Concurrent Use of Alcohol and Sedatives in Finnish General Population

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Background: The epidemiology of independent use of sedatives or alcohol is well reported in previous research. However, the epidemiology of concurrent use of sedatives and alcohol is vastly understudied despite the unpredictable interactions associated with it. **Objectives:** Our aim was to study the prevalence of concurrent use of alcohol and sedatives and further examine the use of sedatives in some subgroups of people with alcohol use. **Methods**: A mailed questionnaire was sent to randomly chosen representative sample of Finnish population (n=5000). The main outcome measure was the prevalence of the use of sedatives in five subgroups of people with alcohol use in the previous week. **Results:** Of the participants, 7.8 % (142/1818) reported use of both alcohol and sedatives in the previous week. Among the people with sedative use, 67.0 % (142/212) reported at least some alcohol use, and 9.9. % (21/212) reported high use of at least 21 units of alcohol in the previous seven days. The prevalence of sedative use was highest among those who had used at least 21 units of alcohol in the previous was especially common among those who reported having used large amounts of alcohol.

Keywords: alcohol; sedatives; benzodiazepines; population study

Introduction

Benzodiazepines and non-benzodiazepine hypnotics are sedatives prescribed for various psychiatric and somatic conditions, making them one of the most prescribed psychotropic medications worldwide (Janhsen, Roser and Hoffmann, 2015). Prescription of these medicines has increased significantly, even though their use has been associated with several public health concerns, such as increased benzodiazepine-related overdose deaths (Bachhuber *et al.*, 2016; Victoria R Votaw *et al.*, 2019b). For example in Finland nearly 10 % of the adult population were using sedatives and 4 % were people with long-term use in 2014 (Kurko *et al.*, 2018). Another Finnish study reported that 39.4 % of those who initiated benzodiazepine medication from 2006 to 2015 continued using these medications in the long-term (Taipale *et al.*, 2020). Most common definition of long-term sedative use is six months during a year, but it varies between studies (Kurko *et al.*, 2015).

Concurrent use of alcohol and sedatives may be problematic for various reasons. They share similar pharmacological properties and present similar sedative and intoxicating effects (Hollister, 1990). Thus, their concurrent use introduces potential unpredictable interactions that can even be fatal (Perera, Tulley and Jenner, 1987; Calhoun *et al.*, 1996; Dåderman and Lidberg, 1999). Sedative use itself has been associated with multiple psychological and physical adverse effects, varying from memory disruption to risks of accidents (Lader, 1999). Risk of dependence also increases on long-term use of sedatives (Lader, 1999).

Previous literature introduces an abundance of studies on the epidemiology of independent alcohol or sedative use, but only a few studies have examined the epidemiology of concurrent use of sedatives and alcohol in the general population (Del Río, Prada and Alvarez, 2002; Veldhuizen, Wade and Cairney, 2009). A great deal of the earlier studies are also focused on a particular clinically relevant sub-group, such as elders (Ilomäki *et al.*, 2013) or people with misuse of alcohol or sedatives (Votaw *et al.*, (2019a, 2019b)).

Despite the risks associated with the concurrent use of sedatives and alcohol, the epidemiology of this phenomenon in the general population has been vastly understudied. Using a sample from Finnish general population, our aim was to study the prevalence of concurrent use of alcohol and sedatives and further examine the use of sedatives among some subgroups of people with alcohol use.

Materials and Methods

Participants

This study uses data from the Regional Health and Well-being Study conducted in 2010 in Finland, designed to obtain data on aspects relating to health and the use of health resources (Härkänen *et al.*, 2014). The study utilized a nationally representative sample of Finland (n=5,000), and the study participants were recruited randomly from the Population Register Centre. A mailed questionnaire was sent to participants over 20 years of age with the options to submit it by mail or via an internet platform. Three versions of the questionnaire were prepared for the age groups of 20–54, 55–74 and 75 or older in four languages: Finnish, Swedish, Russian and English. The overall response rate to the questionnaire was 48 %. The study participants in the final sample represented all age groups.

