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Antidepressant treatment in general practice – An interview study

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Objective **– To elucidate potential problems concerning the use of antidepressants (AD) in general practice.**
Design **– Cross-sectional, descriptive interview study.**
Setting **– General practices, Odense, Denmark.**
Subjects **– Random sample consisting of 98 AD users from 12 general practices.**
Main outcome measures **– Indication for AD treatment, justification of the treatment, duration of AD treatment, daily dose of AD, side effects, Hamilton depression rating, WONCA score.**
Results **– The primary indication for AD treatment was depression (72 patients), partly regular depression (therapeutic/prophylactic treatment) (*n*=39), partly depressive tendencies (*n*=32) (1 unknown). Median treatment duration was 3 years; 25% had been in treatment for more than 10 years. The general practitioners judged the treatment problematic/unacceptable in 23 cases, largely because of uncertain indication or because other or no treatment was considered better for the patient. The daily doses of AD were generally low. Side effects were modest. The patients often had a relatively high depression score and poor status according to the WONCA-scale.**
Conclusions **– The use of low doses, long duration of treatment, and uncertainty about the relevance of the treatment are important features of the use of AD by general practitioners. There seems to be a discrepancy between the use of AD in general practice and the scientifically-based recommendations.**

Key words: **antidepressants, general practice, indications, depression.**

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Depression is a frequent condition with a prevalence of 2-5%. Care and treatment of depressives is thus a significant burden to the health care system. In many countries, the diagnosis and treatment of depressed patients is mainly undertaken by general practitioners (GPs).

The main indication for AD is treatment of major depressive episodes (1), and the treatment should normally last 3-8 months (2). In spite of relatively limited scientific documentation of a beneficial effect of long-term AD treatment (3), maintenance/prophylactic treatment has been recommended for patients with recurrent depression in some reviews (1). According to studies with

imipramine (3) optimal prophylactic effect requires full dosage, as in acute treatment. Some authors claim that ADs are beneficial in mild depression (4). ADs are also effective in the treatment of neuropathy pains and incontinence, and for migraine prophylaxis (5). A review of AD use in general practice found that low doses of AD, i.e. 75 mg of amitriptyline daily or the equivalent, were ineffective in the treatment of depression (6).

In Denmark, 90-95% of all treatments with antidepressant drugs are prescribed by GPs (7). Several studies have pointed out various potential problems related to treatment with antidepressants and treatment of depression outside specialized units: 1. Diagnosis and indication: many depressed patients are not recognized and thereby not offered AD treatment and ADs are used for many other indications than depression (8-12). 2. Dose: ADs are often used in doses lower than those documented for the treatment of depressed patients (7,13,14); the notion that mild depression can be effectively treated with low AD doses is widespread, but without any support in clinical scientific data. 3. Duration of treatment: a New Zealand study found that many patients were treated for years without reconsideration of the indication (15). 4. Therapy control and compliance: compliance with AD treatment is often very poor (16). 5. Finally, the recent introduction of new types of AD, the selective serotonin reuptake inhibitors (SSRI) and the reversible MAO-A-inhibitor, moclobemide, has created a debate on their place in the treatment of depression (17,18).

The present study, based on interviews with a cohort of AD users together with the prescribing GPs, was undertaken with the aim of further elucidating the extent and character of these potential problems.

Materials and methods

The study was carried out in Greater Odense, Denmark (210 000 inhabitants), situated in the County of Funen. Since 1990, a prescription database, Odense Pharmacoepidemiologic Database (OPED), has collected data on all prescriptions subject to health insurance reimbursement (7). Through this database, all recipients of AD can be identified together with the prescriber, the type and amount of drug, and the dispensing pharmacy.

Of the 126 GPs in the index area, only 12 agreed to participate in the rather extensive study. Hence, a random selection procedure could not be adopted, but the representativeness of the participating GPs and the patients could be assessed in various ways (see result section).

