ADVERSE EFFECTS OF BENZODIAZEPINES IN PSYCHIATRIC OUTPATIENTS
Goran Arbanas¹, Dahna Arbanas² & Kata Dujam¹
¹General Hospital Karlovac, Karlovac, Croatia
²Karlovac county pharmacy, Karlovac, Croatia

SUMMARY

Background: Benzodiazepines are among the most frequently prescribed drugs. Of all their side effects, hip fractures and possibility of developing dependence are usually studied.

Objective: The aim of this study was to determine how often do psychiatric outpatients suffer from adverse effects of benzodiazepines, and which adverse effects do they notice.

Subjects and method: 109 patients on two consecutive days were asked to fill in the questionnaire. Among them were 29 women and 80 men. Ten women (1/3) and 20 men (1/4) refused to participate in the study.

Results: 68% of women and 93% of men used benzodiazepines at least once in a lifetime; 40% of women used benzodiazepines in the last seven days, and 93% of men (32% of women and 44% of men used benzodiazepines every day for the last seven days). Unfortunately, 8% of men used more then one benzodiazepine daily.

All of the women who used benzodiazepines had at least one adverse effect; and 91% of men had adverse effects. One third of women and one quarter of men stopped taking benzodiazepines due to adverse effects.

The mean number of adverse effects was 4.8 both in men and women. Those who stopped taking benzodiazepines didn't have more adverse effects in comparison to those who continued to use them.

More than half of the participants suffered from sleepiness, slowness and fatigue. One third of the participants said they noticed the change in sexual drive. More then 30% of women noticed dizziness and only 6% of men. None of the participants said to have jaundice after using benzodiazepines. The same adverse effects were present in those who stopped taking the drugs and in those who continued to use them.

Conclusion: The prevalence of benzodiazepine use is very high in psychiatric patients. Many of them notice adverse effects, but mainly continue to use the drug.

Key words: benzodiazepines - adverse effects - prevalence of use

INTRODUCTION

Although benzodiazepines were developed during 1930s and set into use in 1950s, research on prevalence of adverse effects of these drugs is scarce (Lader 2008). Mainly, there are case reports on special or unusual adverse effects or research on prevalence of adverse effects of special populations (such as older people, because of the possibility of resulting in falls and hip fractures) (Kirby et al. 1999, Johnell & Fastbom 2009, Taylor et al. 1998).

The most common adverse effects are: drowsiness, sedation, dizziness and ataxia (Kaplan & Sadock 1994).

The efficacy of benzodiazepines have been reanalyzed in light of the fact that there is a possibility of developing dependence in long term use (3-6 months or longer) (Schweizer & Rickels 1998). But, despite knowledge to such possibilities, and despite limited evidence to their efficacy (especially in light of newer pharmacotherapeutic possibilities of treating anxiety disorders), benzodiazepines continue to be among the most
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commonly prescribed drugs (Struzik et al. 2004, Stahl 2002).

The aim of this study was to determine how often and which adverse effects do experience psychiatric outpatients.

SUBJECTS AND METHOD

The sample included all the patients on two consecutive days that attended outpatient unit at the General hospital Karlovac. There were 109 patients.

Patients were offered to fill in the questionnaire on adverse effects of benzodiazepines. Patients were told that the questionnaire was anonymous and that they were free to choose whether to participate or not in the study. 30 patients refused to participate in the study.

The questionnaire consisted of three parts. In the first part general sociodemographic date were collected: age, gender, marital status, and educational level. In the second part patients were asked to answer weather they used benzodiazepines in the last seven days, last month and ever in their life. All the benzodiazepines (anxiolytics-sedatives) registered in Croatia were offered, using their trade names. Also, patients were asked who proposed them to use the drug (a doctor, a pharmacist, newspapers, radio or TV, a neighbour, a friend, a nurse or they, themselves). They were asked if the drug was useful to them, and they answered on a Likert scale: my problems/troubles resolved fully; it helped me very much; it helped me; it did not help me; my problems/troubles worsened.

In the third part of the questionnaire patients were offered to choose among 27 side effects if they experienced them during benzodiazepine usage (Kaplan & Sadock 1994). Also, they were asked whether they stopped taking the drug due to these side-effects.

RESULTS

Of 109 patients, who were asked to participate in the study, there were 29 women (26.6%) and 80 men (73.4%). Gender and age characteristics of patients willing to participate and those who didn't want to participate are presented in Table 1. There are no gender differences in these two groups (chi2=0.959; p=0.327). Also, there are no statistical differences in age (women: t=1.03, p=0.31; men: t=1.10; p=0.27).

