Antidepressant drug use in primary care: a record linkage study in Tayside, Scotland

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Depression is a common psychiatric disorder in general practice.¹ There is consensus that antidepressants should be given in sufficient dose and for sufficiently long if treatment is to be effective.² Tricyclic antidepressants carry warnings about their use in patients with cardiac diseases, and they have well known anticholinergic effects that could cause predictable toxicity. Selective serotonin uptake inhibitors are thought to be devoid of such effects. We studied the use and safety of antidepressant drugs in the community, with reference to their labelled warnings.

Patients, methods, and results

We studied patient specific dispensed prescribing³ for antidepressant drugs and admissions to hospital for possible adverse effects over 14 months using a record linkage database that covers the population of Tayside, Scotland (about 400 000 subjects).⁴ The dose and duration of use of antidepressants was determined, as was the number of subjects who had labelled contraindications to and cautions against taking tricyclic antidepressants.

Overall, 20 195 patients received 85 315 prescriptions for an antidepressant drug (14 988 patients received tricyclic antidepressants, 3571 received selective serotonin reuptake inhibitors, and 1636 received both). In comparison with published guidelines,² tricyclic antidepressants were generally given in subtherapeutic doses (10 804 (72%) subjects received only subtherapeutic doses, 1125 (7%) therapeutic or both doses, and 3059 (21%) unknown doses). Selective serotonin reuptake inhibitors tended to be given in therapeutic doses (281 (8%) received

only subtherapeutic doses, 2828 (79%) therapeutic or both doses, and 642 (13%) unknown doses). In both drug groups most prescribing was of short duration (38% of subjects $\leq$ 30 days, 58% $\leq$ 60 days, 68% $\leq$ 90 days).

Despite labelled warnings, 26 out of 16 624 subjects (0.2%) were dispensed a tricyclic antidepressant and 7 out of 5207 subjects (0.1%) a selective serotonin reuptake inhibitor within 30 days of admission for a myocardial infarction. Fourteen subjects (0.1%) had been admitted with heart block, 179 subjects (1.1%) with an arrhythmia, 86 subjects (0.5%) with acute glaucoma, 159 (1.0%) with thyroid disease, 165 (1.0%) with epilepsy, and 1149 (6.9%) with a cardiovascular disorder; all had had one or more prescriptions for a tricyclic antidepressant. Selective serotonin reuptake inhibitors had been prescribed to two (0.04%) patients admitted for heart block, 82 (1.6%) for arrhythmia, 23 (0.4%) for glaucoma, 49 (0.9%) for thyroid disease, 46 (0.9%) for epilepsy, and 357 (6.9%) for a cardiovascular disorder. Tricyclic antidepressants were dispensed to 6303 subjects (37.9%) and selective serotonin reuptake inhibitors to 1897 subjects (36.5%) who had also been prescribed a cardiovascular drug as listed in the second chapter of the *British National Formulary*. Antidepressants did not result in increased admission for known adverse effects (table 1), with the exception of a significantly increased risk of admission for acute retention of urine with tricyclic antidepressants, the odds ratio compared with non-exposure being 1.9 (1.2 to 2.9).

Comment

We found that tricyclic antidepressants were commonly used in low doses that were unlikely to be of benefit in treating major depression,² which confirmed a recent report.⁵ Antidepressants were commonly given for short and probably ineffective durations. Tricyclic drugs were given to some patients who had labelled warnings, but, despite this, and perhaps because tricyclic antidepressants were prescribed in low doses, we found no increased risks of admission for adverse cardiovascular outcomes with tricyclic drugs. There was an increase in the risk of acute

Table 1—Numbers of events, exposures, event rates, and adjusted odds ratios with 95% confidence intervals for each end point studied

End point	No of events	Exposure (1000 patient years)	Event rate	Adjusted odds ratio (95% confidence interval)
Glaucoma:				
Selective serotonin reuptake inhibitor	2	1.27	1.57	1.66 (0.70 to 3.39)
Tricyclic antidepressant	6	5.72	1.05	0.68 (0.39 to 1.16)
Not exposed	19	16.56	1.15	
Convulsions:				
Selective serotonin reuptake inhibitor	1	1.27	0.79	0.53 (0.12 to 2.25)
Tricyclic antidepressant	10	5.72	1.75	1.09 (0.63 to 1.88)
Not exposed	22	16.56	1.33	
Urinary retention:				
Selective serotonin reuptake inhibitor	2	1.27	1.57	1.31 (0.50 to 3.39)
Tricyclic antidepressant	16	5.72	2.80	1.90 (1.24 to 2.94)*
Not exposed	20	16.55	1.21	
Myocardial infarction:				
Selective serotonin reuptake inhibitor	11	1.26	8.70	1.26 (0.63 to 2.51)
Tricyclic antidepressant	50	5.70	8.77	1.02 (0.70 to 1.48)
Not exposed	105	16.48	6.37	
Angina:				
Selective serotonin reuptake inhibitor	24	1.25	19.13	1.36 (0.83 to 2.22)
Tricyclic antidepressant	86	5.67	15.17	0.95 (0.70 to 1.27)
Not exposed	191	16.39	11.65	
Heart failure:				
Selective serotonin reuptake inhibitor	1	1.27	0.79	0.56 (0.12 to 2.68)
Tricyclic antidepressant	10	5.72	1.75	1.28 (0.71 to 2.30)
Not exposed	22	16.56	1.33	
Arrhythmia:				
Selective serotonin reuptake inhibitor	12	1.27	9.47	1.61 (0.87 to 2.97)
Tricyclic antidepressant	32	5.71	5.61	0.75 (0.50 to 1.14)
Not exposed	86	16.49	5.22	

*P<0.05.

