Magic bullets for insomnia?

Patients' use and experiences of newer (Z drugs) versus older (benzodiazepine) hypnotics for sleep problems in primary care

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ABSTRACT

Background

Little is known about patients' perceptions of newer hypnotics.

Aim

To investigate use, experience, and perceptions of Z drug and benzodiazepine hypnotics in the community.

Design of study

Cross-sectional survey of general practice patients who had received at least one prescription for a Z drug or benzodiazepine in the previous 6 months.

Setting

Lincolnshire, UK.

Method

Self-administered postal questionnaire.

Results

Of 1600 surveys posted, 935 (58.4%) responses were received, of which 705 (75.4%) were from patients taking drugs for insomnia. Of those 705 patients, 87.9% (*n* = 620) were first prescribed a hypnotic by their GP, and 94.9% (*n* = 669) had taken a sleeping tablet for 4 weeks or more. At least one side effect was reported in 41.8% (*n* = 295); 18.6% wished to come off hypnotic medication; and 48.5% had tried to stop treatment. Patients on Z drugs were more likely to express a wish to stop (22.7% versus 12.3%; odds ratio [OR] = 1.67, 95% confidence interval [CI] = 1.13 to 2.49), or to have attempted to come off medication, than those on benzodiazepines (52.4% versus 41.0%; OR = 1.54, 95% CI = 1.12 to 2.12). The two groups did not differ significantly in respect of benefits or adverse effects.

Conclusion

There were no significant differences in patients' perceptions of efficacy or side-effects reported by those on Z drugs compared to patients taking benzodiazepines. Side-effects were commonly reported, which may have contributed to a high proportion of responders, particularly patients on Z drugs who were wishing to stop, or who had previously tried to stop taking this medication. Reported prescribing practices were often at variance with the licence for short-term use.

Keywords

attitude; cross-sectional studies; hypnotics and sedatives; prescriptions.

INTRODUCTION

Insomnia is a common, often chronic condition that increases with age and has a reported prevalence rate in Europe ranging from 4% to 37%.[1,2] About half of those with sleep problems seek medical help,[3] which often involves a prescription of hypnotic drugs including benzodiazepines like temazepam, or Z drugs such as zopiclone, zolpidem, or zaleplon. Most hypnotic prescribing takes place in primary care, and drug treatments may be inappropriately prescribed for 4 weeks or longer in up to 50% of new prescriptions.[4]

Over the past decade, a gradual reduction has occurred in the prescribing of older benzodiazepine hypnotics, while the use and cost of hypnotic drugs continues to rise overall.[5] This has been due to fears over benzodiazepine use and abuse and an increase in prescribing of Z drugs, which were marketed as safer and less liable to dependence compared with benzodiazepines.[6] Zopiclone is now the most frequently prescribed hypnotic in the UK at 4 million items (39% of items) costing £10m (43% of total

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How this fits in

Little is known about patients' use, experiences, and perceptions of newer Z drugs compared with older benzodiazepine hypnotics. Efficacy and side-effects reported by those on Z drugs compared with benzodiazepines were similar in this community sample. Side-effects were commonly reported, which may have contributed to a high proportion of participants wishing to stop or having tried to stop taking their medication; this was significantly more likely in those on Z drugs. Reported prescribing practices were often at variance with the licence recommending short-term use of these drugs.

hypnotic cost). Temazepam is the next most commonly prescribed with 3.5 million items (35%) at £4m (19%).[7] As a result, over £22m is spent every year in primary care on 10 million items of hypnotic drugs, and these figures have shown no decline since the early 1990s. This is partly explained by an increasing population, with an average growth per year of 0.4–0.5% since 1991 and an increasing proportion of older people.[8]

