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Choice of antidepressants: questionnaire survey of psychiatrists and general practitioners in two areas of Sweden

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Abstract

Objective—To identify factors that affect physicians' choice of specific antidepressant drugs in order to evaluate the validity of epidemiological studies of the risks (particularly suicide) and benefits of different compounds.

Design—Questionnaire survey of 264 psychiatrists and general practitioners in an urban area and a rural area of Sweden with validation of data by independent prescription surveys.

Setting—Urban area of greater Stockholm and rural county of Jämtland, Sweden.

Subjects—228 physicians (86%) who answered the questionnaire.

Main outcome measures—The drugs used as first line drugs of choice, as drugs of choice in particularly severe depression, and as drugs of choice for disorders other than depression.

Results—Amitriptyline was the most common first line drug of choice among both psychiatrists and general practitioners. The patterns of choice of antidepressants in the two areas accorded with prescribing patterns in two independent prescription surveys. Amitriptyline was chosen even more frequently for severe depression and depression with severe insomnia. Clomipramine was chosen comparatively more often for depression with severe anxiety. Low toxicity compounds (mainly lofepramine, mianserin, and moclobemide) were more often the drug of choice in depression associated with overt risk of suicide. Amitriptyline and clomipramine were used extensively for disorders other than depression (40% and 54% of prescriptions, compared with 13-19% for some other major antidepressants).

Conclusion—Patient groups treated with different antidepressant compounds may not be comparable with respect to diagnoses and severity of disease. In particular, lofepramine, mianserin, and moclobemide, and possibly amitriptyline, seem to be chosen more often for patients prone to suicide.

Introduction

Fatal toxicity indices have been calculated for antidepressants by relating deaths from overdose to prescription rates of the respective substances. Some antidepressants—for example, amitriptyline—have been associated with lethal overdoses significantly more often than others. A few newer antidepressants—for example, mianserin and lofepramine—have been associated with lethal overdoses less frequently.^{1,2} In a recent Swedish study mianserin and moclobemide were detected at necropsy twice as often as amitrip-

tyline when all methods of suicide were included.³ It was not known in any of these studies, however, whether patients treated with the different antidepressants were comparable with regard to diagnoses or severity of the disease.^{4,5}

The purpose of this study was to investigate whether the variation in the risk of different antidepressants being associated with a lethal outcome may partly be due to suicide prone patients being selected for certain drugs. We conducted a survey of psychiatrists and general practitioners in two areas of Sweden in order to evaluate factors that may affect their choices of antidepressants. Independent prescription data in the two areas were available for validation of the survey information.⁶

Subjects and methods

A questionnaire was devised asking which antidepressants doctors prescribed for depression and other disorders (see appendix). It included all 13 antidepressant compounds on the Swedish market in 1991. The questionnaire was mailed to all psychiatrists and general practitioners as well as to residents (licensed physicians in training) in psychiatry or general practice in two areas of Sweden. One was the catchment area of Huddinge University Hospital (300 000 population) in the urban area of southern greater Stockholm. It included 20 primary health care units (74 general practitioners, 43 residents) as well as two psychiatric inpatient units and seven psychiatric outpatient departments (39 psychiatrists, 21 residents). The second area was the rural county of Jämtland (135 000 population). It included 29 primary health care units (59 general practitioners, 19 residents) as well as one psychiatric department for both inpatients and outpatients (11 psychiatrists, two residents). Two of us (GI and IR) as well as two general practitioners in Huddinge, who served as a reference group, were excluded.

The study group comprised over 3% of all Swedish doctors in psychiatry and general practice, serving about 4.5% of the Swedish population. The questionnaire was posted in September 1991 for return within two months. Two reminders were sent.