Table 1. Gender and age characteristics of the sample

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Did not participate</th>
<th>Participated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>10 women, 20 men</td>
<td>19 women, 60 men</td>
</tr>
<tr>
<td>Age /years/</td>
<td>Women 50.90 ± 10.22</td>
<td>Women 45.22 ± 15.66</td>
</tr>
<tr>
<td></td>
<td>Men 49.10 ± 6.99</td>
<td>Men 45.25 ± 8.72</td>
</tr>
</tbody>
</table>

Among the people who participated in the study, 68% of women and 93% of men used benzodiazepines at least once in their lifetime! 40% of women and 93% of men used benzodiazepines in the last seven days! Also, 32% of women and 44% of men used benzodiazepines every day for the last seven days.

More then 40% of the patients who used benzodiazepines used alprazolam, and 20% used diazepam (Figures 1 and 2).

Unfortunately 8% of men used more then one benzodiazepine daily, and none of the women.

In the vast majority of patients they used benzodiazepines prescribed by their physicians (94%). In one case, the drug was advised by a neighbour, a friend, TV or the patient himself.

Adverse effects were prevalent in the sample: all the women had at least one adverse effect; and 91% of men experienced at least one adverse effect. The mean number of adverse effects in both men and women were 4.8.

The most prevalent adverse effects in men were: slowness (59%), sleepiness (55%), fatigue (55%), change in sexual drive (33%), nervousness
(29%), forgetfulness (27%), headache (25%), irritability (24%), weakness in muscles (24%), fear (22%), and confusion (20%).

In women the most prevalent adverse effects were: sleepiness (69%), slowness (69%), fatigue (54%), change in sexual drive (38%), dizziness (31%), irritability (23%), aggressiveness (23%), forgetfulness (23%), amnesia (23%) and changes in body weight (23%). None of the participants reported jaundice as an adverse effect.

The most evident difference was the high prevalence of dizziness in women (31%) and low in men (6%).

One third of women (36.4%) and one quarter of men (26.9%) stopped using benzodiazepines. Interestingly, the number of side effects did not differ in those who stopped to use the drugs, and in those who continued the usage. Also, there was the same profile of adverse effects in those who stopped, and in those who continued to take the drug.

**DISCUSSION**

The aim of this study was to evaluate the prevalence of adverse effects of benzodiazepines. Although benzodiazepines are widely used drugs, the researches on the prevalence of adverse effects in patients attending outpatient clinics are scarce (North et al. 1992).

72.5% of patients consented to participate in the study. Gender and age characteristics of the non-participating and participating patients were the same, so we think we can generalize the results to all the outpatients who were contacted. The gender profile (more than 70% of men) is due to the fact that there are many people with PTSD in Croatia who attend mental health system, and who are mainly men.

There is a very high prevalence of use of benzodiazepines in these patients, higher than in other researches: 40% of women and 93% of men used these drugs in the last seven days (Bartels et
The interesting gender difference was that 30% of women and only 6% of men experienced dizziness. We can not explain why there is such a difference.

We compared patients taking benzodiazepines who stopped taking the drugs and those who continued to use them. There were no difference in terms of age, gender, educational level, marital status, benzodiazepine used, number of adverse effects, type of side effects, or satisfaction with the effect of benzodiazepine. So, we could not differentiate among the patients who will discontinue and those who will continue to take the drug.

Thus, patients suffer often and with many adverse effects, but still use benzodiazepines. The question is why. Possible answers are that these drugs are highly effective, achieve their effect quickly, can be used when needed and because physicians prescribe them (Bendtsen et al. 1999; Hylan T. et al 1999; Valenstein M. et al. 2004). Why do physicians prescribe these drugs so often, despite that guidelines on the treatment of mental disorders do not consider benzodiazepines any more (in case of depression, anxiety disorders and PTSD) as the first line drugs (American Psychiatric Association 2000, Baldwin et al. 2005).

The major shortcoming of this study is that we do not know what disorders the participants suffer from. They were asked to fill in the questionnaire anonymously, and in the questionnaire they were asked which disorder do they suffer from, but their perception is not always the same as the diagnosis of their psychiatrist.

Also, the study relies solely on participants' self-report of the type of medications used and adverse effects experienced, and did not include any of the additional sources, such as medical or pharmacy records or family members.

The second problem is that male and female participants in this sample are not comparable, but this is the reflection of the naturalistic sample in our outpatient unit. In all the Croatia there are many men diagnosed with PTSD, after the war trauma, and they make a high percentage of psychiatric patients, biasing the sample.

Future studies should focus on prevalence of benzodiazepine use and their side effects in specific diagnostic groups.
CONCLUSION

Outpatients use benzodiazepines (too) often. Although more than 90% of them experience adverse effects, they continue to use them. The mean number of adverse effects experienced is 4.8 in both men and women.

REFERENCES


Correspondence:
Goran Arbanas
General Hospital Karlovac, Psychiatric ward, Andrije Stampara 3, 47000 Karlovac, Croatia
E-mail: goran.arbanas@ka.t-com.hr