Primary inclusion criteria for patients were a recent purchase of AD drugs prescribed by one of the participating GPs as recorded in OPED. Patients whom the GPs judged unsuitable for interview were excluded. Each GP then selected 10 patients for participation in the study.

The patients were interviewed and examined (by JUR) in the GPs' offices during spring 1993. A semistructured interview was employed, dealing with various aspects of the AD treatment: the reason for the current use of AD, duration of treatment, type of AD, dose, satisfaction with the treatment, attitudes towards continued treatment versus discontinuation, possible dependence on AD drugs, side effects (including rating by the UKU-scale (19)), general health, including dental status and concurrent medication. In addition, the patients were rated by the Hamilton Depression Scale (HDS) using the 17-item version with detailed item definitions (20). In order to adjust the rating level, the rater (JUR) participated in the DUAG joint ratings (21) prior to and during the study. Finally, the patients completed a rating scale for functional status assessment in family practice (WONCA, 22). Due to high age or disease, some patients did not complete the interview or the ratings. Blood was collected for drug assay from patients treated with imipramine, amitriptyline, nortriptyline, or clomipramine.

A few weeks later, the GPs were interviewed. The interview concerned the individual patients and covered largely the same issues as the patient interview, including a discussion of the justification of the treatment.

The employed daily doses of ADs were expressed in the Defined Daily Doses unit (DDD). DDD is defined as the daily maintenance dose for an adult for the main indication of the drug (23). One DDD for the various ADs should thus in principle express equipotent doses.

Statistical testing was carried out using the Spearman rank correlation and the Fisher exact test. 95%-confidence limits were calculated for

binomial distributed data and for medians. Some results are expressed with interquartile ranges.

The study was approved by the Regional Ethics Committee of Vejle and Funen County and by the Danish National Registry Board. Patients consented to participate on the basis of written and verbal information provided by the GPs.

Results

In total, 98 patients were included; 72 women and 26 men with a median age of 61 years.

All the patients were discussed with their GPs, but only 74 patients were interviewed, because 24 refused. At the time of the GP interviews, 17 patients were no longer taking ADs.

As shown in Table I, the participating GPs appeared to be representative of the AD prescribers in Odense. Similar analyses comparing included patients with all 9 831 AD users in Funen County in 1992 confirmed that the included patients were representative.

Table I. Comparison of various parameters for participating and non-participating GPs. Numbers in brackets are 95%-confidence limits.

Studied parameter	Participating GPs n=12	Non-participating GPs n=114
Percentage of males	92 (76–100)	83 (76–90)
Median age in years	45 (44–48)	46 (33–47)
Percentage of single practices	41 (14–70)	34 (26–43)
AD prescribing in 1992		
Median no. of patients per GP	23 (12–43)	27 (21–32)
Patients' median age in years	62 (58–64)	60 (58–61)
Median no. of prescriptions per GP	78 (38–175)	94 (78–123)
Percentage of patients using older AD	80.7 (76.8–84.5)	78.7 (77.5–79.9)
Daily dose in DDD	0.60 (0.53–0.69)	0.60 (0.57–0.63)

Table II. Primary indication for AD treatment according to GP records and knowledge about the patient.

Indication	No. of patients
Depression	72
Typical depression	40
Depressive episode	23
Prophylaxis	16
No information	1
Depressive tendencies/ no information	32
Pain	7
Anxiety/nervousness	4
Insomnia	3
Other*	9
Not known	3

* neurotic depression (4), asthenia (1), panic attacks (1), alcohol addiction (1), dementia (1), neurosis (1).

Neither the GPs' records nor the information obtained from the patients contained sufficient data to allow for a formal diagnostic classification of the indications for the AD treatment. According to the GPs, the main indication for treatment was depression (72/98 = 73%, Table II). The patients' reasons for the treatment did not agree completely with those of the GPs. Of the 54 GP-indicated depression patients who were interviewed, the reason for AD treatment was stated as depression by 43, nervousness (6), anxiety (1), insomnia (1), pain (2), unknown (1).

