      | 25          |
| 150 mg/day & more        | 15          |
| Fluoxetine (n = 27)      |             |
| 20 to 30 mg/day          | 16          |
| 40 mg/day & more         | 11          |
| Mianserin (n = 5)        |             |
| Less than 30 mg/day      | 3           |
| 30 mg/day & more         | 2           |

* All TCA doses in Imipramine equivalents

Doses used/duration of treatment: TCAs were mostly used in doses less than 150 mg/day Imipramine equivalents. Twenty five patients (63%) received doses less than this, and only 15 patients received 150 mg/day or more. Most patients being treated with Fluoxetine received a dose of 20 - 30 mg daily (n=16; 59%), (table -2).

Antidepressants were withdrawn in 8 cases during the continuation phase. One of these patients was discovered to be pregnant, the other had switched into hypomania. The reasons for stopping drugs in the rest were not clear. In 18 cases the dose of the antidepressant was reduced during continuation treatment. None of these dose reductions could be attributed to onset of side effects, and thus remained inexplicable. Thus, although the majority of patients (n=44; 63%) had received doses similar to those used during acute phases of treatment, at least 24 patients (34%) had their dose reduced or drug withdrawn for unknown reasons (table-2).

TABLE - 3
DOSEAGE STRATEGIES DURING THE CONTINUATION PHASE

| Dose strategies            | No. of cases |
|----------------------------|-------------|
| Same as acute phase        | 23          |
| Dose reduced +             | 12          |
| Drug withdrawn *           | 6           |

* Reasons for reduction in dose in these patients not clear
+ Reasons for stopping drug in two patients was onset of pregnancy and hypomania respectively; in others reasons were unclear

TABLE - 4
OUTCOME OVER SIX M ONTHS

| Dose/outcome*              | Well | Unwell |
|-----------------------------|------|--------|
| Same as acute phase         | 23   | 2      |
| Dose reduced or drug        | 12   | 8      |

* X² = 4.86, df = 1, p < 0.05 (Yates correction applied)

Outcome over six months: Twenty one cases had dropped out before six months, two had not completed six months of continuation therapy, one each had become hypomanic or pregnant. It was thus possible to make an approximate
judgement of the outcome over six months of continuation treatment in only 45 patients, who had followed up, for that duration. These patients had been seen about once every two months during this period (average number of visits - 2.67 ± 1.49).

Whenever the notes indicated that the patient had developed fresh depressive symptoms this was taken as a ‘worsening’ in patient’s clinical state. When the notes indicated that the patient had developed the full complement of depressive symptoms (sufficient to qualify for a depressive episode), this was taken as a ‘relapse’. For comparing outcome these two categories were combined.

The outcome data (table - 4) show that of these 35 patients had remained well during the continuation phase, whereas 10 had either deteriorated or relapsed completely. Table - 4 also shows, that while only a small proportion of patients (9%) on full doses had a poor outcome, a much larger number of patients (67%), whose drugs were either stopped or doses reduced, had worsened or relapsed. These differences were statistically significant ($x^2=4.86; \text{df}=1; p<0.05$).

**DISCUSSION**

A case note study such as this has several limitations. Incomplete records, lack of structured assessments, and the effect of confounding variables make interpretation of data difficult. Several tentative conclusions can nevertheless be made.

Regarding adequacy of continuation treatment, most patients had been continued on antidepressants for a period of six months, unless they had dropped out, or drugs had to be stopped for other reasons. In a small minority drugs had been withdrawn for no apparent reason, and in a much larger proportion their dose had been reduced quite inexplicably. Overall, more than a third of the patients (34%) had received continuation treatment that was inadequate with regard to doses or duration. This is quite similar to the figure of 30% reported by Ramana et al. (1999), although their study was of a much longer duration. In this study cases which had received inadequate treatment were significantly more likely to have worsened or relapsed completely. In contrast, Ramana et al. (1999) had found inadequate treatment to be associated with non-recovery, but not further recurrences. They had thus come to the conclusion that low levels of treatment were not associated with poor outcome. The fact that cases with inadequate treatment had a poorer outcome in this study perhaps lends further credence to the recommendation that continuation treatment should continue for six months at full doses of antidepressants (Frank et al., 1990).

The type of antidepressant treatment used during the continuation period is also of some interest. Not surprisingly drugs were used universally. Use of other modes such as ECT or mood stabilisers was uncommon or non-existent, perhaps partly due to the nature of the sample. In all cases except one the drug(s) used during the acute phase were continued. The commonly used drugs were Fluoxetine (the only SSRI available in India at the time of this study), and Imipramine. Although the efficacy of TCAs in long-term treatment is well established, data regarding SSRIs is still emerging (Montgomery, 1994). However, this study shows that SSRIs are being used for this purpose in clinical situations. Actual doses of drugs used during the continuation phase are highly variable, perhaps a bit on the lower side, especially with regard to TCAs. This was observed in the acute phase of treatment as well, and is perhaps due to lower dose requirements of the Asian population as documented by some studies (Kuruvilla, 1986). However, without further dose-recognition studies, this will remain a mere speculation.

In conclusion, this survey of continuation treatment reveals that although antidepressants are being used for this purpose, either doses or duration of treatment are inadequate in a substantial number of patients. This was despite the study being conducted in a teaching institution where concerted efforts are made to maintain minimum standards of care. The reasons for this ‘treatment gap’ between...
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Knowledge and practice need to be explored, since low levels of continuation treatment seem to be associated with poor outcome. It may thus be necessary to conduct prospective investigations of a similar nature to examine this association further. Such studies also need to be carried out in other settings (e.g. general practice) in India, to learn more about quality of treatment being received by patients with depression. Education of all clinicians about these central aspects of antidepressant treatment remains a priority.

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