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PHARMACOTHERAPY OF TRANSIENT INSOMNIA RELATED TO NIGHT WORK

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Shiftworkers working on the night shift transpose their sleeping hours to the time of day which is inconvenient for sleep because of the endogenous circadian rhythm sleep-wakefulness, the circadian rhythms of other body functions and the environmental schedule. As a result of this, a certain number of workers suffer from insomnia. This study aimed at examining the effects of two hypnotic agents with different elimination times on sleep disturbances which follow night shift work. Three groups of shiftworkers took zopiclone, nitrazepam and placebo capsules during a week of work on the night shift repeating it three times so that each week of capsule taking was separated from the next by a three-week break. In the two groups on hypnotics total length and efficacy of main sleep improved as did the efficacy of all day sleeps at the very beginning of the week, and these sleep characteristics persisted throughout the week. In contrast, in the group which took a placebo sleep was shorter and less efficacious at the beginning but improved towards the end of the week. There was no negative effect of hypnotics on the shiftworker's mood after waking up. To an extent, the hypnotics proved to be useful for periodical pharmacological improvement of the length and efficacy of day sleep after night work in the slowly rotating shift system.

Key terms:
hypnotic agents, shiftwork, sleep characteristics, slowly rotating shift system

Shiftwork has been used in certain branches of industry such as mining for a long time. Today, in the era of modern technology, a large number of people in

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various industries and enterprises are involved in shiftwork. Besides positive effects (better use of capacities, a greater number of workers employed) shiftwork induces numerous biological, social and even medical problems. It not only disturbs physiological functions (meal pattern, sleep schedule), but can also affect the worker's social habits (family and other social relationships, recreational activities) and become the cause of health complaints (1, 2). Major negative effects that are brought about by shiftwork because of work transfer to night hours and of sleep to daytime, are reduced capacity for and safety at work, and disturbed sleep.

Shiftworkers complain of sleep disturbances: inadequate length and quality of sleep. It could be expected that after tiring night work, workers would be able to fall asleep easily and that their sleep would be long-lasting and uninterrupted. However, a very high percentage of workers have difficulties in falling asleep, tend to wake up during sleep and in the end wake up too early (2, 3). Investigations have shown that the sleep which begins in the morning, when most shiftworkers go to bed after working on the night shift, usually lasts four to six hours. In contrast, workers on the day shift get a normal night sleep of between seven and nine hours (3, 4).

It may be expected that day sleep will take shorter than necessary because of the interference of disturbing external factors, especially the noise made by children and that originating in street traffic. However, the investigations where disturbing external factors were controlled and the subjects' sleeping conditions were optimal, demonstrated that day sleep was nevertheless curtailed (5).

According to the results of several investigations the main reason for a shorter sleep in the daytime lies in a discord between the sleep-wakefulness rhythm, which is imposed by shiftwork, and the endogenous circadian (about 24-hour-) sleep-wakefulness rhythm (5). The latter, together with deep body temperature, is one of the basic circadian rhythms. In normal living conditions, with work taking place during the day, the phases of that rhythm in an adult person generally correspond to the two phases of the light-dark cycle. In shiftwork the worker is forced to keep shifting the phases of the sleep-wakefulness rhythm. This is a great burden to the body because the phases of the rhythm, imposed by shiftwork, are at variance with the phases of the endogenous circadian sleep-wakefulness rhythm, as well as with those of the circadian rhythms of the other body functions. In addition, the phases of the imposed sleep-wakefulness rhythm fail to agree with the physical rhythms and living patterns of most people who do not work in shifts.

Some persons appear to be able to cope with disturbances in the quality and quantity of sleep well. Others find it hard, others still are known to have quit shiftwork for that reason. A certain percentage of workers try to find a solution to sleeping problems by taking a hypnotic agent. Reportedly, eleven per cent of shiftworkers often take sleeping pills or do it occasionally (4). The aim of this study was to find out how the sleep characteristics following night shift work were influenced by a hypnotic agent with a relatively short elimination time (zopiclone) as compared to that with a relatively long elimination time (nitrazepam). To examine the effects of hypnotics over a period of several days the study was conducted among workers working in a slowly rotating shift system.