Previous research has documented the attitudes of patients and doctors to benzodiazepines,[9–15] but little has so far been published about their perceptions or experiences of Z drugs, either alone or compared with benzodiazepine hypnotics. Studies of benzodiazepine hypnotics have shown that patients believe that they are more effective and safer than do doctors.[14,15] A recent study of GPs showed that, compared with benzodiazepines, they believed Z drugs to be safer, more effective, less liable to cause side effects, and the drugs of choice for a range of indications,[16] despite a lack of evidence to support such notions.[17]

The clinical benefits of hypnotics have actually been shown to be small, with significant risks of complications arising from adverse cognitive or psychomotor effects, and daytime sleepiness that may persist for several months after stopping the drug.[18] Such unintended reactions are reported most frequently by older patients, who are also the most likely to be prescribed the newer drugs. Complications, such as falls, fractures, and road traffic collisions, have been linked to these drugs,[19] which have considerable potential for tolerance and addiction.

The aim of this community survey was to investigate and compare patients' perceptions of benefits and risks of benzodiazepines and Z drugs. The study formed part of a larger investigation into methods for reducing hypnotic prescribing in primary care, and also aimed to define potential interventions for better management of sleep appropriate to the primary care setting.

METHOD

West Lincolnshire Primary Care Trust (PCT) comprised 40 general practices (now part of Lincolnshire Teaching Primary Care Trust), serving 214 000 patients. Previous attempts to lower relatively high rates of hypnotic prescribing encountered resistance to change. A survey instrument was designed to collect data using a previously published questionnaire,[14] incorporating elements from literature searches, and discussion points raised within the project steering group, as well as advice received from experts in the field.

In 2005, forms were posted to a sample of patients on the lists of GP principals in West Lincolnshire PCT. Selection was made by each participating practice being asked to submit a list of patients who had been prescribed a Z drug or benzodiazepine taken in a single night-time dose to induce sleep in the previous 6 months. From this list of names, a random sample of 50 patients from each practice received the questionnaire for completion. The questionnaire focused on patients' attributes, views about indications for drug treatments (for example, insomnia or anxiety), and their assessment of outcomes.

Returned questionnaires were entered into a spreadsheet according to a predetermined coding frame. SPSS (version 12.1) was used for data analysis. A χ^2 test was used for initial group correlations and logistic regression (both backward conditional and forward conditional) to analyse differences in responses for Z drugs and hypnotic benzodiazepines correcting for age, sex, and duration of drug use. Analysis was restricted to patients who stated that they were taking these drugs for insomnia rather than for other indications, such as musculoskeletal pain or epilepsy. Missing data were not included in the comparisons.

RESULTS

Altogether, 935 of 1600 (58.4%) analysable responses were received from responders who had been prescribed a benzodiazepine or Z drug in the previous 6 months. Thirty-two of the 40 practices surveyed contributed patients to the survey, and the response rate from each varied considerably (mean 44.5%, standard deviation [SD] = 20%). Of the responders, most (705 of 935; 75.4%) were taking their drugs for insomnia rather than other indications, such as anxiety, epilepsy, or drug addiction (Table 1). Further analyses were carried out only for those confirming that they had taken drugs for insomnia. Z drugs were taken more commonly (370 of 705; 52.5%) than benzodiazepines (268 of 705; 38.0%), reflecting current prescribing trends. Hypnotics prescribed included zopiclone (328 responders; 46.5%), zolpidem (39; 5.5%), zaleplon (3; 0.4%), temazepam (161; 22.8%), nitrazepam (48; 6.8%), diazepam (46; 6.5%), or other benzodiazepines (13; 1.8%). Just over half (50.4%; 355 of 705) of responders were aged 65 years of age or older.

The majority of participants, 87.9% (n = 705), were first prescribed a hypnotic by their GP, rather than a psychiatrist or other health professional. Many had been advised to continue treatment for

longer than recommended under the licence: 45.4% (*n* = 320) indicated they were advised to continue treatment for a month or more, and a further 42.3% (*n* = 298) reported not being advised on treatment duration. Most responders, 92.1% (*n* = 649), were on repeat prescriptions of hypnotics, and over two-thirds were taking hypnotics daily rather than intermittently (Table 1).