The most recently prescribed ADs were tricyclic AD (including maprotiline) for 74 patients, SSRI for 20, and moclobemide and mianserin for the remaining.

In 65 of the patients (66%), the AD treatment had been started and was controlled by the GP; 33 patients had started treatment elsewhere, mainly at psychiatric hospitals, but 30 of them were now controlled by the GP.

The median total duration of AD drug treatment, including different AD and treatment-free periods of varying length, was 3 years; it exceeded 10 years in 25 patients. Some of these had been on treatment almost continuously, but precise information on treatment schedules in earlier years could not be obtained. The treatment had been discussed between the patient and the GP at the last or second-last prescription issuing in only 41 cases, and it had been discussed earlier or

never in 43 cases (no information for 14 patients). The treatments not recently discussed had lasted considerably longer than the recently discussed ones (median 468 vs 117 weeks). Of the 67 patients still on AD medication at the time of interview, 33 stated that, largely on their own initiative (n=22), they had tried to stop the medication, but had failed to do so because they felt they could not do without it. Thirty-one of the patients expressed a feeling of being dependent on the treatment.

The GPs judged the AD treatment to be well justified in 71 cases, problematic in 18 cases and unacceptable in 5 cases (no statement for 4 patients). The reasons for these latter judgements were either an uncertain indication, that no drug treatment or psychotherapy was considered better for the patient, or that the patient was unwilling to discontinue the AD treatment.

The stated median daily dose was 0.67 DDD, interquartile range 0.33–1.00. The daily doses tended to be higher in patients treated for depression (DDD median: 0.75, interquartile range: 0.67–1.0) than for other indications (DDD median: 0.42, interquartile range: 0.30–0.67). The drug level monitoring (n=31) suggested that about 2/3 of the patients had AD blood levels below those recommended for AD therapy (24). In the vast majority of cases (80 of 98), the GPs had no concern about the dose given.

As shown in Table III, a fairly large fraction of the patients had depression and/or anxiety-related symptoms in a mild to moderate degree, and the HDS total score corresponded to a mild to moderate depression (HDS>= 12) in about 1/3 of the patients. The WONCA-scale and the general assessments of the patients' well-being made by the GPs also indicated suboptimal functioning in about half the patients. Among the autonomic side effects (Table IV), only reduced salivation was significantly more frequent in users of tricyclic AD than SSRI (Fisher's test, p=0.01).

Comparison of patients on treatment at the time of interview with a large Danish population survey (25) (n=2634) showed significantly more frequent loss of teeth in AD users, in particular in the age group below 65 years (63% versus 31%).

In general, the patients were characterized by a high frequency of somatic disease, cardiopulmonary disease (n=33), locomotion organ disease (31), gastrointestinal disease (21) and other neurological disease (22). Correspondingly, co-medication was frequent, hypnotic/anxiolytic (n=36), cardiovascular drugs (20), gastrointestinal drugs (17), analgesics (18), and neuroleptic (n=6).

Table III. Selected HDS items and total score for interviewed patients. Contingency table, n=70.

	Score				
	0	1	2	3	4
HDS-item no. and content	No. of patients				
1. depressed mood	30	23	14	3	0
2. guilt feeling	33	27	8	2	0
3. suicidal thoughts	50	17	3	0	0
4. insomnia, initial	45	7	18	–	–
5. insomnia, middle	53	7	10	–	–
6. insomnia, late	51	6	13	–	–
7. work and interest	39	20	8	1	0
8. retardation	61	8	1	0	0
9. agitation	37	32	1	0	0
10. anxiety, psychic	18	26	19	7	0
11. anxiety, somatic	30	16	17	7	0
12. somatic, gastro-intest.	46	23	1	–	–
13. somatic, general	21	30	19	–	–
	Score				
	0–3	4–7	8–11	12–15	≥16
HDS total score (17 items)	No. of patients				
	11	19	16	15	9

Table IV. Selected UKU-items for interviewed patients. Contingency table, n=66.