Questionnaire

Use of alcohol

The participants were asked how many glasses, bottles or restaurant servings of various types of alcoholic beverages they had used over the past seven days. The question was asked separately for four alcohol beverage categories: "Medium strength beer, medium cider or long drinks (alcohol content 2.9 % to 4.7 %)"; "stronger beer, strong cider or long drinks (alcohol content over 4.7%)"; "wine"; and "spirits or other strong drinks". The participants were requested to respond "0" if they had not used any alcohol of the type indicated. Using the Finnish standard for drinks, a bottle (33 cl) of beer, cider, or long drink; a glass of wine (12 cl); or a drink of strong alcohol (4cl) corresponds to one unit or approximately 12 grams of pure alcohol.

Use of sedatives

The participants were asked whether they had used sedatives or hypnotics during the past seven days. No further names or visual depictions of these medications were given. The response options were: "No," "yes, other than prescribed medication" and "yes, prescribed medication." The two latter categories were pooled as "yes" due to sample size.

Statistical Analysis

A stratified random sampling design was applied. The probability to be picked was set twice as high in the oldest group (75 or older) in order to correct for the relatively low response rate of the group. The response rates were corrected using the weight factors produced by the Inverse Probability Weighting (IPW) method.

The main outcome measure was the prevalence of sedative use by five categories of

alcohol consumption in the previous week. The categories were determined based on alcohol consumption as 0; 0.1-6.9; 7-13.9; 14-20.9; and 21 or more units of alcohol. The prevalence of alcohol use and the prevalence of concurrent use of alcohol and sedatives were reported as mean values of alcohol use by sex. The confidence interval (CI) was set at 95 %. Post hoc analysis was also conducted to determine whether there were participants with severe alcohol use disorder among the study population. Questionnaire data on self-reported attendance at a detoxification program during the previous 12 months was used for this purpose. Statistical analysis was conducted with PASW Statistics 18 software, using Complex Samples commands.

Results

Of the sample population, 33.9 % (1695/5000) had answered the questions relevant to this study. Of the participants, 749 were men and 946 women. After the weighted correction, the total number of participants was 1818, of whom 895 were men and 923 women. The weight-corrected value was used in the following results.

Of the participants, 76.3 % (1387/1818) had used alcohol in the previous week. The corresponding proportions were 80.6 % (721/895) for men and 72.2 % (666/923) for women. Those who had used alcohol reported an average of 8.1 (95 % CI 7.4-8.8) units of alcohol. The results were 10.5 (95 % CI 9.2-11.8) units of alcohol for men and 5.5 (95 % CI 5.0-5.9) for women. A more detailed description of alcohol use in the sample population is presented in table 1. Of the participants, 11.7 % (212/1818) reported having used sedatives in the previous week. The corresponding proportions were 9.5 % (85/895) for men and 13.8 % (128/923) for women. More detailed prevalence data on the use of alcohol and sedatives is presented in table 2. ** insert Tables 1 and 2 here**

Of the participants, 7.8 % (142/1818) reported use of both alcohol and sedatives in the previous week. The proportions were 6.7 % (60/895) for men and 8.9 % (82/923) for women. Of the participants reporting use of sedatives, 67.0 % (142/212) reported any alcohol use in the previous seven days. The corresponding proportions were 70.6 % (60/85) for men and 64.6 % (82/127) for women. Within this group, 29.5 % (62/212) reported having used at least seven units; 15.4 % (33/212) at least 14 units and 9.9 % (21/212) at least 21 units of alcohol in a week. Of the participants, 0.8 % (21/1818) reported having used sedatives and at least 21 units of alcohol in the previous week. A more detailed description of alcohol use among people with sedative use is presented in table 3.

** insert Table 3 here**

The prevalence of the use of sedatives in the five subgroups by alcohol units is presented in table 4. The prevalence was highest among those who had used at least 21 units of alcohol (19.4 %, 21/108) in the previous seven days. The corresponding proportions were 14.0 % (12/86) for men and 39.1 % for women (9/23). The prevalence of the use of sedatives was the second highest among those who had not used any alcohol (16.2 %, 70/431) and lowest among those who had used 7-14 units of alcohol (9.0 %, 29/321) in the previous seven days.

