Effects of licence change on prescribing and poisons enquiries for antipsychotic agents in England and Scotland

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Aims To examine the effect of licence change for thioridazine at the end of 2000 on the prescription of antipsychotic drugs in England and Scotland, and investigate changes in poisons information inquiries and, for Edinburgh, poisons admissions.

Methods Prescription data for antipsychotic drugs were obtained for England and Scotland and quarterly trends examined for 2000 and 2001. Accesses to the UK National Poisons Information Service website TOXBASE for antipsychotic products were examined for the same period. For Scotland telephone enquiry data, and admission data to the Edinburgh Poisons Unit were also evaluated. Trends in poisonings were compared with prescribing change.

Results In England prescriptions for thioridazine fell rapidly in 2001 from approximately 35% of market share to less than 5%, and were replaced by risperidone, chlorpromazine and olanzapine. TOXBASE accesses fell from 39.3% of antipsychotics to 4.4%. Accesses for chlorpromazine, olanzapine and risperidone increased. In Scotland prescribing of thioridazine was similar to changes in England, but it was principally replaced by chlorpromazine. These changes were mirrored by TOXBASE accesses, telephone enquiries and in-patient admissions. The ratio of TOXBASE accesses for thioridazine to prescription numbers for the drug increased after the licence change.

Conclusions Licence change produced rapid change in prescribing behaviour within 3 months. Prescribing behaviour in England and Scotland was different. Changes in prescribing were mirrored by changes in accesses for poisons information in both England and Scotland, and in Edinburgh by hospital admissions. The increase in the ratio of TOXBASE accesses to prescriptions for thioridazine suggests doctors may have become more aware of its potential toxicity.

Keywords: antipsychotics, drug licensing, pharmacoepidemiology, poisoning, poisons information, thioridazine

Introduction

Antipsychotic drugs have been known for some years to cause arrhythmias in overdose, in particular *torsade de pointes*. One of the drugs to do this most commonly in overdose has been thioridazine [1–5]. Antipsychotic phenothiazines have a wide range of pharmacological properties, but it is believed that this arrhythmogenic action is due to an effect on potassium ion channels on the myocardium [6]. It has also been suggested that this effect

may be partially due to a metabolite of thioridazine rather than the parent compound [2, 7–9].

In an epidemiological study published in 2000 Reilly and colleagues [10] demonstrated significant QT prolongation in patients receiving thioridazine therapeutically. Since QT prolongation is known to be a risk factor for sudden death, and predisposes to *torsade de pointes*, licence changes were made by the Committee on Safety of Medicines in the UK with stringent changes in the advised prescribing advice [11]. These changes were publicized both by the pharmaceutical company involved, and the Medicines Control Agency at the beginning of 2000. No clear advice was offered at that time about appropriate substitution therapy for patients receiving thioridazine.

We have investigated the effects of this licence change

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on prescribing of thioridazine and other antipsychotics in England and Scotland. We have also examined the effect on poisoning by examining information accesses to the TOXBASE database from England and Scotland and telephone enquiries to the National Poisons Information Service (NPIS) Edinburgh Centre from Scotland. Finally, we have documented the effect on admissions to our own poisons treatment unit at the Royal Infirmary of Edinburgh.

Methods

The change in thioridazine licensing and relevant publicity occurred in December 2000 and January 2001. This study therefore concentrates on prescribing behaviour and overdose patterns for oral antipsychotics for 2000 and 2001.

Prescription data

Prescription data for the years 2000 and 2001 were kindly supplied by the Prescription Pricing Authority for England, and the Prescription Division of the Scottish Executive Health Department's Information and Statistics Division for Scotland. These are expressed as items dispensed per month (i.e. individual general practitioner prescriptions). We have not corrected these figures for population, but the population of Scotland is 5.2 million, which is approximately a tenth of the population of England. There are no major differences in the way drugs are licensed, prescribed and dispensed in England and Scotland, since both countries operate under the terms of the National Health Service. Virtually all patients in the UK obtain their drugs in the community via their general practitioners on NHS prescriptions.