Data on drug prescription rates were obtained from two independent sources. All pharmacies in the Huddinge catchment area (n=20) monitor purchases of prescription drugs during one month each year.¹⁰ Similar data were obtained from the individual based drug monitoring survey in Jämtland, which has been in progress since 1970.¹¹ These two sets of data were compared with the corresponding questionnaire responses by using Spearman's rank correlation test for

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TABLE I—Choice of first line antidepressant as ascertained by questionnaire and actual prescriptions reported by independent surveys

	Psychiatrists		General practitioners		Huddinge (A)		Jämtland (B)		Prescriptions	
	No	%	No	%	No	%	No	%	Huddinge	Jämtland
Desipramine	0	0	0	0	0	0	0	0	0	0
Imipramine	2	4	0	0	1	1	1	1	132	441
Clomipramine	7	15	14	13	28	19	10	12	1980	2067
Opipramol	0	0	0	0	0	0	0	0	48	0
Trimipramine	0	0	0	0	0	0	0	0	456	46
Lofepramine	1	2	11	10	14	10	5	6	360	479
Amitriptyline	16	35	55	52	64	44	40	49	2520	4157
Nortriptyline	8	17	6	6	13	9	2	2	492	144
Protriptyline	0	0	0	0	0	0	0	0	36	0
Maprotiline	0	0	4	4	3	2	4	5	468	426
Mianserin	1	2	0	0	0	0	2	2	60	631
Fluvoxamine	1	2	0	0	0	0	1	1	36	122
Moclobemide	0	0	0	0	0	0	0	0	324	281
No response	10	22	16	15	23	16	17	21	—	—
Total	46	100	106	100	146	100	82	100	6912	8794
Correlation	$r_s=0.66, P<0.05$				$r_s=0.90, P<0.01$				$r_s=0.82, P<0.01^*$	$r_s=0.86, P<0.01^\dagger$

*Correlation with Huddinge (A).

†Correlation with Jämtland (B). The two prescription surveys were not quite comparable.^{10,11}

TABLE II—Proportions of respondents who did not switch antidepressant according to particular types of depression and respondents who indicated they switched

	Severe depression		Severe insomnia		Severe anxiety		Overt suicide risk	
	No	%	No	%	No	%	No	%
No response	14	6	18	8	13	6	30	13
Did not switch	178	78	117	51	111	49	144	63
Switched	36	16	93	41	104	46	54	24
Total	228	100	228	100	228	100	228	100

TABLE III—First line antidepressants preferred and choices in particular types of depression

	First line choice		Severe depression		Severe insomnia		Severe anxiety		Overt suicide risk	
	No	%	No	%	No	%	No	%	No	%
Imipramine	2	1	3	1	0	0	2	1	0	0
Clomipramine	38	17	32	14	20	9	87	38	32	14
Trimipramine	0	0	1	>1	12	5	4	2	0	0
Lofepramine	19	8	15	7	6	3	6	3	36	16
Amitriptyline	104	46	124	54	158	69	104	46	86	38
Nortriptyline	15	7	16	7	6	3	2	1	13	6
Maprotiline	7	3	6	3	14	6	5	2	8	4
Mianserin	2	1	3	1	1	>1	4	2	12	5
Fluvoxamine	1	>1	2	1	1	>1	2	1	2	1
Moclobemide	0	0	1	>1	0	0	1	>1	14	6
No first line	40	18	25	11	10	4	10	4	25	11
Total	228	100	228	100	228	100	228†	100	228	100

†Includes one choice of opipramol.

TABLE IV—Proportions of respondents with any experience or wider experience (more than 20 patients) of prescribing antidepressants for indications other than depression

	All prescribers		Prescribers to > 20 patients		Drugs used (No (%) of prescribers)
	No	%	No	%	
Anxiety disorder	161	71	31	14	Clomipramine (149 (65))
Obsessive-compulsive disorder	64	28	11	5	Clomipramine (61 (27))
Pain	151	66	35	15	Amitriptyline (92 (40))
Other	46	20	13	6	Clomipramine (38 (17))
					Amitriptyline (27 (12))

statistical analyses.¹² Data were also taken from the diagnosis and therapy survey,¹³ in which a sample of Swedish physicians was asked to complete prescription forms with the symptoms or diagnoses of the patients. These provided an estimate of the prescription rate of antidepressants for indications other than depression.