** insert Table 4 here**

Severe alcohol disorders were rare among this study population as only one participant reported attendance at a detoxification program.

Discussion

The concurrent use of alcohol and sedatives was common in the general population (7.8 %) and even more common among those who used alcohol at least 21 units in a week (19.4 %). One tenth of those with sedative use reported alcohol use of at least 21 units in a week. These are concerning findings because even lesser amount of alcohol use might be a risk when used concurrently with sedatives (Hollister, 1990).

We also found that rate of sedative use among women compared to men was pronounced in the sub-group of highest alcohol use in our study. This may relate to overall higher prevalence of sedative use in women, which may be explained by higher prevalence of anxiety disorders (Martin, 2003).

Some of our findings are aligned with previous literature (Del Río, Prada and Alvarez, 2002; Veldhuizen, Wade and Cairney, 2009). Sedatives were more frequently used by women and alcohol was more frequently used by men. Similar to previous studies, the prevalence of any alcohol use was lower with people who use sedatives. The Canadian study presented that even heavy drinking was less frequent among those who use sedatives (Veldhuizen, Wade and Cairney, 2009). However, our study suggests that the prevalence of sedative use may increase after certain number of alcohol units. It should be noted that prevalence figures between studies are not directly comparable due to different methodological approaches.

There are several reasons, which might explain concurrent use being more prevalent among those who drink. Alcohol use has been associated with increased risk of depression and anxiety disorders (Haynes *et al.*, 2005). Those who use alcohol may experience more severe symptoms of depression and anxiety, and therefore may use sedatives in attempt to better cope with them. Similarly, sedatives may be used in attempt to relieve possible symptoms caused by alcohol, e.g. withdrawal symptoms. Among people with non-medical use of sedatives, most common motives for simultaneous alcohol use were to relieve stress, to sleep and to change mood (Nattala *et al.*, 2012). Previous studies have suggested that index dependence increases the risk of another dependence (McGrath *et al.*, 2020). Thus, dual dependence of alcohol and sedatives might also partly explain our findings of higher prevalence sedative use among those who report using high doses of alcohol.

The sample used in this study is part of a large national data collection, which renders it representative of the general Finnish population. The results are thus generalizable at least in most western countries with similar trends in alcohol and sedative use. In sensitive matters such as alcohol use, it is suggested that a self-reported questionnaire, which was used in the present study, may reflect participants' real behavior better than an interviewed survey (Hochstim, 1967). The questions about medication use and drinking were dispersed across the questionnaire, which probably decreased the effect of social desirability bias related to the simultaneous use of alcohol and medication.

The response rate was relatively low, which is typical for mailed questionnaires. It is likely that the concurrent use of alcohol and sedatives was higher among individuals who did not participate. Only one participant reported attending a detoxification program, which indicates that individuals with an alcohol use disorder may be underrepresented in the sample. If so, the results might underestimate the prevalence of concurrent use of alcohol and sedatives. A similar effect would occur if the self-reported use of alcohol was underestimated, which is possible. Due to limitations in the questionnaire, it was not possible to determine if the use of sedatives occurred simultaneously with the use of alcohol. Less than five reported other than prescribed use of sedatives in the past seven days. Therefore, it was not possible to separate prescription use and misuse of sedatives from this data. Relative weakness of the questionnaire was that it did not include examples of sedative or hypnotic medicines. Thus, it is possible that the participants may have reported other medication as sedatives. However, we estimate that in Finland sedatives are widely understood to refer to benzodiazepines by general public.

As a conclusion, the concurrent use of alcohol and sedatives is common. Subsequent studies should examine if this is explained by sociodemographic or psychosocial factors. Based on our findings, it is important to assess patients' alcohol use before prescribing sedatives.

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Declaration of interest statement

JP has received travel fees from Otsuka and Lundbeck.

Data availability statement

The data is stored and administered by THL (Finnish Institute for Health and Welfare). Users can obtain the survey data as follows:

1) For researchers employed by/ in cooperation with THL: a research plan should be addressed to the THL research board with a description of how the data will be used. (The data is available for free provided that the research plan is accepted and a contract on data use signed).