	Score			
UKU-item	0	1	2	3
Concentration difficulty	40	19	7	0
Sedation	24	11	30	1
Memory difficulty	24	32	10	0
Tension	28	24	13	11
Reduced salivation	21	23	13	9
Orthostatic dizziness	32	15	17	0
Increased sweating	26	28	10	2

Discussion

In spite of the non-random fashion in which the present material was selected, there was no observable selection bias. The participating GPs and included patients thus appeared representative of the index area, with respect both to general characteristics such as age and sex, and to patterns of AD prescribing, and AD use. The index area may differ from other geographical regions by the frequent use of nortriptyline as first choice AD (7), and the relatively cautious introduction of the new ADs, in particular the SSRIs. Both features may reflect the policy recommended by the regional psychiatry service and the influence of AD research in Denmark, which has shown that the SSRIs are considerably less effective than tricyclic AD in severely depressed in-patients (17).

The primary indication for ADs in the majority of patients being depression (Table II) contrasts somewhat with other studies on use of ADs in general practice, where other indications have been more prominent (8,9,26). In most cases, the indication for treatment had been established long before the interview, and a further validation was not attempted through the patient interview. The recorded indication for treatment was the GP's reason for prescribing AD. The lack of formal diagnostic inventories as a basis for this procedure may have contributed to the apparent diversity of indications for AD use.

A distinct feature was the large number of patients who had been treated for very long periods, often for several years without drug-free intervals and with infrequent discussion of the treatment between the GP and the patient. Indeed, long-term treatment might well be justified in the patients suffering from rapidly relapsing depression or more chronic depression of the dysthymia type, etc. The acute treatment period is often set at 4-6 months (2), and the discontinuation of the treatment at the time of the interview, taking place 2-4 months after the primary registration, may be a simple consequence of this. However, an indirect effect of the study on the discontinuation rate cannot be excluded.

The uncertain indication, the use of long-term AD treatment in many patients, and the many unsuccessful attempts to discontinue the treatment seem to be the main reason why so many GPs had reservations about the justification of the treatments. The discontinuation problems may have been secondary to withdrawal symptoms, but distinct symptoms indicative of such a reaction were not reported in any patient.

As suggested by a previous analysis of prescription data, we found that lower doses were employed for the tricyclic AD than those usually required to obtain optimal effect in the acute treatment of depression (7). For long-term treatment, lower doses than for acute therapy have previously been recommended, but recent controlled studies indicate that the doses should be the same as in acute treatment (3). For the SSRIs, the dose-effect relationships are poorly defined in the literature (18), and the doses employed by the participating GP cannot be evaluated. It is interesting that the GPs generally considered the employed doses adequate and had no concern about underdosing despite the many studies demonstrating underdosing of AD in general practice (7,13,14). One of the reasons may be the uncertain diagnosis, and the belief that the depressions in general practice are "different"/milder than in-patient depressions (11), and therefore should be treated differently.

Since most of these patients had been on treatment for some time, it is not surprising that the complaints of side effects were generally modest. However, the patients had significantly poorer dental status with more loss of teeth than an age-matched Danish control population. It is tempting to associate this with the anticholinergic effects of the tricyclic AD, but the high frequency of somatic co-morbidity and co-medication may have contributed.

The symptom rating scale (HDS) showed that several patients had symptoms of depression and/or anxiety, and the WONCA rating and the GP general assessment showed that about half the patients had a suboptimal well-being. The extent to which this related to insufficient treatment of the depression, or resulted from the patients' general health and social situation, remains to be elucidated.

In conclusion, this study points out that the use of low doses, long duration of treatment, difficulties in discontinuing the treatment, and uncertainty about the relevance of the treatment are important features with respect to the use of ADs by GPs. There seems to be a discrepancy between

the use of ADs in general practice and the scientifically-based recommendations.

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