Data on poisoning

Within the UK clinicians may obtain information on the management of poisoning in two ways, via telephone enquiries to the regionally based individual centres of the UK NPIS, or increasingly by access to the national web-based dedicated poisons information system TOXBASE [12]. We have examined data on enquiries by both approaches for 2000 and 2001 in Scotland, and for England have examined the pattern of TOXBASE access. Accesses to TOXBASE have increased steadily since it was introduced to the internet in August 1999. Rates of access from different parts of the UK differ [12]. The majority of TOXBASE use on the UK mainland has been traditionally in Scotland and the north of England. We have therefore expressed TOXBASE accesses for the total of all antipsychotics as a percentage of all TOXBASE accesses, by country of origin, and examined the pro-

portion of antipsychotic accesses for each of the marketed antipsychotic agents.

For Scotland we have analysed the number of telephone enquiries to our NPIS Centre that involved antipsychotics. We have also examined the relative proportion for those agents for which telephone enquiries were made. Enquiries were not made about every antipsychotic on the market.

Finally, to confirm that in Scotland the pattern of enquiries mirrors hospital presentations, we have examined our records of patients admitted to the Royal Infirmary of Edinburgh with poisoning. Amongst these the proportion for which an antipsychotic drug was part of the ingestion have been identified, and changes in agent use are reported. Where informative we have included 95% confidence intervals.

Prescribing and overdose

To allow comparison of the relationship between overdose enquiry rates before and after licence change, we have related TOXBASE accesses for individual agents to prescribing. To do this we have compared the percentages of TOXBASE accesses among antipsychotics with that of percentage of antipsychotic prescriptions for each product and expressed this as a ratio. We have also compared the relationship between TOXBASE accesses and prescribing for thioridazine and that for other antipsychotics by calculating an odds ratio.

Results

Prescribing in England

A total of 25 antipsychotic preparations were prescribed in general practice during the study period (see Table 1). Of these, seven accounted for the vast majority of prescribing and individually each accounted for more than 5% of prescribing in 2001 (Table 2). For visual illustration we have shown data for four antipsychotics (chlorpromazine, olanzapine, risperidone and thioridazine) of most interest and pooled data for the remainder.

It can be seen from Figure 1 that, prior to change in licensing, thioridazine was the most frequently prescribed antipsychotic, with more than 140 000 scripts per month and over 35% of market share throughout 2000. Prescribing dropped rapidly in 2001 to less than 5% of total sales of antipsychotics. There was no single drug that replaced thioridazine, but prescriptions for risperidone (20.7%), chlorpromazine (17.1%) and olanzapine (17%) appear to be the main ones that have been used in place of thioridazine by the end of 2001. In the first quarter of 2000 9.4% (95% confidence interval [CI] 9.35, 9.46) of antipsychotic scripts were for drugs not included in the 'top

Table 1 Antipsychotic medications prescribed in general practice during the study period.

Amisulpride
Benperidol
Chlorpromazine hydrochloride
Clozapine
Droperidol
Flupenthixol hydrochloride
Fluphenazine hydrochloride
Haloperidol
Loxapine succinate
Methotrimeprazine hydrochloride
Methotrimeprazine maleate
Olanzapine
Oxypertine
Pericyazine
Perphenazine
Pimozide
Promazine hydrochloride
Quetiapine
Risperidone
Sulpiride
Thioridazine
Trifluoperazine
Zotepine
Zuclopenthixol acetate
Zuclopenthixol hydrochloride

seven'; by the end of 2001 this was 13.6%. Total prescriptions for antipsychotics fell from 4.77 million in 2000 to 4.53 million in 2001.