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retention of urine, possibly because of the anticholinergic effect of tricyclic drugs.

These results are reassuring in that tricyclic antidepressants seem to be safe in the doses used in clinical practice. Although antidepressants are given for indications other than depression, the results are worrying because tricyclic antidepressants were mostly prescribed in low doses and both types of antidepressant were given only short term. These two factors mean that the treatment of major depression is less likely to be effective. Further research should determine why antidepressant drugs are prescribed in this way.

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Cross sectional database analysis of antidepressant prescribing in general practice in the United Kingdom, 1993-5

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Consensus guidelines for the treatment of depression in general practice were published in 1992.¹ We investigated whether the prescription of antidepressants in general practice had changed since these guidelines and related educational materials had become available through the Defeat Depression Campaign and the Royal College of General Practitioners' senior mental health education fellowship.²

Methods and results

Cross sectional data for two periods of 12 months ending June 1993 and June 1995 were obtained from the database of the doctors' independent network (DIN-LINK); this is maintained by the independent company Compufile (Woking, Surrey), which provides general practice data mainly to the pharmaceutical industry. It contains data from 100 general practices (377 general practitioners, 750 000 patient records) across the United Kingdom that use AAH Meditel practice computer systems. Prescriptions for antidepressants linked to a general practitioner's diagnosis of

depression were included in the study. Antidepressants that accounted for less than 2% of the total were excluded. The effective dose of tricyclic antidepressants was taken as 125 mg daily from the consensus guidelines¹ and that of selective serotonin reuptake inhibitors as the value in the manufacturers' data sheets.

Since 1993 the number of prescriptions issued for the treatment of depression increased overall by nearly 33%. The prescription rate for all antidepressants increased, but the increase was much lower in the older tricyclic antidepressants (12.4%) than in the selective serotonin reuptake inhibitors (133.8%). The number of people receiving an effective dose increased from 41% in 1993 to 53% in 1995. For amitriptyline, clomipramine, and dothiepin the percentage of prescriptions for an effective dose and the average dose prescribed changed only marginally (table 1).

Comment

In this large population the number of prescriptions for antidepressants issued to patients with a diagnosis of depression increased substantially between 1993 and 1995. We emphasise, however, that antidepressants are far from being the only effective treatment for depression.

Prescriptions for all antidepressants increased but more for selective serotonin reuptake inhibitors than for tricyclic antidepressants. This suggests that general practitioners are not prescribing selective serotonin reuptake inhibitors to patients who have been taking tricyclic antidepressants long term.

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Table 1—Prescription of antidepressants to patients with diagnosis of depression

	Tricyclic antidepressants						Selective serotonin reuptake inhibitors			
	Total	Amitriptyline	Clomipramine	Dothiepin	Total older tricyclics	Lofepiramine	Fluoxetine	Paroxetine	Sertraline	Total
No of prescriptions:										
1993	58646	10763	2413	18777	31953	4864	5720	2710	1329	9759
1995	77738	11873	2693	21334	35900	6317	13675	6480	2657	22812
Increase in numbers (%) of prescriptions between 1993 and 1995	19092 (32.6)	1110 (10.3)	280 (11.6)	2557 (13.6)	3947 (12.4)	1453 (29.9)	7955 (139.1)	3770 (139.1)	1328 (99.9)	13053 (133.8)
1993:										
No of prescriptions with dose specified	37091	7754	1828	14383	23965	4090	5422	2523	1091	9036
No (%) of prescriptions at effective dose	15145 (40.8)	442 (5.7)	278 (15.2)	2188 (15.2)	2908 (12.1)	3205 (78.4)	5422 (100)	2519 (99.8)	1091 (100)	9032 (99.9)
1995:										
No of prescriptions with dose specified	52633	8193	1992	16847	27032	5318	13203	6101	1720	20283
No (%) of prescriptions at effective dose	28113 (53.4)	640 (7.8)	240 (12.1)	2666 (15.8)	3546 (13.1)	4309 (81.0)	13203 (100)	6076 (99.6)	1720 (100)	20258 (99.9)
Average dose (mg/day)*:										
1993		55.4	63.8	75.8		131.5	21.3	22.2	81.4	
1995		58.5	58.9	77.1		134.7	21.4	22.7	79.8	

*Based only on prescriptions with dose specified.