In a number of important respects those prescribed Z drugs differed from those taking benzodiazepines (Table 2); they were more likely to be younger, to have received their first prescription from a psychiatrist, stated a wish to come off hypnotics, and made at least one attempt to come off medication. These differences were significant at $P<0.05$ (but not at $P<0.01$). Over two-fifths of responders (41.8%; *n* = 295) reported at least one side-effect from hypnotic use. Withdrawal effects were commonly reported among those who had tried to stop their treatment, even if they were on intermittent rather than daily therapy. Responders who felt they may be at risk of becoming drug dependent were more likely to want to stop medication than those who already acknowledged dependence or felt that they were not dependent on hypnotics ($P<0.001$).

No significant differences between Z drugs and benzodiazepines were found in respect of perceived benefits or adverse effects, including withdrawal or dependence (Table 3). Almost one in five patients (18.6% overall) expressed a desire to come off hypnotic medication. Patients on Z drugs were more likely to wish to stop (22.7% versus 12.3%; odds ratio [OR] = 1.67; 95% confidence interval [CI] = 1.13 to 2.49), and to have attempted to come off medication than those on benzodiazepines (52.4% versus 41.0%; OR = 1.54, 95% CI = 1.12 to 2.12).

Most patients using hypnotics stated they took less time to get to sleep (Z drugs versus benzodiazepines, 76.2% versus 79.1%), and woke less during the night (60.8% versus 55.6%), but half the users or fewer agreed that they slept longer (48.6% versus 47.8%), felt rested on waking (47.0% versus 45.1%), were more active (37.0% versus 35.8%), or felt better overall (48.1% versus 50.0%); these differences were not significant. Side-effects including daytime drowsiness (20.5% versus 19.0%), headache (18.1% versus 14.9%), dizziness (13.5% versus 17.2%), difficulty concentrating (16.7% versus 14.2%), or difficulty thinking (14.9% versus 14.6%), confusion (11.6 versus 7.8%), shaking (9.2% versus 7.5%), and falls (5.9% versus 7.8%) were not significantly different between those on Z drugs or benzodiazepines (Appendix 1).

Table 1. Demographic data for responders prescribed hypnotics for insomnia in the previous 6 months.

Characteristics	Number (*n* = 705)	(%)
Sex		
Male	223	(31.6)
Female	379[a]	(53.8)
Age, years		
18–44	69	(9.8)
45–64	198	28.0)
65–84	305	(43.3)
85+	51	(7.2)
Responder		
Patient	618	(87.7)
Relative	46	(6.5)
Carer	19	(2.7)
Medication type		
Z drug	370	(52.5)
Benzodiazepine	268	(38.0)
First prescriber		
GP	620	(87.9)
Psychiatrist	53	(7.5)
Advised duration of treatment		
Days	14	(2.0)
Weeks	30	(4.3)
Months	35	(5.0)
Years	28	(4.0)
Indefinitely	257	(36.4)
Not advised	298	(42.3)
Duration of treatment		
0–2 weeks	13	(1.8)
2–3 weeks	11	(1.6)
4–52 weeks	101	(14.3)
Over 1 year	568	(80.6)
Medication type		
Repeat prescription	649	(92.1)
Acute (one-off) prescription	48	(6.8)
Frequency of taking medication		
Daily	475	(67.4)
As needed	222	(31.5)
Advised about side-effects		
Yes	301	(42.7)
Not sure	164	(23.3)
No	213	(30.2)
Would like to come off medication		
Yes	131	(18.6)
No	508	(72.1)
Tried to come off medication		
Yes	342	(48.5)
No	300	(42.6)
Dependency		
Dependent	323	(45.8)
At risk of becoming dependent	75	(10.6)
Not dependent	247	(35.0)
Improvement in insomnia		
Yes	613	(87.0)
No	57	(8.1)

