

## ORIGINAL ARTICLE

# Analysis of the consumption of sedative and hypnotic drugs in Yemen and the Czech Republic

## Analýza spotřeby sedativ a hypnotik v Jemenu a v České republice

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### Summary

The aim of this project is to analyze the consumption and reasons for the use of sedative and hypnotic drugs (ATC: N05B and N05C) (SHD) in Yemen (YEM) and to compare this with the consumption of SHD in the Czech Republic (CZ) and in YEM, in the years 2000–2005. In 2005 the consumption of SHD in YEM and in CZ was 0.20 and 6.9 USD/1000 citizens/day, respectively. The consumption of SHD in YEM and in CZ increased after 2000 by 637% and 85%, respectively. A pilot questionnaire tested the factors influencing the consumption of SHD in YEM. 72% of respondents were male; 48% had obtained SHD the first time without a prescription; 90% had engaged in the long term use of SHD; 43% did not know the risks of SHD and the majority of users are most likely young people. The increasing consumption of SHD may be caused by the frequent prescribing of drugs for off-label use, obtaining SHD in the pharmacy without prescription and the common chewing of qat and the lack of warnings about long term risks.

**Keywords:** sedative and hypnotic drugs • consumption of ATC groups N05B and N05C • Yemen • Czech Republic

### Souhrn

Cílem tohoto projektu je analyzovat spotřebu a důvody pro použití léčiv ze skupiny sedativ a hypnotik (SHD) (N05B & N05C) v Jemenu a porovnat je se spotřebou SHD v České republice v letech 2000–2005. V roce 2005 byla spotřeba v Jemenu 0,2 a v České republice 6,9 USD/1000 obyvatel a den. Spotřeba SHD vzrostla v Jemenu o 637 % a v České republice o 85 %. Pilotní dotazník v Jemenu testoval faktory ovlivňující spotřebu SHD. Respondenti byli většinou muži (72 %). Čtyřicet osm procent respondentů získalo poprvé SHD bez předpisu; 90 % užívá tyto léky dlouhodobě a 43 % neznalo rizika, které přináší užívání SHD. Většina uživatelů byli mladší lidé. Z těchto signálů se zdá, že za zvyšující se spotřebou SHD v Jemenu by mohla být snadná dostupnost těchto léčiv v lékárně, časté žvýkání Katu a nedostatek varování odborné veřejnosti o škodlivých účincích dlouhodobého užívání SHD.

**Klíčová slova:** sedativní a hypnotické drogy • spotřeba ATC skupin N05B a N05C • drogy v Jemenu • drogy v České republice

### Introduction

The Department of Social and Clinical Pharmacy, Faculty of Pharmacy, Charles University, Hradec Králové, Czech Republic, co-operates with various students and experts engaged in research into drug consumption worldwide<sup>1)</sup>. Drug consumption analysis is an important source of signal information in pharmacoepidemiology. Drug consumption data can inform us about, e.g., 1. the habits of medicine prescription strategies, 2. rates of particular diseases, 3. willingness of the public to use particular drugs and 4. rates of potential adverse drug effects (e.g. lactulose consumption can be an indicator of constipation, perhaps due to drug use). It can indirectly monitor the harm to patients caused by the misuse of particular drugs as well. There are a variety of barriers to obtaining consumption figures in developing countries – mainly a lack of relevant databases (due to the absence of health insurance companies) and the inaccessibility of many particular drugs in a pharmacy without a medical

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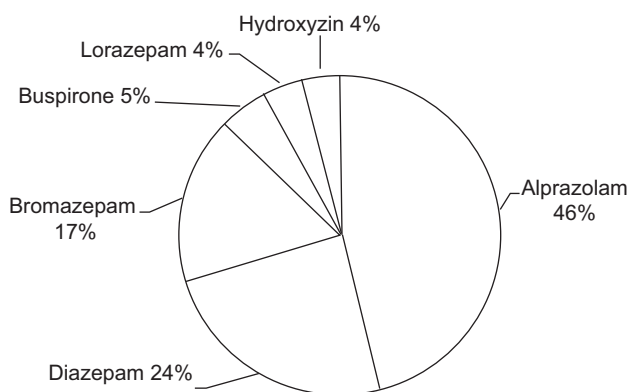


