Is the Clinical Test for Impairment a Reliable Tool in Evaluating Impairment from Zopiclone and Ethanol?

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Abstract

Background
When the police stop a driver on the suspicion of drugged driving, it is essential to have the correct tools to help evaluate whether the apprehended driver is impaired or not. In Norway, a comprehensive clinical test for impairment (CTI) is performed by a physician, as a routine procedure, shortly after apprehension. Former research has indicated that such testing is suited for detecting alcohol impairment, but less sensitive for detecting impairment in driving caused by other drugs.

Aim
To compare CTI results with experimental laboratory test results for zopiclone, a commonly used benzodiazepine-like drug, with alcohol as verum.

Methods
A double-blind placebo-controlled randomized trial on 16 healthy male volunteers was performed. The volunteers each attended the research unit in 4 sessions, receiving placebo, 5 mg of zopiclone, 10 mg of zopiclone, or 50 g of ethanol. Blood samples were collected, and psychomotor performance was measured by computerized tests and by selected subtests from the Norwegian CTI.

Results
The performance on the CTI and the computerized psychomotor tests show both a clear concentration-dependant deterioration after consumption of an active substance (zopiclone or ethanol). Seven hours after intake, the performance was again comparable to baseline.

Discussion and Conclusions
The results show that the CTI may be of value in evaluating whether an individual is impaired or not, for zopiclone as well as for alcohol, with a sensitivity similar to that of computerized psychomotor tests.

Introduction
The negative effects of alcohol on driving performance are well documented. Several studies have shown a blood alcohol concentration (BAC)-related increasing risk of traffic accidents (Blomberg, Peck, Moskowitz, Burns, & Fiorentino, 2009) and deteriorating performance in experimental studies (Schnabel, Hargutt, & Krüger, 2010). The detection of drunk driving, in practice, is well established by the combined use of various standardized field sobriety tests (SFST) and breath alcohol screening.
During the last few decades, driving under the influence of non-alcoholic drugs has received considerable attention and yielded increasing concern (Gjerde, Normann, Christophersen, Samuelsen, & Morland, 2011; Schulze H, Schumacher M, Urmeew R, & Auerbach K, 2012).

As rapid quantitative saliva tests, for all of the non-alcoholic drugs of interest, are not yet available for screening cases of suspected drugged driving, it is important to have a systematic set of observations available to help indicate impairment. This again becomes important both for detecting cases which should be subjected to further examination, and for documenting impairment with the possible subsequent handling of the cases in court. For these purposes, different approaches are presently being applied in different countries, such as the SFST and various other clinical tests of impairment (CTIs).

There is no awareness of any systematic comparison of the SFST or any CTI with the psychomotor performance on the three core levels of traffic-relevant behavior (automotive behavior, level 1; control behavior, level 2; and executive planning behavior, level 3) considered of importance to safe driving (Walsh, Verstraete, Huestis, & Morland, 2008). A systematic evaluation of the psychomotor performance, with reference to the recommended three core levels, cannot be performed roadside, as it has to be done in a laboratory setting and requires special equipment, in contrast to the SFST and the CTIs, which can easily be performed in an actual traffic-related setting.

One of the most frequently detected non-alcoholic drugs among Norwegian drivers is zopiclone (Gjerde et al., 2008), and the risk of being involved in a traffic accident involving person injury is increased among patients being prescribed zopiclone (Gustavsen et al., 2008). Zopiclone may represent other similar drugs acting through the GABA-receptor, and has also been shown to be a drug inducing impairment in an on-the-road driving test (Verster, Spence, Shahid, Pandi-Perumal, & Roth, 2011).

A controlled study was performed on how the outcome of a simple field sobriety test compared to the outcome of psychomotor testing on the three core levels in subjects given one of two doses of zopiclone, ethanol or placebo, in a double-blind crossover design.