Results

Response rates—The overall response rate was 86% (228/264). It was 84% (146/174) in Huddinge and 91% (82/90) in Jämtland and 94% (46/49) among psychiatrists, 81% (106/131) among general practitioners, and 90% (76/84) among residents.

First line drug of choice (table I; appendix, question 3)—Amitriptyline was the most common first line drug of choice, both among general practitioners (52%; 55/106) and among psychiatrists (35%; 16/46) in both areas. The second most common choice among general practitioners was clomipramine (13%; 14/106) and among psychiatrists nortriptyline (17%; 8/46). Lofepramine was the first line choice among general practitioners five times more often than among psychiatrists (table I).

Drugs of choice in particular types of depression (appendix, questions 4–7)—A minority of respondents indicated that their choice of antidepressant was different when the depression had any of the following characteristics: particular severity, severe insomnia, severe anxiety, overt suicide risk (table II). Compared with its use as a first line drug, amitriptyline was chosen even more frequently in severe depression and in depression with severe insomnia (table III). Other sedating compounds (trimipramine, maprotiline) were also chosen more frequently in the presence of severe insomnia. Clomipramine was chosen more often when there was pronounced anxiety. Lofepramine, mianserin, and moclobemide were chosen more often for depression with an overt suicide risk (table III). The pattern of first line choice as well as choice in particular types of depression was the same when answers from the 86 respondents who reported the greatest experience with antidepressants were analysed separately (not shown).

Use of antidepressants for other indications (appendix, question 8)—Ninety eight per cent of the psychiatrists (45/46) and 96% of the general practitioners (102/106) reported prescribing antidepressants for indications other than depression. The most common of these indications were anxiety, obsessive-compulsive disorders, and pain. The drugs used were almost exclusively clomipramine and amitriptyline (table IV). Quantitative estimates calculated from the diagnosis and therapy survey data showed that 35% of the prescriptions of clomipramine were for anxiety and 12% of the amitriptyline prescriptions were for pain, the two main indications other than depression. Only 46% and 60% of prescriptions for these drugs respectively were for depression (table V).

Validation—The 13 antidepressants were ranked according to how frequently they were chosen as the first line drugs of choice in Huddinge and Jämtland (table I). These ranks were compared with the rank orders received from the prescription surveys in the respective areas. Strong correlations were found (Spearman's rank correlation coefficient: Huddinge $r_s=0.82, P<0.01$; Jämtland $r_s=0.86, P<0.01$).

TABLE V—Prescriptions per diagnostic category. Data are from diagnosis and prescription survey 1990-2. Prescription numbers are extrapolated from sample of prescribers. Drugs with fewer than 100 observations excluded

	Clomipramine		Lofepramine		Amitriptyline		Maprotiline		Mianserin		Moclobemide	
	No	%	No	%	No	%	No	%	No	%	No	%
Depression	164 486	46	86 448	87	188 381	60	68 524	82	69 743	86	58 390	81
Anxiety disorder	123 975	35	471	>1	18 634	6	1 799	2	7 008	9	5 681	8
Obsessive-compulsive disorder	13 689	4	0	0	1 184	>1	0	0	0	0	506	1
Pain	15 781	4	2 207	2	38 258	12	1 266	2	800	1	581	1
Other psychiatric symptoms	23 383	7	4 160	4	52 651	17	6 879	8	2 345	3	3 203	4
Other somatic symptoms	17 168	5	6 301	6	17 078	5	4 614	6	1 020	1	4 019	6
Total	358 482	100	99 587	100	316 186	100	83 082	100	80 916	100	72 380	100

Discussion

In risk-benefit comparisons of antidepressant compounds it is essential to know whether the compounds are prescribed to comparable patient groups. This issue was approached by questioning the prescribers about their treatment rationale. The study group comprised over 3% of all Swedish doctors in psychiatry and general practice. Taken from one urban area with a medical school and from one rural area, the sample was likely to provide an accurate picture of the prescribing habits of Swedish psychiatrists and general practitioners.