SUBJECTS AND METHODS

A group of 32 workers employed in a security company were recruited to the study as subjects. Three workers had left the company before the study was over. The remaining 29 workers were aged between 24 and 58 years and had been engaged in shiftwork in the company from 0.4 to 22.8 years. They reported to have had night-work related insomnia for an average of 5.4 years (SD 3.3 years). The subjects were placed in three groups which did not differ from one another in respect to age, experience of shiftwork and duration of insomnia. The first group (n=9) received capsules with 7.5 mg zopiclone (a tranquilizer and hypnotic from the cyclopyrolone family with a relatively short elimination time), the second (n=11) was given capsules containing 5 mg nitrazepam (a benzodiazepine preparation that is characterized by a relatively slow elimination from the body), and the third group (n=9) was given placebo capsules. The subjects took capsules after work on the night shift before main sleep.

The study spread over three cycles of seven successive night shifts each. The cycles started on a Monday and ended on a Sunday. Between two cycles of night shifts there were three intervening weeks: a week of rest days, a week of morning shifts and a week of afternoon shifts. The working hours on the night shift were from 22.00 to 06.00 hours.

Throughout each study week the subjects kept detailed sleep diaries, especially constructed for the purpose, in which qualitative and quantitative changes of main sleep and of all sleeps of 30 minutes or more were entered on awakening.

The following main sleep characteristics were analysed: time in bed, length of sleep episode (from the sleep beginning to final waking up), total sleep time (duration of the sleep episode minus duration of all awakenings during sleep), sleep efficacy (the percentage of total sleep length in the time in bed), sleep latency, sleep quality rated on a visual-analogue scale by means of descriptions "Worst sleep for a long time" or "Best sleep for a long time" on the extreme poles, the number of awakenings during sleep and the proportion of spontaneous final awakenings.

For all day sleeps (including main sleep) the following characteristics were analysed: time in bed, length of sleep episode, total sleep time, sleep efficacy and the number of sleeps during the day.

The subjects rated their moods half an hour after having woken up by means of an eighteen item list of bipolar moods and the associated visual-analogue scales (6). Eleven moods made the wakefulness scale and seven pertained to the tranquillity scale.

The results were analysed by means of the three factor analysis of variance which made it possible to test the significance of the effects of three different agents, seven days of sleep after night shift and three study weeks, as well as of their interactions.

RESULTS

Table 1 shows the results of testing the significance of differences in sleep and mood characteristics between the groups on zopiclone, nitrazepam and placebo, day of week and week of study, as well as their interactions.

Table 1 *Results of analysis of variance (F-ratios, degrees of freedom and P) of sleep characteristics and moods in three groups of shiftworkers who were given zopiclone, nitrazepam and placebo seven days in a week, for three study weeks*

	T	D	T × D	W	T × W	D × W	T × D × W
Degrees of freedom	**2/26**	**6/156**	**12/156**	**2/52**	**4/52**	**12/312**	**24/312**
A. MAIN SLEEP							
Time in bed	0.49	2.14	1.56	2.49	0.52	1.20	0.83
Sleep episode	0.77	2.26*	1.76	4.23*	0.77	1.26	0.74
Total sleep time	0.85	2.29*	1.89*	4.97*	0.71	1.40	0.76
Sleep efficacy	1.86	1.79	2.09*	11.57***	0.94	0.88	0.71
Sleep latency	1.24	1.48	1.18	7.30**	0.65	1.01	0.90
Sleep quality rating	0.92	2.50*	1.16	1.02	1.24	0.98	0.80
Number of awakenings	0.55	0.85	0.66	0.52	1.26	1.41	0.83
Percentage of spontaneous final waking up	1.92	1.98	0.63	1.76	0.79	0.86	1.29
Alertness after waking up	0.11	0.85	1.08	0.05	0.32	0.83	1.10
Tranquillity after waking up	0.04	1.56	1.26	0.29	0.43	1.16	0.77
B. ALL SLEEPS							
Time in bed	1.68	44.99***	0.76	2.05	1.51	1.89	1.07
Sleep episode	2.33	48.05***	0.94	4.33*	1.81	1.57	1.10
Total sleep time	2.74	47.33***	0.86	5.65*	1.62	1.69	1.12
Sleep efficacy	1.39	4.19*	1.86*	11.94***	1.05	0.90	0.83
Number of sleeps	0.30	21.67***	1.15	0.79	0.38	2.00*	0.99