Fig. 1. Arrived value of sedative drugs to Yemen 2000–2005

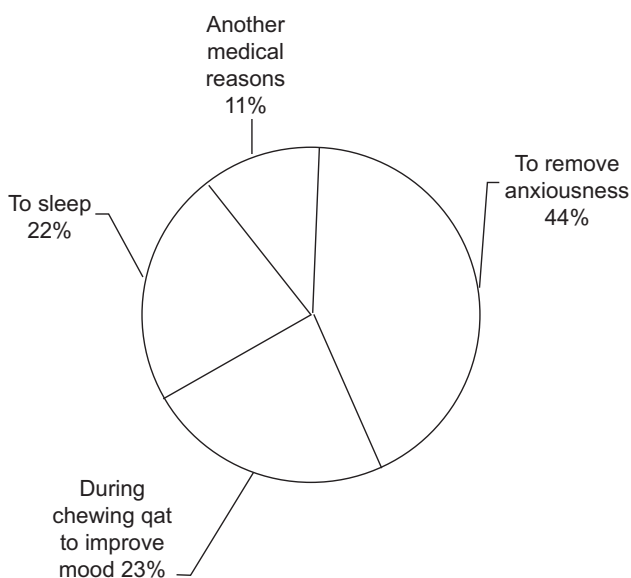


Fig. 2. Reason of using sedatives drugs

prescription<sup>2</sup>). Sedatives and hypnotic drugs (SHD) are compounds which cause the physiological and mental slowdown of body processes and functions.

SHDs have many legitimate medical uses. Benzodiazepines are invaluable in the treatment of anxiety disorders, depression and insomnia; however they also have the potential for abuse and may cause dependence or addiction. It is important to distinguish between addiction to and normal physical dependence on benzodiazepines. Intentional abusers of benzodiazepines usually also have other substance abuse problems. Benzodiazepines are usually a secondary drug of abuse, used mainly to augment the high received from another drug or to offset the adverse effects of other drugs<sup>3</sup>. Physicians may sometimes prescribe these drugs for other conditions, such as muscle spasms, epilepsy and other seizure disorders, phobias, panic disorder, withdrawal from alcohol syndrome, and sleeping problems. However, this type of medicine should not be used regularly for sleep problems that last more than a few days. If used this way, the drug loses its effectiveness within a few weeks<sup>4</sup>.

High percentage of the population in Yemen is chewing “Qat” daily. The broad use of “Qat” in Yemen is one of the main causes of anxiousness and insomnia. Qat (pronounced

cot), also referred to as khat, quatt, kat, and that (in Ethiopia) is a leafy narcotic popular in certain areas of Africa and, more recently, Britain. The term Qat, is taken from the Catha Edulis tree from which the substance is taken. Cathinone, the active component of Qat, closely resembles ephedrine and amphetamine in chemical structure<sup>5</sup>). The substance is regularly chewed daily by a high proportion of the adult population in YEM for its resultant pleasant mild stimulant action. The pleasurable central stimulant properties of qat are commonly believed to improve work capacity and are used on long journeys as well as by students preparing for examinations and to counteract fatigue<sup>6</sup>).

Due to a number of reasons, using sedative drugs in Yemen is quite complicated: using them while chewing Qat to heighten the euphoric effect or as a sleep aid post-usage. For Yemeni citizens it is easier to obtain SHDs from a pharmacy without prescription, which is not the case in the Czech Republic. Therefore it is expected that a Qat user is likely to try to purchase SHDs more frequently, in which case physicians would be less inclined to inform the patient about the risks of chronic use. In Yemen it is very difficult to obtain consumption data to conduct research in this field. Moreover it is difficult to acquire accurate data directly from Yemeni citizens because of an absence of awareness about the problem; discussion about it would be a very sensitive issue. The problem is hidden and not spoken about, which makes the task of the researcher more difficult. With 10 years' experience in community pharmacy, one of the present researchers can verify the fact that sedative use and misuse is widespread in Yemen.

The aims of this study are:

1. to find a source for longitudinal and ecological consumption studies of sedative and hypnotic drugs (SHD) in YEM;
2. to analyze retrospectively the consumption of these drugs in Yemen and compare it with the consumption in the Czech Republic in the period of 2000–2005;
3. to analyze the reasons for consumption and the lack of knowledge about SHD in a pilot cross-sectional study of Yemeni citizens.