The high correlation between the responses from the two study areas (table I) suggests that the sample was representative. The high response rate (86%) indicates that the survey was judged not to be controversial or intrusive by the physicians approached and that the topic was important. The high correlation between the responses regarding the first line choice of antidepressant and the actual prescribing practice, as found in independently conducted prescription surveys in the two areas, strongly supports the validity of our findings⁹ (table I). Further support comes from comparison of the responses regarding prescribing for other indications with those reported in the diagnosis and therapy survey (tables IV and V), from the intergroup consistency of responses (table I), and from the face validity of the findings (tables II and III).

Forty respondents either preferred not to or could not answer the question regarding their first line drugs of choice. Probably they did not have a first line drug of choice but chose drugs according to patients' symptoms (table III). This subgroup was at least as experienced as the whole study group. Some commented that they had two "first line drugs," one sedating and one non-sedating, and 36 (90%) answered at least one of the subsequent questions regarding particular types of depression. This reflects the difficulties in devising an uncomplicated questionnaire to investigate a complex problem.

Particularly severe depression and depression characterised by severe insomnia or by an overt risk of suicide may be associated with a higher risk of suicide.¹⁴ Most respondents (49-78%) did not switch from their first line choice in these types of depression (table II). However, a minority indicated that they switched to amitriptyline for severe depression, to the sedating compounds amitriptyline, trimipramine, and maprotiline for severe insomnia, and to the compounds with lower toxicity in overdose (lofepramine, mianserin, and moclobemide) in cases of overt risk of suicide (table III). This suggests that more severely ill patients are treated with these drugs. In particular, more suicidal patients may be treated with lofepramine, mianserin, and moclobemide. This may explain why moclobemide and mianserin were associated with an excess risk of suicide compared with amitriptyline in a Swedish toxicological study of 3400 suicides.³ Clomipramine was chosen more often for depression with severe anxiety, which may increase the association of clomipramine with suicide, as comor-

bidity between major depressive disorder and anxiety disorder has been reported.¹⁵

Almost all prescribers had prescribed antidepressants for disorders and symptoms other than depression. Clomipramine or amitriptyline was used almost exclusively (table IV). Half of the clomipramine prescriptions and a third of the amitriptyline prescriptions were for diagnoses other than depression according to the diagnosis and therapy survey¹³ (table V). This pattern of use might give a weaker association with suicide for these drugs compared with those used exclusively for depression.

That lofepramine was the first line choice five times more often among general practitioners than among psychiatrists (table I) might possibly weaken the association of lofepramine with suicide. But this would be true only if depressed patients consulting general practitioners were at lower risk of suicide than those consulting psychiatrists. In a study in Jämtland more patients committing suicide were being treated by general practitioners than by psychiatrists.¹¹

CONCLUSION

Clomipramine and amitriptyline seem to find substantial use in patients other than those with depression, possibly tending to weaken the association of these drugs with suicide. On the other hand, the use of amitriptyline was also comparatively greater in depression with features associated with increased risk of suicide (severity, insomnia). The less toxic substances lofepramine, mianserin, and moclobemide seem to be in proportionally greater use in overtly suicidal patients, which may strengthen their association with suicide. These factors should be taken into account when comparing the associations of different antidepressants with suicide in epidemiological

Key messages

- In epidemiological studies the varying associations of different antidepressant drugs with suicide are due to different pharmacological properties or factors such as selective prescribing
- In this Swedish study amitriptyline and clomipramine were most commonly the first line drugs of choice for severe depression and are also the drugs most often used for disorders other than depression
- Antidepressants of less toxicity in overdose—lofepramine, mianserin, and moclobemide—were more often chosen for overtly suicidal patients
- Diagnoses and severity of disease must be taken into account when comparing the outcome of treatment with different antidepressants

studies, as they may confound the impact of pharmacological properties of the drugs.

