The Effects of Tandospirone and Diazepam on Actual Driving Performance

Tsutomu Asoh*, Mitsusaka Uchiumi** and Mitsukuni Murasaki**

* Japan Automobile Research Institute, Inc., 2530 Karima, Tsukuba, Ibaraki 305, Japan
** Department of Psychiatry, Kitasato University School of Medicine, 2-1-1 Asamizodai, Sagamihara, 228 Japan

ABSTRACT

The acute effects of tandospirone, a new anxiolytic agent, on actual driving performance were investigated in 12 healthy male subjects according to a double blind, cross-over design. Drug treatments were tandospirone 30mg, diazepam 5mg and placebo. The time of administration was 30 minutes prior to beginning of the driving test. Subjects were instructed to drive continuously for two hours at a speed of 60 kilometers an hour. Eye movement, steering wheel operation, speed variability and the Stanford Sleepiness Scale were continuously measured during driving.

Diazepam significantly increased the frequency of long closure duration blinks and large steering reversals, the variability of driving speed and the Stanford Sleepiness Scale in comparison with tandospirone and placebo. These findings suggest a dangerous tendency to fall asleep during driving for the drivers administered diazepam. On the other hand, on all measurement items there was no difference between tandospirone and placebo. So it is concluded that tandospirone does not indicate the central nervous system depressant action and does not impair driving performance.

INTRODUCTION

Anxiolytic drugs such as diazepam are in frequent use by persons carrying out skilled tasks such as driving. In addition, there is some evidence that therapeutic dose levels of such drugs can produce impairments in performance related to driving and in driving itself. Thus, it is warned in a prescription for conventional anxiolytic drugs that “This drug may cause drowsiness. Pay great attention to workers receiving this drug not to be engaged in risky operations of machines including car driving”. However, it is thought that a large number of peoples actually engaged in car driving under the influence of drugs.

Skegg et al. (1979) found, when he compared prescriptions for the previous 3 months in fatal car accident victims to controls, that those involved in the accidents were 4.9 times more likely to have obtained a prescription for minor tranquilizer such as a benzodiazepine.

Tandospirone is a new non-benzodiazepine anxiolytic, that is a highly potent and selective 5HT1A receptor agonist, and have a less the central nervous system adverse reaction than benzodiazepines. In this study, we have continuously monitored drivers’ physiological
reactions and driving performance during driving on the road, and compared the effects of tandospirone on driving with those of a conventional benzodiazepine and placebo.

METHODS

Twelve healthy male subjects participated in the experiment. They were Japanese volunteers, between the ages of 19 and 43, usually driving a vehicle. The test vehicle was a four-door sedan equipped with an additional steering wheel and a foot break pedal at the passenger’s side taking an emergency case in account. The experimenter seated on the passenger’s side throughout driving. The driving tests were carried out on a two-lane circular paved road in the Japan Automobile Research Institute, which was 5.5m wide, 7km one round and had appropriate numbers of curves and traffic signs.

The drug treatments were tandospirone 30mg, diazepam 5mg and placebo. The drug administration was made once a day according to a randomized double blind cross-over design. The drug was administered at 14:30. Taking the carry-over effect of each test drug into consideration, an interval of more than one week was taken between tests and one subject was scheduled to complete all three tests within one month.

During driving, electrooculogram (EOG), steering wheel movement and driving speed were continuously recorded by a data recorder. Every round of driving, the subject was asked to evaluate the subjective sleepiness by the Stanford Sleepiness Scale (SSS).

The driving test was started at 15:00 after the drug administration. The subjects were instructed to drive continuously for 2 hours at a constant speed of about 60 Km/h. When the subjects fell into a state of dozing at the wheel and the experimenter on the passenger’s seat sensed danger to continue driving, the test was not continued immediately. The subjects were not allowed to listen to the radio during driving.

All data were analyzed by the cross-over analysis of variance. When the hypothesis of uniformity among three test drugs was abandoned, the statistical significance of difference was tested for every pair of drugs by Tukey’s multiple comparison method.

RESULTS

Two hours continuous driving was completed by 10 subjects in the placebo condition and by 12 subjects in the tandospirone condition. On the other hand, in the diazepam condition, only 7 subjects completed the driving, and remaining 5 subjects were judged by the examiner to be incapable to continue driving and instructed to stop. The mean time of continuous driving was not significantly different between placebo and tandospirone, while the value for diazepam was significantly shorter than tandospirone (p<0.05) (Figure 1).