Prescribing in Scotland

In Scotland the profile of antipsychotic prescribing in 2000 was somewhat different from England. Thioridazine accounted for 45% and, in contrast to England, chlorpromazine was the next most frequently prescribed drug. The same seven antipsychotics were most frequently prescribed in Scotland as in England (Table 3). After the change in licensing, chlorpromazine became the single most frequently prescribed drug (31%), followed by risperidone (18.75%) and olanzapine (14.7%) in the last quarter of 2001. In the first quarter of 2000 9.3% (9.14, 9.49) of antipsychotic scripts were for drugs not included in the 'top seven'; by the end of 2001 this was 13.5%, almost identical to the proportion in England. Prescription numbers for antipsychotics fell from 529 800 in 2000 to 484 400 in 2001.

Poisoning in England

All accesses to the TOXBASE website from England were counted and those relating to a product containing an antipsychotic ingredient were analysed. The number of web accesses for all products increased month on month

Table 2 Quarterly prescription number for antipsychotics, England 2000–2001.

	2000				2001			
	Jan–Mar	Apr–Jun	Jul–Sept	Oct–Dec	Jan–Mar	Apr–Jun	Jul–Sept	Oct–Dec
<i>England prescription numbers</i>								
Chlorpromazine	129 080	126 445	125 964	128 090	171 615	193 423	195 133	199 527
Haloperidol	94 065	92 761	93 247	95 916	120 317	121 335	119 569	121 123
Olanzapine	95 582	105 014	117 868	130 557	143 416	161 338	178 157	198 713
Risperidone	102 267	112 903	125 946	141 501	175 065	201 296	220 184	241 738
Sulpiride	60 957	60 947	61 051	61 015	62 169	62 459	61 224	61 490
Thioridazine	431 190	429 410	432 374	416 287	165 843	76 414	55 881	46 921
Trifluoperazine	135 688	134 922	133 653	133 438	143 531	144 539	139 987	140 156
Others	109 002	114 006	118 545	123 454	149 789	151 411	151 076	160 037
Total	1 157 831	1 176 408	1 208 648	1 230 258	1 131 745	1 112 215	1 121 211	1 169 705
<i>England prescriptions, %</i>								
Chlorpromazine	11.15	10.75	10.42	10.41	15.16	17.39	17.40	17.06
Haloperidol	8.12	7.89	7.71	7.80	10.63	10.91	10.66	10.36
Olanzapine	8.26	8.93	9.75	10.61	12.67	14.51	15.89	16.99
Risperidone	8.83	9.60	10.42	11.50	15.47	18.10	19.64	20.67
Sulpiride	5.26	5.18	5.05	4.96	5.49	5.62	5.46	5.26
Thioridazine	37.24	36.50	35.77	33.84	14.65	6.87	4.98	4.01
Trifluoperazine	11.72	11.47	11.06	10.85	12.68	13.00	12.49	11.98
Others	9.41	9.69	9.81	10.03	13.24	13.61	13.47	13.68

Upper panel prescription numbers, lower panel percentage of prescriptions. Others, Eighteen other antipsychotics, see text.

and the proportion for antipsychotics per quarter declined from 4.24% (3.95, 4.53) to 2.86% (2.74, 2.98) over the 2-year period. In the first quarter of 2000 thioridazine accounted for 39.31% (35.90, 42.72) of TOXBASE antipsychotic accesses and remained at a similar level throughout that year. Chlorpromazine was the next highest agent at 15.9% (13.3, 18.5). In 2001 accesses

for thioridazine dropped rapidly and fell to 4.39% (3.54, 5.24) by the last quarter, those for chlorpromazine, olanzapine and risperidone all increased by approximately the same amount (Table 4). There was a small increase in accesses for the antipsychotics not included in the 'top seven' group, but no obvious 'favourite' within this category of 18 drugs.

Figure 1 Prescribing of antipsychotic drugs per quarter 2000–2001 expressed as % of total antipsychotics. a, Percentage England. ♦, Others; ■, risperidone/olanzapine; ▲, chlorpromazine; ×, thioridazine. b, Percentage Scotland. ■, Risperidone/olanzapine; ♦, others; ▲, chlorpromazine; ×, thioridazine. (Others – haloperidol, sulpiride, risperidone + 18 other antipsychotics – see text.)