T groups treated; D day of week; W week of study
* P<0.05; ** P<0.01; *** P<0.001

In groups which took hypnotics most differences indicated an improvement of the sleep characteristics. The improvement was greatest in the group that was given zopiclone, but the differences between the groups were not statistically significant either for a single sleep characteristic analysed or for the after sleep mood.

However, significant interactions were determined between the groups (i.e. treatments) and days of week for the total sleep time ($F(12/156) = 1.89$; $P<0.05$) and the efficacy of the main sleep ($F(12/156) = 2.09$; $P<0.05$) as well as for the efficacy of all sleeps during the day ($F(12/156) = 1.86$; $P<0.05$). Figures 1–3 show modified sleep characteristics during the week of night work for groups on different treatments.

As is evident from the figures, at the very beginning of the week, the groups that used hypnotics had a longer total length of main sleep and better efficacy

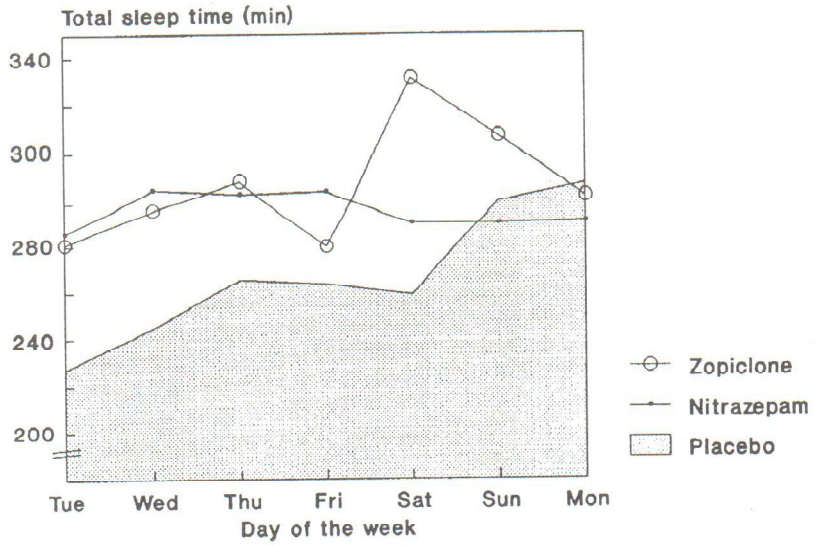

Figure 1 *Changes in total sleep time of the main sleep during a week of night work in groups of workers on zopiclone, nitrazepam and placebo*

