



Original article

Maintenance pharmacotherapy for recurrent major depressive disorder in primary care: A 5-year follow-up study

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ABSTRACT

Background: Most practice guidelines recommend maintenance antidepressant treatment for recurrent major depressive disorder. However, the degree to which such guidance is actually followed in primary health care has remained obscure. We investigated the provision of maintenance antidepressant treatment within a representative primary care five-year cohort study.

Methods: In the Vantaa Primary Care Depression Study, a stratified random sample of 1119 adult patients was screened for depression using the Prime-MD. Depressive and comorbid psychiatric disorders were diagnosed using SCID-I/P and SCID-II interviews. Of the 137 patients with depressive disorders, 82% completed the prospective five-year follow-up. A graphic life chart enabling evaluation of the longitudinal course of episodes plus duration of pharmacotherapies was used. In accordance with national guidelines, an indication for maintenance treatment was defined to exist after three or more lifetime major depressive episodes (MDEs); maintenance treatment was to commence four months after onset of full remission.

Results: Of the cohort patients, 34% (46/137) had three or more lifetime MDEs, thus indicating the requirement for maintenance pharmacotherapy. Of these, half (54%, 25/46) received maintenance treatment, for only 29% (489/1670) of the months indicated.

Conclusions: In this cohort of depressed primary care patients, half of patients with indications for maintenance treatment actually received it, and only for a fraction of the time indicated. Antidepressant maintenance treatment for the prevention of recurrences is unlikely to be subject to large-scale actualization as recommended, which may significantly undermine the potential public health benefits of treatment.

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1. Introduction

Depressive disorders are mostly evaluated and treated in primary care settings, where chronic and recurrent depressions are common [1]. Most practice guidelines produced by national health care organizations or professional societies recommend antidepressant maintenance pharmacotherapy for patients with three or more major depressive episodes (MDEs) [2–5]. However, the degree to which such guidance is actually followed in primary care has remained obscure. Although registry-based studies [6,7] indicate a large proportion of patients receiving long-term

antidepressant medication, indications for patients' long-term treatment remain unclear. Long-term antidepressant treatment may reflect the chronicity of depression, nonspecific long-term use of antidepressants, deliberate maintenance treatment, or antidepressant treatment for other indications. A major methodological obstacle for clinical-epidemiological studies in this field is that evaluating continuity and adequacy of maintenance treatment of depression necessitates both determining treatment phases (acute, continuation or maintenance) using labor-intensive life-chart methodology, and concurrently incorporating accurate data on the temporal course of pharmacological treatment. Therefore, such studies are scarce. In our previous life-chart-based study from secondary care regional psychiatric services, we documented major shortcomings in the implementation of maintenance treatment [8].

To our knowledge, no primary care study has examined how recommendations for antidepressant maintenance treatment are

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implemented. We investigated its prevalence, duration and predictors, and roles of attitudes and adherence in a naturalistic prospective long-term Finnish cohort of primary care patients with depressive disorders.

2. Material and methods

2.1. Patients and procedures

The methodology of the Vantaa Primary Care Depression Study (PC-VDS) has been published in detail elsewhere [9,10]. In brief, based on stratified sampling, altogether 373 of 1119 general practitioners' (GP) patients aged 20–69 screened with the PRIME-MD had a positive screen for depression. The presence of at least one core symptom of major depressive disorder (MDD) according to the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I/P) [11] was confirmed by telephone. All of the 175 potentially eligible patients were interviewed face-to-face using the SCID-I/P with psychotic screen. Inclusion criteria were current (1) MDD, (2) dysthymia, (3) subsyndromal MDD with two to four depressive symptoms (minimum one core symptom) and lifetime MDD and (4) minor depression otherwise similar to subsyndromal MDD, but without an MDD history. Refused (15%) and consented patients did not differ significantly in age or gender. The diagnostic reliability for current depressive disorder was excellent (κ -pa = 1.0). The PC-VDS was approved by the pertinent Ethics Committee in 2001.