## Experimental part

The data regarding YEM drug consumption of N05B and N05C were obtained from the annual report of the Ministry of Public Health & Population – the Supreme Board of Drugs and Medical Appliances, which controls drug registration and regulation as well as allows pharmaceutical companies to import drugs. It publishes an annual report showing the prices in American dollars (USD) for the total quantity of drugs imported to Yemen; drug consumption is expressed in local currency. We asked for data from ATC group N05 about imports into the Yemen in 2000, 2001, 2002, 2003, 2004 and 2005 respectively<sup>7–12</sup>). The Czech consumption figure of N05B and N05C was analyzed based on the data from AISLP (Automated Information System of Medicines) versions 2002.2; 2007.3<sup>13</sup>). The consumption of SHD in the Czech Republic is here expressed in USD. The exchange rate used from the Czech National Bank was 24CzK = 1USD for 28.12.2005<sup>14</sup>).

In Yemen the questionnaire was allocated into fifteen pharmacies in the city of Ibb, and visitors who sought to

Table 1. Arrived value (in USD) of sedative drugs in Yemen for the five-year period from 2000–2005<sup>7–12)</sup>

| No    | Drug        | 2000    | 2001    | 2002    | 2203    | 2004    | 2005      | Total     |
|-------|-------------|---------|---------|---------|---------|---------|-----------|-----------|
| 1     | Alprazolam  | 25.256  | 299.297 | 478.047 | 294.431 | 655.232 | 593.589   | 2.345.852 |
| 2     | Diazepam    | 51.983  | 195.977 | 236.446 | 203.065 | 133.254 | 413.141   | 1.233.866 |
| 3     | Bromazepam  | 60.383  | 185.506 | 66.583  | 91.261  | 69.492  | 375.101   | 848.326   |
| 4     | Buspirone   | 27.895  | 45.298  | 35.651  | 66.057  | 17.334  | 50.850    | 243.085   |
| 5     | Lorazepam   | 12.190  | 57.343  | 11.766  | 16.709  | 29.182  | 78.677    | 205.867   |
| 6     | Hydroxyzine | 27.274  | 26.821  | 67.360  | 53.156  | 26.480  | 79.443    | 201.170   |
| Total |             | 204.981 | 810.242 | 895.853 | 724.679 | 930.974 | 1.511.437 | 5.078.166 |

Table 2. Annual drug consumption (in USD) of N05B and N05C in the Czech Republic for 2000–2005<sup>13)</sup>

| Years | N05B       | N05C       | total      | Δ% of 2000 |
|-------|------------|------------|------------|------------|
| 2000  | 6.859.037  | 6.946.257  | 13.805.294 |            |
| 2005  | 10.357.064 | 15.232.787 | 25.589.850 | 85.36      |

Table 3. Comparison of Yemen and Czech Republic consumptions of N05B and N05C (in USD/1000 citizens/day (UTCD))

| Country        | Year | Consumption | Population <sup>15)</sup> | UTCD* |
|----------------|------|-------------|---------------------------|-------|
| Czech Republic | 2000 | 13.805.294  | 10.272.322                | 3.68  |
|                | 2005 | 25.589.850  | 10.235.828                | 6.85  |
| Yemen          | 2000 | 204.981     | 17.723.186                | 0.03  |
|                | 2005 | 1.511.437   | 20.648.643                | 0.20  |

\*UTCD = USD/1000 citizens/day

buy any SHD were asked to fill in a questionnaire, which 127 patients agreed to do from January 2006 to April 2006. Each questionnaire contains questions monitoring the respondent's gender, age, the strategy of SHD use (time of medication use; diagnosis; is it a first or repeated

Table 4. Demographic characteristics of the participants (127)

|        |             |     |
|--------|-------------|-----|
| Gender | male        | 72% |
|        | female      | 28% |
| Age    | 20–40 years | 73% |
|        | > 40 years  | 24% |
|        | < 20 years  | 3%  |

Table 5. How participants(127) obtained sedative drugs the first time

|                      |     |
|----------------------|-----|
| By prescription      | 52% |
| From a friend        | 29% |
| From a health worker | 11% |
| Alone                | 8%  |