Poisoning in Scotland

In Scotland total accesses to the database were less than in England, as Scotland serves a smaller population. In 2001 approximately 10% of total TOXBASE accesses were Scottish in origin. The main changes seen in antipsychotic accesses were a decline for thioridazine, from 34.5% (28.7, 40.3) to 5.22% (2.87, 7.57), and an increase in chlorpromazine from 27.52% (22.07, 32.97) to 41.16% (35.97, 46.35). Olanzapine and risperidone had started from a lower baseline, but by the end of 2001 together accounted for 20% of accesses. Very little change in accesses was seen for all other agents (Table 5).

Telephone calls to the Edinburgh centre of the NPIS regarding antipsychotic agents averaged between 3% and 4.5% of total calls per quarter. The proportion of calls for individual antipsychotics mirrors the percentage of TOXBASE accesses (Table 6).

Admissions

Over the 2-year period approximately 6% of admissions to the Royal Infirmary of Edinburgh poisons

Table 3 Quarterly prescription number for antipsychotics, Scotland 2000–2001.

	2000				2001			
	Jan–Mar	Apr–Jun	Jul–Sept	Oct–Dec	Jan–Mar	Apr–Jun	Jul–Sept	Oct–Dec
<i>Scotland prescription numbers</i>								
Chlorpromazine	17 589	17 520	17 436	18 393	32 406	37 090	36 703	38 600
Haloperidol	6 825	6 871	7 103	7 863	11 431	10 942	10 575	10 722
Olanzapine	8 691	9 501	10 388	11 645	12 719	14 777	15 937	17 820
Risperidone	11 200	12 278	13 096	14 818	17 665	20 304	21 489	23 370
Sulpiride	5 718	5 919	5 886	5 833	6 005	6 175	6 056	6 096
Thioridazine	60 825	60 954	60 401	57 502	19 538	8 134	6 063	5 376
Trifluoperazine	6 008	6 005	6 115	6 000	6 017	5 951	5 793	5 798
Others	11 963	12 625	13 019	13 821	15 844	15 996	16 141	16 854
Total	128 819	131 673	133 444	135 875	121 625	119 369	118 757	124 636
<i>Scotland prescriptions, %</i>								
Chlorpromazine	13.65	13.31	13.07	13.54	26.64	31.07	30.91	30.97
Haloperidol	5.30	5.22	5.32	5.79	9.40	9.17	8.90	8.60
Olanzapine	6.75	7.22	7.78	8.57	10.46	12.38	13.42	14.30
Risperidone	8.69	9.32	9.81	10.91	14.52	17.01	18.09	18.75
Sulpiride	4.44	4.50	4.41	4.29	4.94	5.17	5.10	4.89
Thioridazine	47.22	46.29	45.26	42.32	16.06	6.81	5.11	4.31
Trifluoperazine	4.66	4.56	4.58	4.42	4.95	4.99	4.88	4.65
Others	9.29	9.59	9.76	10.17	13.03	13.40	13.59	13.52

Upper panel prescription numbers, lower panel percentage of prescriptions. Others, Eighteen other antipsychotics, see text.

unit involved an antipsychotic drug. These admissions were all due to deliberate or recreational drug use. It is often difficult to distinguish these presentations in this patient group, but the vast majority are deliberate overdoses. In 2000 54.2% (46.1, 62.3) of antipsychotic ingestions involved thioridazine and 23.6% (16.7, 30.5) chlorpromazine, but in 2001 chlorpromazine (58.3%; 50.8, 65.8) replaced thioridazine (10.7%; 6.0, 15.4) as the 'drug of choice'. This change occurred between the last quarter of 2000 and the first of 2001 (Table 7).

There were no clear changes in self-harm from other antipsychotics apart from trifluoperazine, for which there were no admissions in 2000 and six in 2001.