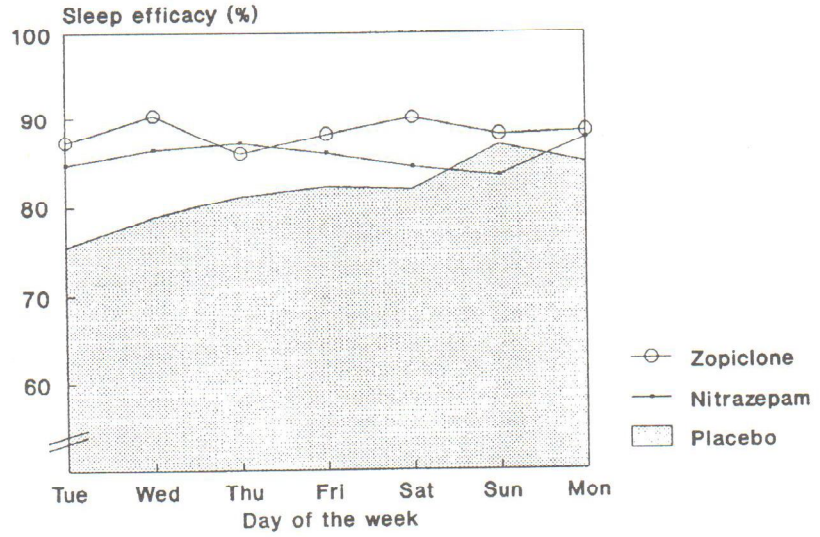

Figure 2 *Changes in efficacy of main sleep during a week of night work in groups of workers on zopiclone, nitrazepam and placebo*

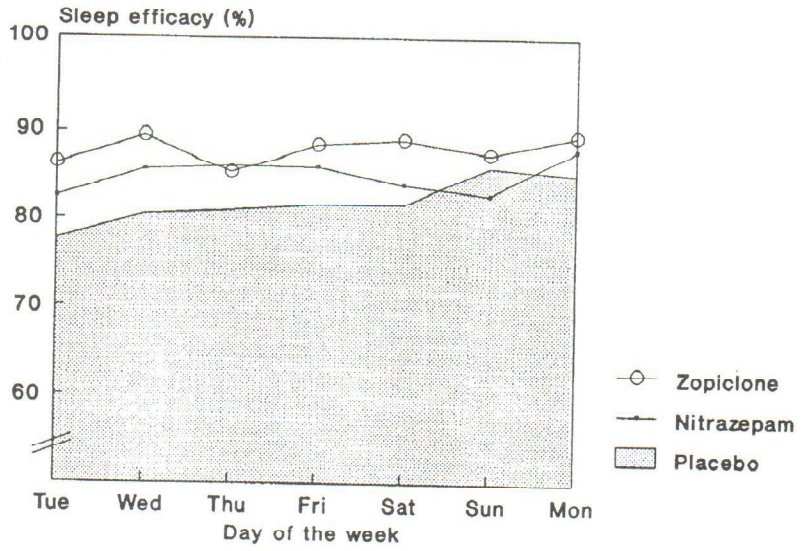

Figure 3 *Changes in efficacy of all day sleeps during a week of night work in groups of workers on zopiclone, nitrazepam and placebo*

of main sleep and all sleeps during the day than the control group. Their sleep did not change throughout the week. On the other hand, the group that took a placebo had a shorter lasting main sleep and poorer efficacy of main sleep and all day sleeps at the beginning of the week. In that group, however, during the week of night shift work, sleep characteristics improved so that by the end of the week the sleep length and efficacy were similar to those of the groups on nitrazepam and zopiclone. For the group which did not take sleeping pills this could be taken as sign of a certain adjustment to night work.

At the same time, there was no significant interaction between the groups (i.e. treatments) and day of week as concerns the feeling of wakefulness and tranquility after sleep. This was taken to indicate that the hypnotics used did not produce a prolonged negative effect on the workers' mood after final waking up.

DISCUSSION AND CONCLUSIONS

Before prescribing a hypnotic agent as a means of improving sleep it is essential to establish the factors responsible for sleep disturbances. It is equally important to consider the possibility of eliminating the cause of insomnia and of administering

a non-pharmacological means to improve sleep. This applies to shiftworkers' insomnia too (7, 8). There is general agreement that hypnotics are to be given only in cases of transient insomnia, because the treatment with hypnotics is symptomatic and the good effects usually disappear in a few weeks' time. The choice of hypnotic depends on the type of insomnia. If circadian rhythms are disturbed, as is the case with shiftworkers and passengers flying over several time zones, hypnotics with short to medium-long effects are recommended, as are administered to patients in hospital, for instance on the night before a surgical operation (9).