[a]*Missing values account for totals less than 705 or 100%.*

DISCUSSION

Summary of main findings

This study shows that in a sample of patients whose GPs had prescribed hypnotics during the previous 6 months, there was no significant group difference in reported effectiveness or adverse reactions evoked by

Table 2. Comparing Z drugs with benzodiazepines according to patients' characteristics and treatment factors

	Z drug[a]		Benzodiazepine		χ^2
	Number (n = 370)	(%)	Number (n = 268)	(%)	P-value
Sex					
Male	122	(33.0)	77	(28.7)	0.23
Female	198	(53.5)[b]	145	(54.1)	
Age, years					
18–44	42	(11.4)	22	(8.2)	0.012
45–64	118	(31.9)	65	(24.3)	
65–84	147	(39.7)	120	(44.8)	
85+	19	(5.1)	27	(10.1)	
First prescriber					
GP	320	(86.5)	242	(90.3)	0.027
Psychiatrist	34	(9.2)	13	(4.9)	
Duration of treatment					
Up to 4 weeks	13	(3.5)	10	(3.7)	0.27
4–52 weeks	64	(17.3)	32	(11.9)	
Over 1 year	286	(77.3)	225	(84.0)	
Medication type					
Repeat prescription	339	(91.6)	248	(92.5)	0.87
Acute (one-off) prescription	24	(6.5)	19	(7.1)	
Frequency of taking medication					
Daily	246	(66.5)	186	(69.4)	0.41
As needed	120	(32.4)	79	(29.4)	
Advised about side-effects					
Yes	157	(42.4)	121	(45.1)	0.54
Not sure	92	(24.9)	57	(21.2)	
No	108	(29.2)	82	(30.6)	
Would like to come off medication					
Yes	84	(22.7)	33	(12.3)	0.001[c]
No	254	(68.6)	211	(78.7)	
Tried to come off medication					
Yes	194	(52.4)	110	(41.0)	0.001[c]
No	141	(38.1)	137	(51.1)	
Dependency					
Dependent	161	(43.5)	126	(47.0)	0.01
At risk of becoming dependent	53	(14.3)	18	(6.7)	
Not dependent	125	(33.8)	101	(37.7)	
Improvement in insomnia					
Yes	317	(85.7)	239	(89.2)	0.012
No	39	(10.5)	13	(14.5)	

[a]*Comparisons include patients who confirmed that they were taking Z drug or benzodiazepine.* [b]*Missing values account for totals less than the stated denominator or 100%.* [c]$P<0.01$.

Z drugs or benzodiazepine hypnotics. Adverse effects were common, affecting over two-fifths of those on either drug. Almost half the responders had tried to stop taking their medication, and this was more likely for those on Z drugs. Withdrawal effects were common, with almost one-quarter of those who had tried to discontinue the drug regime experiencing panic or other withdrawal symptoms. Almost one in five patients on either agent expressed a desire to come off hypnotic medication, and those on Z drugs were more likely to want to stop than those on benzodiazepines. Despite this, the majority of patients, whether on Z drugs (68.6%; 254) or benzodiazepines (78.7%; 211), wished to continue taking this medication.

Strengths and limitations of the study

This study is the first to compare the experiences of those on Z drugs with those taking benzodiazepine hypnotics. The study surveyed a random sample of 705 patients from 32 general practices who had been prescribed hypnotics (at least one prescription) over the previous 6 months. The response rate to the survey was satisfactory for a self-administered postal survey of patients. The study was conducted within a single PCT, and not all practices agreed to participate in the survey. Patients from practices that did participate may have had different experiences from those that did not. There may have been a higher response rate among patients on repeat prescriptions than among those

Table 3. Logistic regression of clinical effects related to hypnotic type.