Prescribing and TOXBASE use

The ratio of percentage accesses for a product to the percentage of prescribing related to that drug provides an insight into whether licence changes result in a more frequent use of TOXBASE. A change in this ratio would suggest a different pattern of use of the system, and that poison enquiries after the licence change had been affected by this change. In England and Scotland the ratio of accesses to prescriptions for thioridazine increased after the licence change, while for other antipsychotics the ratio remained relatively stable (Figure 2). The rank order of this ratio of proportion of TOXBASE usage to proportion of thioridazine prescribing did not change statis-

Table 4 England TOXBASE enquiries.

	2000				2001			
	Jan-Mar	Apr-Jun	Jul-Sept	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sept	Oct-Dec
Total products	18 536	30 823	38 356	40 750	84 149	57 502	87 608	77 208
Total antipsychotics	786	1 300	1 563	1 594	2 059	2 030	2 083	2 210
Percentage antipsychotics	4.24	4.22	4.07	3.91	2.45	3.53	2.38	2.86
<i>Individual antipsychotic agents, %</i>								
Chlorpromazine	15.90	15.62	14.59	15.68	20.88	28.67	24.53	29.59
Haloperidol	4.33	3.69	4.93	4.64	6.02	7.88	6.53	5.79
Olanzapine	6.62	10.15	7.87	9.79	10.73	13.40	13.87	13.62
Risperidone	4.33	4.46	5.18	5.52	8.11	8.03	10.42	10.41
Sulpiride	6.36	5.62	5.57	4.45	4.13	4.58	4.08	4.57
Thioridazine	39.31	37.62	36.72	36.45	17.48	8.97	6.43	4.39
Trifluoperazine	9.16	8.38	8.32	7.72	9.03	8.82	10.23	9.91
Others	13.99	14.46	16.83	15.75	23.60	19.66	23.91	21.72

Upper panel total number of accesses and antipsychotics as a percentage of total; lower panel individual antipsychotics. Others, Eighteen other antipsychotics, see text.

Table 5 Scotland TOXBASE enquiries.

	2000				2001			
	Jan-Mar	Apr-Jun	Jul-Sept	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sept	Oct-Dec
Total products	5740	6672	7331	7595	8827	8610	8965	9227
Total antipsychotics	258	281	286	344	348	417	330	345
Percentage antipsychotics	4.49	4.21	3.90	4.53	3.94	4.84	3.68	3.74
<i>Individual antipsychotic agents (%)</i>								
Chlorpromazine	27.52	21.71	26.22	18.60	37.93	40.53	45.76	41.16
Haloperidol	10.08	5.69	6.29	12.21	5.75	7.43	6.36	9.57
Olanzapine	3.88	8.54	5.94	5.52	7.47	9.11	8.79	11.59
Risperidone	2.71	5.34	3.85	6.98	6.03	7.43	6.36	8.41
Sulpiride	2.33	3.20	1.75	1.45	4.02	5.28	4.24	3.19
Thioridazine	34.50	38.79	32.17	41.28	20.98	7.43	6.67	5.22
Trifluoperazine	2.71	2.14	3.85	2.33	2.87	3.12	3.94	2.03
Others	16.28	14.59	19.93	11.63	14.94	19.66	17.88	18.84

Upper panel total number of accesses and antipsychotics as a percentage of total; lower panel individual antipsychotics. Others, eighteen other antipsychotics, see text.

tically significantly compared with other individual antipsychotics. In Scotland odds ratios (95% CI) for the proportion of antipsychotic TOXBASE accesses for thioridazine *vs* the proportion of all antipsychotics prescriptions for thioridazine in 2000 were 0.71 (0.63, 0.80), and in 2001 1.26 (1.06, 1.51). In England the odds ratios for the same two comparators were 1.06 (1.01, 1.13) in 2000 and 1.23 (1.14, 1.33) in 2001.