In this investigation we examined how two hypnotics with different elimination times affected shiftworkers' day sleep after the night shift. One was zopiclone, whose elimination time is reported to be five hours (range 4-7 hours) in young persons and eight hours (range 7-10 hours) in older persons. The other was nitrazepam with respective elimination times of 26 hours (range 19-31 hours) and 38 hours (range 26-64 hours). Our results show that in the case of disturbed sleep after the night shift the use of both hypnotics could have a good effect on the duration and efficacy of sleep, but did not prove to have significant effects on the time of falling asleep, the quality of sleep and the frequency of awakenings during sleep. Taking into account that differences in the quantitative sleep characteristics between the groups which were given hypnotics and the group on placebo were especially pronounced on the first days of work on the night shift, the use of hypnotics on these very days could be recommended for a slowly rotating shift system. In a rapidly rotating shift system there is a possibility of making up for shorter sleep after the night shift by prolonging sleep on subsequent days (10, 11), so it is questionable whether the use of hypnotics in such system would make any sense.

It is known that the use of hypnotics may bring about a number of adverse effects and that there are great interindividual differences concerning those effects (9, 12). Among possible negative effects induced by hypnotic agents is a residual effect which manifests itself by impairing mood, alertness and performance efficiency, may lead to increased risk of accident and may interfere with normal night sleep. In addition, hypnotics can induce temporary amnesia, especially in the elderly. Their prolonged use threatens to become a habit, or can even turn into "rebound insomnia" i.e. insomnia that is more pronounced than before treatment with hypnotics. The use of hypnotics could develop into an addiction. A negative action of hypnotics may stem from interaction with other pharmacological preparations if those are taken at the same time. Most of these negative effects come as a result of a long-lasting use of hypnotics. In this study hypnotics were used over a period of three weeks, each of which was separated by three weeks of non-use. In those circumstances there was no immediate mood impairment after waking up, nor were any changes noticed, during a week or three weeks, that could point to a negative effect of hypnotics.

To conclude, the hypnotics used in this study were found to be useful, to a certain extent, for periodical pharmacological improvement of the length and efficacy of day sleep after work on the night shift.

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Sažetak

UČINCI HIPNOTIKA NA DNEVNO SPAVANJE SMJENSKIH RADNIKA

Smjenski radnici koji rade noću pomiču svoje spavanje u ono razdoblje dana koje je nepovoljno za spavanje s obzirom na unutrašnji cirkadijurni ritam budnost – spavanje, cirkadijurne ritmove ostalih funkcija u organizmu te ritmove u okolini. Kao posljedica toga kod određenog broja radnika dolazi do poremećaja spavanja. Cilj ovog rada bio je ispitati djelovanje dvaju hipnotika s različitim vremenom poluraspada, zopiklona i nitrazepama, na poremećeno spavanje nakon rada u noćnoj smjeni. U tu svrhu tri skupine radnika uzimale su kapsule zopiklona, nitrazepama, odnosno placeba tijekom tjedan dana rada u noćnoj smjeni u tri navrata, tako da je svaki tjedan uzimanja kapsula

bio odijeljen od sljedećeg s tri tjedna pauze. U ovakvim uvjetima utvrđen je različit oblik promjene nekih karakteristika spavanja tijekom tjedan dana rada u noćnoj smjeni u skupinama koje su uzimale hipnotike u odnosu na skupinu koja je uzimala placebo. U skupinama koje su uzimale hipnotike došlo je do poboljšanja ukupnog trajanja i efikasnosti glavnog spavanja, kao i efikasnosti svih spavanja u danu odmah na početku tjedna, a spavanje je ostalo ovakvih karakteristika sve do kraja tjedna. Za razliku od toga, u skupini koja je uzimala placebo spavanje je na početku bilo kraće i manje efikasno, ali se do kraja tjedna poboljšalo. Istodobno nije došlo do negativnog djelovanja hipnotika na raspoloženje nakon buđenja. Upotrijebljeni hipnotici pokazali su se u određenoj mjeri korisnim za povremeno farmakološko poboljšanje trajanja i efikasnosti dnevnog spavanja nakon rada u noćnoj smjeni u sustavu sporotirajućih smjena.

Ključne riječi:
hipnotici, karakteristike spavanja, smjenski rad, sustav sporotirajućih smjena

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