	Z drug		Benzodiazepine			
	Number (n = 370)	(%)	Number (n = 268)	(%)	OR	95% CI
Would like to come off medication						
Yes	84	(22.7)	33	(12.3)	1.67	1.13 to 2.49[a]
No	254	(68.6)	211	(78.7)		
Tried to come off medication						
Yes	194	(52.4)	110	(41.0)	1.54	1.12 to 2.12[a]
No	141	(38.1)	137	(51.1)		
Dependency						
Dependent/at risk of becoming dependent	214	(57.8)	144	(53.7)	1.31	0.94 to 1.8
Not dependent	125	(33.8)	101	(37.7)		
Withdrawal						
Any withdrawal symptom	74	(20.0)	43	(16.0)	0.79	0.54 to 1.16
No withdrawal symptom	296	(80.0)	224	(83.6)		
Improvement in insomnia						
Yes	317	(85.7)	239	(89.2)	0.85	0.49 to 1.42
No	39	(10.5)	13	(14.5)		
Benefit						
Any benefit	333	(90.0)	249	(92.9)	1.45	0.74 to 2.84
No benefit	17	(4.6)	7	(2.6)		
Adverse effect						
Any adverse effect	161	(43.5)	113	(42.2)	0.74	0.49 to 1.13
No adverse effect	68	(2.2)	47	(17.5)		

Backwards stepwise conditional regression using terms: medication type (Z drug or benzodiazepine hypnotic), sex (male or female), age group (≥75 years), length of treatment (≥4 weeks). Similar results were obtained using forward stepwise conditional regression. OR = odds ratio. [a]*P<0.01.*

who only took hypnotics for a short time, although comparisons were adjusted for length of treatment.

There was no opportunity within this study design to survey non-responders. However, it is likely that response biases were similar for participants on Z-drug or benzodiazepine hypnotics; therefore, the group comparisons, in which logistic regression was used to account for age and sex of patients as well as duration of treatment, are likely to be valid.

Comparison with existing literature

Benzodiazepines and Z drugs are known to be prescribed for longer than is recommended and in excessive doses, particularly in older adults:[4,20] a finding that was confirmed in this study. Given that the incidence of insomnia tends to increase with age (at least until 80 years of age), that it is often chronic or recurrent, and that once started, hypnotics tend to continue being used in almost one-third of patients, an ageing population could lead to increased hypnotic prescribing in the long term.[21]

In a previous study it was shown that perceptions of GPs towards hypnotics tended to be in favour of newer hypnotics despite a lack of evidence showing benefit of newer Z drugs compared to benzodiazepines.[16] This may partly explain why Z drugs have overtaken benzodiazepines as hypnotics of first choice, and why they were more likely to be prescribed for younger patients in this community study.

Although Z drugs have been promoted as being effective and safe, and compared favourably with benzodiazepines in terms of side-effect profile and dependence,[22] these findings are not supported in this study. Reported rates of adverse reactions to Z drugs were similar in nature and incidence to benzodiazepines in responders, and comparable with the findings of other studies in hospital settings.[23] Cognitive problems[24] and psychomotor impairment[25] similar to those of benzodiazepines have also been demonstrated in other studies, and recent evidence suggests that Z drugs may also increase the risk of depression.[26]

Implications for future research and clinical practice

Sleep problems are often chronic and therefore there is a mismatch with pharmacotherapy which is only suitable for the short term.[27] This study supports the lack of demonstrable improved efficacy of Z drugs, similar rates of adverse events, and the possibility of higher rates of dependence of Z drugs compared to benzodiazepine hypnotics.

The lack of difference between these two types of drugs and the importance of restricting hypnotics for short-term use need to be emphasised to patients and practitioners. Hypnotic drugs continue to be prescribed instead of safer alternatives when they have not been shown to be superior to placebo in primary insomnia

for improving function or quality of life.[28] Their routine use is likely to reinforce help-seeking behaviour,[29] involving further requests for hypnotic prescriptions.