Table 6. Participants responses about their reasons for using sedative drugs along with time used, understanding side effects

|            |            |     |
|------------|------------|-----|
| Time used  | > 6 months | 90% |
|            | > 2 weeks  | 5%  |
|            | one week   | 5%  |
| Addiction* | yes        | 57% |
|            | no         | 43% |

\* Do you know that using this drug for more than two weeks causes health and psychological problems (addiction)?

experience). If the respondent is a chronic user he/she was asked how and why the SHD was obtained the first time, how well the patient understood medication's side effects as well as about the prescribing doctor's specialty and instructions given on medication use.

### Result

Consumption of SHD increased in YEM and in CZ in the five years by 637% (Table 1) and by 85% (Table 2) respectively. Consumption in YEM and in CZ in 2005 was 0.20 and 6.85 USD/1000 citizens/day respectively (Table 3).

The top imported SHD to YEM was alprazolam at 46%, followed by diazepam at 24% (see Fig. 1). 73% of respondents were 20–40 years old (see Table 4). 52% of respondents obtained SHD the first time by a prescription (Table 5).

68% of participant obtained sedative drugs the first time by prescription, did not get any advice from doctors (how long to use it). Only 20% of the prescribing physicians were psychiatrist. 89% of respondents used SHD for non-medical purposes (Fig. 2), 90% of respondents had used SHD for more than six months and 43% had undetermined side effects (Table 6). 23% of respondents had used SHD while using Qat to heighten their euphoria (Table 7).

Table 7. Participants using sedative drugs while chewing Qat to enhance mood (23% of respondents)

|   |        |             |      |
|---|--------|-------------|------|
| 1 | Gender | female      | 0%   |
|   |        | male        | 100% |
| 2 | Age    | 20–30 years | 59%  |
|   |        | 31–40 years | 30%  |
|   |        | > 40 years  | 11%  |

### Discussion

Worldwide sales of prescription drugs, including tranquillizers and sleeping pills, exceed \$300 billion yearly. An estimated 4 million people in the United States have used prescribed benzodiazepine tranquillizers and hypnotics (sleeping pills) regularly for 5–10 years or more according to a US study in the early 1990s. Similar figures apply in the UK, Europe and in some Asian countries with the trend continuing. An estimated 60% of users of

tranquilizers and sleeping pills suffer a mixture of adverse effects and withdrawal syndrome after 2–4 weeks of use due to increased tolerance and addiction<sup>16</sup>.

Researchers on the consumption of drugs in developing countries like Yemen, however, face many difficulties, not only the lack of information and complications in the information that is available, but also the inability to obtain research samples of patients who use such medications. This is undoubtedly a factor which may explain the lack of previous studies. In deferent of CZ, where annual consumption of medicine used to be calculated by DDD methodology, Ministry of Health in Yemen releases the final annual cost (USD) for each pharmacological group.

The trend of an increase in total sales figures in currency is not linked to consumption in DDD and only partly to the number of units sold. It can be interpreted that maybe it is higher consumption of drugs for parenteral use, which are more expensive as per-oral drugs. Of course, there are limits in the interpretations of the State Institute for Drug Control data<sup>2</sup>: it is not possible to calculate consumption of many active substances on the 5<sup>th</sup> level of ATC code, we cannot identify a particular drug formulation and in some cases drug consumption figures can be calculated several times, e.g. one wholesaler sells data to another one and he sells it to pharmacies. The drawback of using consumption in currency is that changes in consumption in longitudinal and ecological studies can be influenced by changes in unit price of medicines, the currency conversion rate if drugs are imported, and the variety of size of the package. We did not discover in YEM so many changes in prices (very frequently cheap generics are imported from India and the market is conservative) and we also factored in population growth. In comparison to CZ in YEM the population grows very quickly but the same results are included in the relative consumption figure of consumption as well.