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Appendix

Questionnaire items

(1) How many patients do you treat at present with antidepressants? Alternative answers: 0, 1 or 2, 3 or 4, 5-10, > 10.

(2) How many patients do you estimate that you have ever treated with antidepressants? Alternative answers: 0, 1-9, 10-19, 20-100, > 100.

(3) Which antidepressant do you prescribe as first line (one alternative)? Alternative answers: Saroten (amitriptyline), Tryptizol (amitriptyline), Tofranil (imipramine), Ensidon (opipramol), Tolvon (mianserin), Tymelyt (lofepramine), Concoridin (protriptyline), Fevarin (fluvoxamine), Anafranil (clomipramine), Noritren (nortriptyline), Sensaval (nortriptyline), Surmontil (trimipramine), Aurorix (moclobemide), Pertofrin (desipramine), Ludiomil (maprotiline), "not applicable."

(4) Is there any one of these drugs that you mainly prescribe if you consider the depression to be particularly severe? Alternative answers: see question 3.

(5) Is there any one of these drugs that you mainly prescribe if the depression is associated with particularly severe insomnia? Alternative answers: see question 3.

(6) Is there any one of these drugs that you mainly prescribe if the depression is associated with a particu-

larly severe anxiety state? Alternative answers: see question 3.

(7) Is there any one of these drugs that you mainly prescribe if you think there is a risk of suicide? Alternative answers: see question 3.

(8) Have you ever prescribed antidepressants for indications other than depression? If "yes" state which other indications (for example, obsessive-compulsive disorder, panic disorder, pain), which drugs you have chosen, and roughly how many patients you have treated in this way. [A table is provided for answers in which the drug used and the number of patients should be stated for each indication.]

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Impact of HIV infection on Zambian businesses

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Women attending antenatal clinics in Zambia have rates of HIV infection of 11-30%.¹ Deaths from the disease are likely to affect the economy of individual families and, if widespread, that of the country. Since December 1990 the Kara Counselling and Training Trust has offered education about HIV to local companies. We therefore studied the impact of HIV infection on businesses in Zambia as reported by senior management staff.

Methods and results

A questionnaire designed to assess the quantitative and qualitative impact of HIV infection on businesses was delivered to the personnel managers of 33 companies, including banks, car manufacturers, food and drink manufacturers, and farms. One week later it was collected and any ambiguities were clarified. Death rates were calculated by dividing the annual number of deaths by the total number of employees at the end of each year. Mortality and morbidity trends over the past six years were studied by χ^2 analysis.

All 33 companies filled in questionnaires: 25 were

based in Lusaka, the capital (population 982 000, 1990 census) and eight in the Copperbelt, the other main conurbation (total population 1 200 000, 1990 census). Thirty two questionnaires were returned fully completed. One company could not find its mortality records. The total number of employees in 1993 was 10 204 (79% men, 21% women); the range for individual companies was 19 to 1836. The total number of employees did not change significantly over the study period. Most companies had a workforce aged between 18 and 55 years. Four companies had employees over 55 and one over 65.

The crude death rate in this population increased sequentially ($P < 0.001$, χ^2 test for trend) from 0.25 per 100 person years in 1987 to 1.83 per 100 person years in 1993 (table).

Comment

In the developing world average annual mortality between the ages of 15 and 60 is estimated to be around 0.5 per 100 person years.² Vital registration systems are rare in developing countries, but in Zambia company mortality records are likely to be accurate because funeral benefits are substantial. Some employees could have retired early because of ill health and so would not appear in the mortality figures when they died. We believe, however, that few deaths will have been missed because normal employment practice allows employees to remain on sick leave for prolonged periods. Buve *et al* found that mortality in female nurses from two hospitals in Zambia rose from 0.2-2.7 per 100 person years between 1980 and 1991.³ Our

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