Further research is recommended into the process that takes place during the consultation for sleep presentations. More research is needed using non-pharmacological approaches to insomnia, such as cognitive behavioural therapy which includes the techniques of sleep education, sleep hygiene, muscle relaxation, stimulus control, and sleep restriction.[30,31] Research, including recent studies of cognitive behavioural therapy for insomnia in general practice, has demonstrated benefits in primary insomnia, and also in secondary insomnia due to physical disorders, such as painful conditions or psychological problems such as anxiety and depression.[32,33]

The findings point to a need for primary care service improvements that focus on helping patients stop their use of hypnotics as well as preventing their use as long-term treatments. This will need careful evaluation of evidence-based assessment tools and techniques applied to real-world primary care settings.[34,35] Implementation will require commitment to change from patients, practitioners, and primary care organisations.

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Competing interests

The authors have stated that there are none

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Appendix 1. Patients' perceptions of benefits and disadvantages of Z drugs and benzodiazepines.

	Z drugs (*n* = 370)			Benzodiazepine (*n* = 268)			
	Agree or strongly agree, *n* (%)	Not sure, *n* (%)	Disagree or strongly disagree, *n* (%)	Agree or strongly agree, *n* (%)	Not sure, *n* (%)	Disagree or strongly disagree, *n* (%)	χ^2 test, *P*-value
Perception of associated benefits							
I take less time to get to sleep[a]	282 (76.2)	19 (5.1)	16 (4.3)	212 (79.1)	12 (4.5)	10 (3.7)	0.82
I wake less during the night	225 (60.8)	25 (6.8)	37 (10.0)	149 (55.6)	22 (8.2)	28 (10.4)	0.61
I sleep longer overall	180 (48.6)	37 (10.0)	54 (14.5)	128 (47.8)	18 (6.7)	42 (15.7)	0.38
I feel rested on waking up	174 (47.0)	53 (14.3)	51 (13.8)	121 (45.1)	36 (13.4)	34 (12.7)	0.98
I am more active during the day	137 (37.0)	68 (18.4)	50 (13.5)	96 (35.8)	38 (14.2)	49 (18.3)	0.14
I feel better overall	178 (48.1)	64 (17.3)	38 (10.3)	134 (50.0)	38 (14.2)	26 (9.7)	0.59
Perception of associated side-effects							
Headaches	67 (18.1)	26 (7.0)	140 (37.8)	40 (14.9)	12 (4.5)	108 (40.3)	0.27
Dizziness	50 (13.5)	24 (6.5)	148 (40.0)	46 (17.2)	13 (4.9)	109 (40.7)	0.38
Sickness	22 (5.9)	16 (4.3)	163 (44.1)	18 (6.7)	9 (3.4)	120 (44.8)	0.77
Drowsiness (during the daytime)	76 (20.5)	28 (7.6)	132 (35.7)	51 (19.0)	13 (4.9)	95 (35.4)	0.48
Confusion	43 (11.6)	23 (6.2)	152 (41.1)	21 (7.8)	16 (6.0)	106 (39.6)	0.47
Difficulty thinking	55 (14.9)	29 (7.8)	142 (38.4)	39 (14.6)	9 (3.4)	108 (40.3)	0.073
Difficulty concentrating	62 (16.7)	29 (7.8)	144 (38.9)	40 (14.9)	14 (5.2)	102 (38.1)	0.54
Falls	22 (5.9)	12 (3.2)	176 (47.6)	21 (7.8)	5 (1.9)	122 (45.5)	0.37
Fractures	6 (1.6)	10 (2.7)	187 (50.5)	12 (4.5)	5 (1.9)	126 (47.0)	0.07
Road traffic accidents	5 (1.4)	8 (2.2)	190 (51.4)	4 (1.5)	3 (1.1)	130 (48.5)	0.65
Visual disturbance	23 (6.2)	20 (5.4)	165 (44.6)	16 (6.0)	9 (3.4)	116 (43.3)	0.56
Shaking	34 (9.2)	16 (4.3)	157 (42.4)	20 (7.5)	11 (4.1)	114 (42.5)	0.79

[a]*Missing values account for totals less than 370 or 268.*