Discussion

We were interested to examine the change in profile of prescribing and overdoses with individual antipsychotic agents following the change in licensing advice, as no central advice on a drug switch had been offered. This lack of advice has been criticised by others [13]. In the UK there are limitations on use of clozapine as an alternative. It is licensed for use in patients unresponsive or intolerant to conventional

antipsychotic drugs. Advice has subsequently been issued by the National Institute for Clinical Excellence (NICE) in England [14] recommending use of an atypical antipsychotic as first-line treatment for newly diagnosed schizophrenics or where there are unacceptable side-effects with conventional antipsychotics. Clozapine is recommended for those whose symptoms have not been controlled by two successive antipsychotics (one atypical). This advice was not generally available at the time of our study.

We concentrate on two aspects of drug use, prescribing and overdose, which are unusual comparisons in pharmacoepidemiological studies, but allow a unique insight into the effects of a licence change on behaviour of doctors and their patients.

Prescribing data clearly show a rapid response in reduction of thioridazine prescriptions, occurring from the first quarter of 2001. This change was seen in England and Scotland to a similar degree. What is unexpected is the difference between the replacement thera-

Table 6 Scottish phone calls 2000–2001.

	2000				2001			
	Jan–Mar	Apr–Jun	Jul–Sept	Oct–Dec	Jan–Mar	Apr–Jun	Jul–Sept	Oct–Dec
Total enquiries	1401	1396	1305	1151	1169	1266	1229	1128
Total antipsychotics	62	41	40	51	48	38	42	43
Percentage antipsychotics	4.43	2.94	3.07	4.43	4.11	3.00	3.42	3.81
<i>Individual antipsychotic agents (%)</i>								
Chlorpromazine	17.74	26.83	10.00	9.80	27.08	31.58	26.19	48.84
Haloperidol	12.90	0.00	5.00	1.96	0.00	2.63	2.38	6.98
Olanzapine	3.23	4.88	0.00	3.92	8.33	18.42	14.29	4.65
Risperidone	3.23	7.32	7.50	9.80	2.08	0.00	16.67	9.30
Sulpiride	3.23	2.44	5.00	5.88	6.25	0.00	11.90	0.00
Thioridazine	35.48	41.46	45.00	45.10	29.17	13.16	4.76	4.65
Trifluoperazine	1.61	4.88	2.50	0.00	2.08	0.00	0.00	2.33
Others	22.58	12.20	25.00	23.53	25.00	34.21	23.81	23.26

Others, Eighteen other antipsychotics, see text.

Table 7 Antipsychotic poisoning admissions to Edinburgh Royal Infirmary.

	2000					2001				
	Jan–Mar	Apr–Jun	Jul–Sept	Oct–Dec	Total 2000	Jan–Mar	Apr–Jun	Jul–Sept	Oct–Dec	Total 2001
Chlorpromazine	9	7	11	7	34	19	23	38	18	98
Haloperidol	0	2	4	0	6	2	2	3	1	8
Olanzapine	0	1	1	0	2	0	0	0	0	0
Risperidone	0	2	0	2	4	1	2	4	2	9
Sulpiride	2	3	2	2	9	1	2	4	1	8
Thioridazine	15	16	15	32	78	7	4	6	1	18
Trifluoperazine	0	0	0	0	0	1	0	3	2	6
Others	3	0	4	4	11	3	5	5	8	21
Total	29	31	37	47	144	34	38	63	33	168

Others, Eighteen other antipsychotics, see text.

Figure 2 Ratio of percentage of antipsychotic TOXBASE accesses to percentage of antipsychotic prescribing by quarter. a, England ratio, b, Scotland ratio. ▲, Chlorpromazine; ×, thioridazine; ●, olanzapine; ◆, risperidone. (Others – haloperidol, sulpiride, risperidone + 18 other antipsychotics – see text.)

pies used for thioridazine in the two countries. In Scotland this was primarily chlorpromazine, while in England it was a combination of three drugs, the older agent chlorpromazine and two new compounds, risperidone and olanzapine (Tables 1 and 2).