The frequency of long closure duration blinks, which were longer than 0.3s in duration, is shown in Figure 2. The mean frequency was 1.81/min for placebo, 0.85/min for tandospirone and 4.16/min for diazepam. The value for tandospirone was significantly smaller than placebo (p<0.01) and diazepam (p<0.05).
Figure 1
Mean Number of the Length of Driving Time in Each Drug Condition

Figure 2
Mean Number of Long Closure Duration Blinks per Minute in Each Drug Condition

Figure 3 shows the frequency of coarse (more than 10 degrees) steering reversals. The mean frequency was 0.65/min for placebo and 0.46/min for tandospirone; there was no significant difference between these values. On the other hand, the value for diazepam was greater than placebo and tandospirone.
Results of the SSS score on driving are shown in Figure 4. The mean SSS score was 3.58 for placebo, 4.04 for tandospirone and 5.04 for diazepam. The value for tandospirone was significantly smaller than placebo ($p<0.05$) and diazepam ($p<0.01$).

**Figure 3**
Mean Number of Coarse Steering Reversals per Minute in Each Drug Condition

![Chart showing mean number of coarse steering reversals per minute for placebo, tandospirone, and diazepam.](chart1)

**Figure 4**
Mean Score of the Stanford Sleepiness Scale in Each Drug Condition

![Chart showing mean SSS scores for placebo, tandospirone, and diazepam.](chart2)
Decreasing ratio of the critical flicker fusion frequency (CFF) after driving are shown in Figure 5. The CFF scores were 0.17 for placebo, -1.24 for tandospirone and -4.77 for diazepam. There was no significant difference between tandospirone and placebo, while the value for diazepam was significantly smaller than placebo (p<0.01) and tandospirone (p<0.05).

**DISCUSSION**

Since the sense of danger, motivation etc. in the simulator or laboratory studies are largely different from those in actual driving on the road, it has been questioned to what extent the parameters obtained by simulation or laboratory experiments are related to actual driving. Thus, O’Hanlon et al. (1980) have pointed out that a driving test on the road is the most suitable method to evaluate drug effects on driving.

If the effect of a test drug is not strong enough, subject’s short-term performances are not affected by the drug in many cases because of an elevated mental tension in the subject facing the test. From this point of view, we investigated the effect of tandospirone on actual driving by means of the dozing-inducing, monotonous and continuous driving test on the road.

In the present study, the blinking waves induced by vertical eye movements were focused. The degree of sleepiness on driving was evaluated from sleepiness-induced changes in blinking waves. With the progression of sleepiness, the blinking frequency was increased in order to overcome sleepiness, and the arousal level was not largely lowered at this stage. When the sleepiness advanced further, the blinking frequency decreased and long closure duration blinks appeared in turn. Then, long closure duration blinks increased in number and driving became impossible to continue. Finally, eye movements almost disappeared,
watching the front could not give any visual information and the driver fell into a state of driving asleep. In the diazepam condition, the frequency of long closure duration blinks was significantly higher as compared with the tandospirone condition. This indicates that sleepiness on driving was more intense in the diazepam condition than in two other conditions. On the other hand, the tandospirone is not thought to cause central sedation-induced sleepiness during driving.

A high arousal level allowed the driver to control the vehicle along the lane mark on the road by fine operation of the steering wheel, while a low arousal level makes the driver not to perform such an accurate tracking but to control the vehicle by coarse operation of the steering wheel. The frequency of coarse steering operation in the diazepam condition was greater than that in the placebo and the tandospirone conditions, suggesting that diazepam impaired the driving performance.

The score by SSS indicated that all drop-out cases showed SSS scores of 6 or 7, indicating claiming of fairly strong sleepiness. In the diazepam condition, many subjects claimed sleepiness before the driving test and their SSS scores during driving were significantly higher than the tandospirone condition. Thus, tandospirone is not thought to have the side effect causing drowsiness on driving.

From these results, it may be concluded that diazepam induced sleepiness on driving and impaired the driving performance, probably because its central depressant action is stronger than driving-induced mental tension. On the other hand, the tandospirone showed no such effects on driving, hence the drivers received the tandospirone could drive as if they received the placebo. This indicates that there is no risk for tandospirone to cause the depression of the central nervous system.

REFERENCES