2) For researchers outside THL: through FinData (https://www.findata.fi/en/).

ATH study is a cross-sectional study and it has been conducted annually starting from 2010. ATH study was approved by the Coordinating Ethics Committee of Finnish Institute for Health and Welfare (THL) in 2010 (approval number THL107/6.01.00/2010)

References

Bachhuber, M. A. *et al.* (2016) 'Increasing benzodiazepine prescriptions and overdose mortality in the United States, 1996-2013', *American Journal of Public Health*. American Public Health Association Inc., pp. 686–688. doi: 10.2105/AJPH.2016.303061.

Calhoun, S. R. *et al.* (1996) 'Abuse of flunitrazepam (rohypnol) and other benzodiazepines in Austin and South Texas', *Journal of Psychoactive Drugs*, 28(2), pp. 183–189. doi: 10.1080/02791072.1996.10524390.

Dåderman, A. M. and Lidberg, L. (1999) 'Flunitrazepam (Rohypnol) abuse in combination with alcohol causes premeditated, grievous violence in male juvenile offenders', *Journal of the American Academy of Psychiatry and the Law*, 27(1), pp. 83–99. Available at: https://europepmc.org/article/med/10212029 (Accessed: 23 September 2020).

Härkänen, T. *et al.* (2014) 'Inverse probability weighting and doubly robust methods in correcting the effects of non-response in the reimbursed medication and self-reported turnout estimates in the ATH survey', *BMC Public Health*. BioMed Central Ltd., pp. 1–

10. doi: 10.1186/1471-2458-14-1150.

Haynes, J. C. *et al.* (2005) 'Alcohol consumption as a risk factor for anxiety and depression: results from the longitudinal follow-up of the National Psychiatric Morbidity Survey', *The British journal of psychiatry : the journal of mental science*, 187(DEC.), pp. 544–551. doi: 10.1192/BJP.187.6.544.

Hochstim, J. R. (1967) 'A Critical Comparison of Three Strategies of Collecting Data from Households', *Journal of the American Statistical Association*, 62(319), pp. 976–989. doi: 10.1080/01621459.1967.10500909.

Hollister, L. E. (1990) 'Interactions between alcohol and benzodiazepines.', *Recent developments in alcoholism : an official publication of the American Medical Society on Alcoholism, the Research Society on Alcoholism, and the National Council on Alcoholism*, pp. 233–239. Available at: https://europepmc.org/article/med/1970665 (Accessed: 23 September 2020).

Ilomäki, J. *et al.* (2013) 'Prevalence of concomitant use of alcohol and sedativehypnotic drugs in middle and older aged persons: a systematic review', *The Annals of pharmacotherapy*, 47(2), pp. 257–268. doi: 10.1345/APH.1R449.

Janhsen, K., Roser, P. and Hoffmann, K. (2015) 'Probleme der Dauertherapie mit Benzodiazepinen und verwandten Substanzen: Verschreibungspraxis, Epidemiologie und Entzugsbehandlung', *Deutsches Arzteblatt International*, 112(1–2), pp. 1–7. doi: 10.3238/arztebl.2015.0001.

Kurko, T. *et al.* (2018) 'Trends in the long-term use of benzodiazepine anxiolytics and hypnotics: A national register study for 2006 to 2014', *Pharmacoepidemiology and Drug Safety*, 27(6), pp. 674–682. doi: 10.1002/pds.4551.

Kurko, T. A. T. *et al.* (2015) 'Long-term use of benzodiazepines: Definitions, prevalence and usage patterns - a systematic review of register-based studies', *European psychiatry : the journal of the Association of European Psychiatrists*, 30(8), pp. 1037–1047. doi: 10.1016/J.EURPSY.2015.09.003.

Lader, M. H. (1999) 'Limitations on the use of benzodiazepines in anxiety and insomnia: Are they justified?', *European Neuropsychopharmacology*, 9(SUPPL. 6). doi: 10.1016/S0924-977X(99)00051-6.

Martin, P. (2003) 'The epidemiology of anxiety disorders: A review', *Dialogues in Clinical Neuroscience*. Les Laboratoires Servier, pp. 281–298. doi: 10.31887/dcns.2003.5.3/pmartin.