The effects of these differences in prescribing behaviour were mirrored in the parameters we measured to investigate the effects on overdose. In Scotland the ward admission data from our hospital clearly show that the population of patients who previously took thioridazine as part of their overdose in 2000 presented in 2001 having taken predominantly chlorpromazine. This pattern mirrors the changes seen in prescribing across Scotland, but also mirrors the changes we saw in enquiries to our poisons centre both by telephone, and electronically via accesses to the TOXBASE database. We have thus been able to show in three different ways a decrease in the presentation of patients who might be deemed most at risk of thioridazine-induced arrhythmias as a result of the change in licensing as measured.

In England poisons telephone enquiries go to four centres of the National Poisons Information Service (Birmingham, Cardiff, London and Newcastle). TOXBASE enquiries increased throughout the period of the study from England (Table 3), though the proportion of enquiries relating to antipsychotics as a whole tended to fall. However, amongst antipsychotics the proportion of TOXBASE accesses relating to thioridazine fell in line with the

observed changes in prescribing behaviour in England and Scotland. There was an increased proportion of TOXBASE accesses for chlorpromazine, olanzapine and risperidone. The stable relationship between the proportion of accesses to TOXBASE and the proportion of drug prescribed (Figure 2) for all antipsychotics except thioridazine supports the hypothesis that there is a relationship between overdose enquiries and prescribing volume, and indicates this differs for different antipsychotics. As these agents may be used for different populations of patients, it is likely that the overdose rate will not be the same in all groups, and this is the most likely reason for our observation. Thus in our clinical experience of overdose, thioridazine and chlorpromazine tend to be used by young impulsive males with behaviour disturbances. The change in the relative proportion of prescriptions resulting in TOXBASE accesses for thioridazine is in keeping with doctors making more enquiries about this drug, probably because of increased awareness of its toxicity.

If it was the aim of the Medicines Control Agency to reduce risk of toxicity by reducing patient population exposure, the effects of the licence change are clear and may be seen as beneficial. Perhaps an unexpected benefit has been the very large reduction in overdose presentations relating to thioridazine. The impact of these changes on clinical features in patients with antipsychotic poisoning will be reported separately. Speed of change in prescribing behaviour and speed of change in overdose patterns illustrate the rapidity with which a licence change can affect both prescriber behaviour and, as a secondary effect, patterns of use in self-harm. It is interesting to compare the magnitude and speed of this effect with the smaller effect on paracetamol sales and self-harm seen in Scotland and England following changes in over-the-counter availability of this product.

With thioridazine the change in the licensing produced an immediate reduction in prescriptions and a ten-fold reduction within 1 year. For poisoned patients in Edinburgh Royal Infirmary this was seen in a reduction of overdoses from 32 in the last quarter of 2000 to one in the last quarter of 2001. The actual number of antipsychotic poisonings admitted to the ward rose but the drugs changed. Change in pack size of over-the-counter paracetamol in England reduced the annual number of deaths from paracetamol poisoning by 21%. The rate of nonfatal self poisoning with paracetamol decreased by 11% over the year after the pack size change [15], but there is no information on whether there was a decrease in the total number of overdoses, or if they changed to a more or less toxic substance. In Scotland this change in mortality was not mirrored [16].

In conclusion, we have shown different responses in prescribing in England and Scotland to the prescribing warning. In future such warnings might usefully include

prescribing advice [13]. We have shown a marked reduction in thioridazine overdoses in our own unit, changes in overdose telephone enquiries and TOXBASE enquiries that indicate a beneficial effect in an at-risk population. Comparison of prescription data with computer database accesses suggests a stable relationship over time in England, and suggests different patterns of overdose presentation with different antipsychotic drugs.

The change in thioridazine use in overdose following the MCA warning compares very favourably with attempts to reduce over-the-counter availability of paracetamol using pack size changes, and indicates different methods are needed to address the control of over-the-counter drugs compared with prescription medicines.

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