The final sample comprised 137 patients. Current and lifetime psychiatric disorders were assessed with SCID-I/P and SCID-II interviews [11,12]. In addition to face-to-face interviews, observer- and self-report scales and all medical and psychiatric records were used to assess retrospective and prospective course of depression, comorbid disorders and psychosocial and socioeconomic factors. After baseline, patients were prospectively investigated at 3, 6 and 18 months and 5 years [10]. The 5-year investigation included all the same diagnostic interviews, scales and records as at baseline. The timing and duration of episodes of depression (MDEs and partial and full remission) and indications for acute, continuation and maintenance antidepressant treatment were integrated into a graphic life chart. We defined maintenance indication to exist after three or more lifetime MDEs (before or during the follow-up) and then achieved full remission for more than two months; treatment was to commence four months after the onset of full remission (National Finnish Current Care Guideline 2016). We have previously reported methodology and findings related to acute phase treatment [13].

Of the 137 patients initially included in the study, 127 (93%) participated in the 18-month and 112 (82%) in the 5-year follow-up. Patients remained in the cohort until they were censored due to change of diagnosis to bipolar disorder (4%, 5/137) or death (4%, 6/137). The final follow-up group consisted of the 134 patients with some follow-up information, 110 of them had had lifetime MDD. The dropouts (18%) did not significantly differ from participants in terms of socio-demographic or clinical features [10].

2.2. Measures of attitudes, adherence and contacts with general practitioners (GP)

Attitudes towards different treatments were rated very positive, positive, neutral, negative and very negative, and analyzed in two groups: favorable and negative. Patient adherence to antidepressants was rated (1) regularly, (2) somewhat irregularly (whether this would affect treatment goals was unknown), (3) very irregularly (treatment did not proceed according to plan), or (4) not at all (provided treatment could not be implemented). All contacts with GPs concerning any health problems were totaled;

the monitoring comprised all contacts where depression-related symptoms or treatments were discussed. The primary reasons for poor adherence were classified into patient-, GP- and organization-related factors with a semi-structured questionnaire, based on interviews and records.

2.3. Statistical methods

Between-group comparisons were carried out using Fisher's exact test, the two-sample *t*-test, and the Mann-Whitney or Kruskal-Wallis tests. Logistic and linear regression models were used to investigate associations of different variables; models were controlled for age, gender and duration of maintenance indication, and in the final models, the non-significant variables were omitted. SPSS, version 23, was used.

3. Results

3.1. Proportion and duration of indicated and received maintenance antidepressant treatment during the 5-year follow-up

Altogether 34% (46/137) of the cohort patients had three or more lifetime MDEs, and thus an indication for maintenance pharmacotherapy. Half (54%, 25/46) of them actually received it. The most frequently prescribed antidepressants were selective serotonin reuptake inhibitors. Characteristics of patients with an indication of maintenance, comparing those who received it with those who had not, are presented in Table 1.

Among the 46 patients, maintenance treatment would have been indicated for a mean 36.3 months (median 41.8, SD 20.6, 1–74 months). However, the mean observed duration of maintenance treatment was 19.6 months (median 12.0, SD 18.0, 1–60 months). It covered 29% (489/1670 months) of the time the indication was in force (Fig. 1).

3.2. Follow-up contacts with general practitioners (GP) and psychosocial treatments during the 5-year follow-up

During the follow-up, the patients visited GPs overall (for any reason) for a mean of 19 times (median 13, SD \pm 21, 0–153). The mean number of GP contacts due to depression was 8 (median 4, SD \pm 12, 0–83). A fourth (24%) of the patients also sought psychiatric care, often ambulatory. One fifth (20%) were treated in psychiatric outpatient units and one tenth (11%) received inpatient care. Some kind of psychosocial support other than that from a GP was offered to one third (38%); one fifth (20%) actually received it.

3.3. Patients' attitudes and adherence to antidepressant treatment

Patients' attitudes to antidepressants were very positive in 29%, positive in 42%, neutral in 17%, negative in 7% and very negative in 5%; to maintenance in 26%, 36%, 23%, 8% and 8%, respectively, and for comparison, to psychotherapeutic support in 45%, 40%, 13%, 3% and 0%. There were no statistically differences in attitudes towards different treatments.

The patients receiving maintenance antidepressant treatment had reportedly adhered to it regularly in 29%, moderately in 25%, incompletely in 23% and not at all in 23% of the cases.

The reasons for poor adherence included patient-related factors in 37%, GP-related factors in 43% and organization-related factors in 20% of the cases. Patients-related factors included inability to adhere, lack of motivation, negative attitudes, recovery, and inadequate effects, side effects or costs of antidepressants. GP-related factors included incomplete follow-up (41%), antidepressant not offered (20%), inadequately small dosage (0%), dosage not increased (10%), antidepressant not changed (3%), maintenance

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