McGrath, J. J. *et al.* (2020) 'Comorbidity within mental disorders: a comprehensive analysis based on 145 990 survey respondents from 27 countries', *Epidemiology and Psychiatric Sciences*, 29. doi: 10.1017/S2045796020000633.

Nattala, P. *et al.* (2012) 'Motives and simultaneous sedative-alcohol use among past 12month alcohol and nonmedical sedative users', *The American journal of drug and alcohol abuse*, 38(4), pp. 359–364. doi: 10.3109/00952990.2011.643987.

Perera, K. M. H., Tulley, M. and Jenner, F. A. (1987) 'The Use of Benzodiazepines Among Drug Addicts', *British Journal of Addiction*, 82, pp. 511–515.

Del Río, M. C., Prada, C. and Alvarez, F. J. (2002) 'Do Spanish patients drink alcohol while undergoing treatment with benzodiazepines?', *Alcohol*, 26(1), pp. 31–34. doi: 10.1016/S0741-8329(01)00195-1.

Taipale, H. *et al.* (2020) 'Incidence of and Characteristics Associated With Long-term Benzodiazepine Use in Finland', *JAMA network open*, 3(10), p. e2019029. doi: 10.1001/jamanetworkopen.2020.19029.

Veldhuizen, S., Wade, T. J. and Cairney, J. (2009) 'Alcohol consumption among Canadians taking benzodiazepines and related drugs', *Pharmacoepidemiology and Drug Safety*, 18(3), pp. 203–210. doi: 10.1002/pds.1702.

Votaw, Victoria R. *et al.* (2019a) 'Nonmedical prescription sedative/tranquilizer use in alcohol and opioid use disorders', *Addictive Behaviors*, 88, pp. 48–55. doi: 10.1016/j.addbeh.2018.08.010.

Votaw, Victoria R *et al.* (2019b) 'The epidemiology of benzodiazepine misuse: A systematic review* HHS Public Access', *Drug Alcohol Depend*, 200, pp. 95–114. doi: 10.1016/j.drugalcdep.2019.02.033.

	Men		Women		Total	
Units of alcohol	%	n	%	n	%	n
0	19.4	174	27.8	257	23.7	431
0.1-6.9	39.0	349	54.0	499	46.7	848
7-13.9	22.9	205	12.6	116	17.7	321
14-20.9	9.0	81	3.1	29	6.0	110
<u>≥</u> 21	9.6	86	2.5	23	6.0	108
Total	100	895	100	923	100	1818

Table 1. Prevalence of alcohol use by units of alcohol in the previous seven days in the sample population (n=1818).

	Men		Womer	1	Total	
Use of:	%	n	%	n	%	n
Alcohol	80.6	721	72.2	666	76.3	1387
Sedatives	9.5	85	13.8	128	11.7	212

Table 2. Prevalence of the use of alcohol and sedatives in the sample population (n=1818) in the previous seven days.

	Men		Women		Total	
Units of alcohol	%	n	%	n	%	n
0	29.2	25	35.3	45	32.9	70
0.1-6.9	31.7	27	41.6	53	37.7	80
7-13.9	16.0	13	12.8	16	14.1	29
14-20.9	9.1	8	3.0	4	5.5	12
<u>></u> 21	13.8	12	7.3	9	9.9	21
Total	100	85	100	127	100	212

Table 3. Prevalence of alcohol use by units of alcohol in the previous seven days among the people with sedative use (n=212).

	Men		Women		Total	
Units of alcohol	%	n/N	%	n/N	%	n/N
0	14.4	25/174	17.5	45/257	16.2	70/431
0.1-6.9	7.7	27/349	10.6	53/499	9.4	80/848
7-13.9	6.3	13/205	13.8	16/116	9.0	29/321
14-20.9	9.9	8/81	13.8	4/29	10.9	12/110
<u>></u> 21	14.0	12/86	39.1	9/23	19.4	21/108

Table 4. Prevalence of the use of sedatives in subgroups by alcohol units in the previous seven days in the sample population (N=1818).