One of the authors of this article has 10 years' experience in community pharmacy practice in Yemen, which recognized that more and more pharmacy customers ask for SHD. Therefore we tried to provide a consumption study and to look for a reason for this in a pilot study. In Yemen no consumption study had ever been conducted until ours; it is not required from authorities. We found only one source possible to use for a consumption study, a source which computes the costs of imported drugs. Since this database is quite valid and because Yemen has no pharmaceutical industry, we can use it for a consumption study. One disadvantage is that data are expressed in currency only and therefore can be influenced by differing costs per unit, a shift to more expensive drugs by particular group and fluctuations in the exchange rate of Rial to USD. Another disadvantage is the limited access to this database, which can be received only in printed form. An increased consumption of SHD is not due to currency exchange rate. During these five years the rate of Rial to USD was quite stable. For this reason we believe that the increased cost of imported drugs signifies both a higher consumption in DDD and more units sold as well. It can be seen that Yemen's consumption in comparison to the Czech Republic is low – but the cost per package of HSD is very low, so maybe

there is not such a big difference between the two countries in trends of a change in consumption of SHD. What is alarming – it a stark increase in SHD consumption in YEM in five years. From the pilot questionnaire study we wanted to find the reasons. It seems that a significant factor can be the growing number of users of Qat and their attempt to solve problems of insomnia or phobia. Respondents to our questionnaire numbered only 127, hardly a representative group of the population of Yemen. Still our study shows that males required SHD more often – maybe because shopping is their role in family and they possibly use Qat more often.

We were not able to find any study to compare with our results. We were surprised that the majority of our respondents were young people who used Qat, and they have no clue about the risks of exposition to SHD. The abuse of Qat has been traditionally accepted in society. If patients are more addicted to Qat nowadays and thus there is increasing usage of other drugs associated with Qat, this would pose a grave risk for society and we see that in our sample of respondents that, in addition to being prescribed by physicians for intended use, SHD is often used off-label.

That drugs are available without prescription in the pharmacy (to avoid asking a physician is cheaper) is a trend not only in Yemen. Patients can find that very often a physician does not conduct any test and simply prescribes drugs without any diagnostic process. We have seen this trend in the Czech Republic as well when we asked Czech citizens if they are prepared to self-medicate by using antibiotics<sup>17</sup>. Another way from our till now unpublished results it seems to signal that the majority of Czech pharmacists do not dispense “prescription only drugs” without prescription.

It seems to us that maybe the risk of HSD abuse is higher for young men and for qat users. Young men formed the majority of our respondents and many respondents engaged in non-medical usage. Chewing Qat daily, which is one of the most frequent habits of use, is a leading cause of anxiety and insomnia. About half of respondents used SHD to remove anxiety and one fifth to enhance mood while chewing Qat. We discovered that the use of Qat is not only in and of itself very risky for the population because of the harmful side effects, but this problem is compounded by a long term use of SHD as well. It remains to be seen if changes in availability – e.g. to stop selling SHD without a prescription – will be a solution to the problem. It is necessary for pharmacists and physicians to educate citizens that it is necessary to be more careful not only in using Qat and also in using SHD. Physicians seem to play a very important role in consumption of SHD – half of respondents obtained SHD the first time by prescription from doctors of various specialization; patients were often not advised as to the drugs' risks and benefits and thus consented to the drug therapy without requisite knowledge. Because of the lack of rules and regulations regarding the sale of drugs in pharmacies, a patient can obtain any medicine from any pharmacy without prescription. We are going to continue with this research and try to compare the years 2008–2013. We try to stimulate regulation bodies in YEM to make available more precious data for consumption studies as well.

## Conclusion

Sedative use and misuse is a worldwide problem. The consumption of sedative and hypnotic drugs in YEM and in CZ increased after 2000 by 637% and 85%, respectively, and the consumption in YEM in 2005 was in 0.20 and in CZ 6.85 USD/1000 citizens/day respectively.

In Yemen it is very difficult to obtain consumption data to conduct research in this field. Moreover, it is difficult to acquire accurate data directly from Yemeni citizens because of an absence of awareness about the problem; discussion about it would be a very sensitive issue.

A pilot questionnaire tested the factors influencing the consumption of SHD in YEM. 90% had engaged in the long term use of SHD; 43% did not know the risks of SHD and the majority of users are most likely young people, 52% had obtained SHD the first time with a prescription. About half of respondents used SHD to remove anxiety and one fifth to enhance mood while chewing Qat, which is one of the most frequent habits of use, is a leading cause of anxiety and insomnia.

**Conflicts of interest:** none.

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