**Materials and Methods**

**Study procedure**

A double-blind placebo-controlled randomized trial with a crossover design was performed, including 16 healthy male volunteers. The volunteers attended a research unit for four study days, and received in a randomized order either placebo, 5 mg of zopiclone, 10 mg of zopiclone, or 50 g of ethanol. Blood samples were collected on the study day and analyzed for zopiclone and ethanol. Psychomotor performance was measured by a simplified CTI and by three licensed computerized tests. The study procedure is described in detail elsewhere (Gustavsen, Hjelmeland, Bernard, & Morland, 2011).

The blood drug concentrations were grouped into 4 drug concentration quartiles, based upon the measured blood drug concentrations at 1, 3.5, and 6.5 hours after intake (Figure 1). Pearson’s Chi-square test was used to calculate differences in the shares of impaired observations between the different concentration levels, using the lowest quartile as a reference.
Impairment measured by CTI
A simplified version of the Norwegian CTI was performed at 1.5 and 7 hours after intake of the study medication (Figure 1): Gait on line, turning on line, finger-to-finger test, finger-to-nose test, and Romberg’s test (standing on one foot for at least 5 seconds, with arms stretched out and eyes closed). Based upon the subtest performance and an “overall judgment”, the raters concluded on the subjects being either “impaired” or “not impaired”, which was used as a basis for the calculations in this manuscript.

Impairment measured by computerized tests
The computerized tests, including 15 test components, were performed at baseline, and at 1, 3.5, and 6.5 hours after study medication intake (Figure 1). Any test performance worse than the individual’s baseline performance was defined as “impaired”, and vice versa (Gustavsen, Hjelmeland, Bernard, & Morland, 2012).

Figure 1 Study day flowchart showing the procedures included in the present paper: Intake of study medication (#); arrows indicating blood sampling; black boxes indicating the time intervals for the psychomotor performance as measured by the computerized tests; and stars indicating the CTIs.

Results and discussion
Figure 2 The percentages of impaired individuals as judged by the CTI, and the percentages of impaired observations at the three levels of behavior, both related to blood drug concentrations of zopiclone and to BACs. The concentration levels are divided into quartiles, and for each quartile the percentages of impaired subjects as judged by the CTI, and the percentages of impaired observations at the three levels of behavior, are presented. The number of observations in each quartile is given in each bar. Significant differences are calculated with Pearson’s Chi-square test using the lowest quartile as a reference, and are marked by asterisks in the figure: *p<0.05, **p<0.01, ***p<0.001.
For the impairment assessed by the CTI, a positive relationship was found for the blood zopiclone concentrations, but not for the BACs. There was, however, twice as many zopiclone observations compared to that of ethanol, which may explain a stronger dose-dependent correlation for zopiclone.

The results indicate that the CTI is a more reliable tool for revealing zopiclone impairment than ethanol impairment. This stands in contrast to a former study, were a Finnish clinical test for impairment was found to be more sensitive to the intake of 0.8 g/kg of alcohol than that of 7.5 mg of zopiclone (Kuitunen, Mattila, & Seppala, 1990; Kuitunen, Mattila, Seppala, Aranko, & Mattila, 1990). In the previous study, the sensitivity for evaluating dosages, but not for evaluating concentrations, was tested.

For the impairment assessed by the computerized tests, a positive concentration relationship was found for impaired observations for level 1 and level 2, but not for level 3, for both zopiclone and ethanol. Tests for all three levels of behavior are recommended when investigating traffic-relevant impairment. The revealed impairment in automotive- and control behavior but not in executive planning was somewhat surprising. However, it is likely that at higher concentration levels, impairment in executive planning would also have been detected.

The results indicate that the performance of the CTI may be a valuable aid for discriminating between blood zopiclone concentration levels above and below 20 µg/L, and BACs above and below 0.05%. The previous concentration level for zopiclone corresponds approximately to the maximal concentration level achieved within 6 - 10 hours after intake of a regular sleeping dosage of 7.5 mg of zopiclone.

Reference List


