BENZODIAZEPINE AND TRICYCLIC ANTIDEPRESSANT USE AND MOTOR VEHICLE CRASH RISK AMONG OLDER DRIVERS

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The psychomotor and autonomic effects of benzodiazepines (BZ) and tricyclic and related antidepressants (TCA) have led to the concern that these medications can impair driving. Older drivers may be particularly affected because of their increased prevalence of medication use and susceptibility to adverse medication effects. To determine whether BZ and TCA were associated with increased rates of injurious motor vehicle crashes among older drivers, we conducted a retrospective cohort study among Medicaid enrollees 65 to 84 years of age who had a valid driver's license and who met other criteria designed to exclude persons unlikely to be drivers and to assure availability of necessary study data. Data were obtained from computerized files from the Tennessee Medicaid program, driver's license files, and police reports of injurious crashes. There were 12,262 persons in the study cohort with 38,701 person-years of followup and involvement in 495 injurious crashes. Adjusted risk of crash involvement was calculated with Poisson regression medels that controlled for demographic characteristics and use of medical care as an indicator of health status. The relative risk (95% CI) of injurious crash involvement for current users of BZ was 1.5 (1.2–1.9) and that for TCA was 2.2 (1.3–3.5). For these drugs, relative risk increased with dose and was substantial for high doses: 2.4 (1.3–4.4) for $\geq$ 20 mg diazepam and 5.5 (2.6–11.6) for $\geq$ 125 mg amitriptyline. Analysis of Data for the crash-involved drivers suggested that these findings were not due to confounding by alcohol use or driving frequency. These data underscore the need to prescribe psychoactive drugs cautiously for older drivers.

EFFECTS OR ALPIDEM, LORAZEPAM AND PLACEBO ON ACTUAL DRIVING PERFORMANCE OF ANXIOUS PATIENTS

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This study compared the effects of a benzodiazepine-like anxiolytic (alpidem) with those of a benzodiazepine (lorazepam) and placebo on anxious patients' abilities to perform skilled tasks, particularly car driving, during the first week of therapy. Volunteers suffering from either general anxiety disorder or adjustment disorder with anxious mood (DSM III-R) participated in a 3-leg, double blind, parallel group design with an 8-day treatment period, preceded and followed by single-blind placebo run-in (7 days) and washout (6 days). Entry into the treatment period was contingent upon the patients scoring higher than 17 on the 14-item Hamilton Anxiety Rating Scale (HARS), and less than 20 on the Montgomery Asberg Depression Rating Scale. Patients were randomly assigned to three parallel groups. The groups respective treatments were alpidem 50 mg b.i.d., lorazepam 2 mg b.i.d. and placebo b.i.d. A total of 56 volunteers either completed treatment or dropped out after providing usable data. Patients' performance in a standardized actual driving test as well as in a battery of psychometric tests (Critical Flicker/Fusion, Choice Reaction Time, Word Learning, Spatial Memory, Tracking and Divided Attention) was measured prior to treatment (baseline) and after 1 and 8 days of treatment. Efficacy was assessed before treatment and at the end of each period using the HARS and the Clinical Global Impression scales. Patients recorded their anxiety using the Zung Self-Rating Scale and sleep quality/duration on a daily basis. Baseline performance levels were essentially normal and comparable between groups. Lorazepam profoundly impaired performance in all tests, including driving, on the 1st day of treatment. Most performance changes diminished, but were still highly significant on the 8th day. Patients in this group were aware of their driving disability on the 1st day, but thought erroneously that they had recovered by the 8th day. Alpidem significantly impaired driving performance on both test days though far less than lorazepam. The former's impairing effects were also significant in psychometric tests that primarily measure perceptual/motor coordination, but in none of the tests measuring memory functions. Anxiety symptoms diminished significantly and similarly in all groups during treatment but increased significantly in the lorazepam group during washout. Side effects during treatment and withdrawal phenomena during washout were markedly greater in the lorazepam group than the others, which were similar.

Patients drove normally before treatment. Lorazepam 2 mg b.i.d. seriously impaired patients driving performance for a week after the beginning of therapy; with their knowledge at the beginning but without it at the end. Alpidem 50 mg b.i.d. also impaired patients driving but to a relatively moderate degree.

A DOUBLE-BLIND STUDY OF THE THERAPEUTIC EFFECTS OF CHRONICALLY ADMINISTERED BUSPIRONE AND DIAZEPAM AND THEIR EFFECTS ON ACTUAL DRIVING PERFORMANCE IN OUTPATIENTS WITH GENERALIZED ANXIETY DISORDER

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Two groups of 12 outpatients each (6 men and 6 women) with generalized anxiety disorder, diagnosed according to DSM-IIIR criteria, participated in this study. Each patient was treated single-blind with placebo during the first 7 days *(baseline)*, followed by double-blind drug treatment for 4 consecutive weeks *(active)* and ending again within 7 days single-blind placebo treatment *(washout)*. One group received buspirone 5 mg t.i.d. during the first week, and thereafter 10 mg in the morning followed by separate 5 mg doses in the afternoon and evening. The other group received diazepam 5 mg t.i.d. over all four weeks. Clinical assessments and driving performance measurements were made on the evening of the seventh day of each treatment week. These included the Hamilton Anxiety Scale and the Symptom Check List (90 items), followed by an on-the-road driving test which started 1.5 hours after the last drug or placebo intake. The test consisted of operating an instrumented vehicle over a 100 km highway circuit while attempting to maintain a constant speed and a steady lateral position within the right traffic lane. Two patients in the diazepam group were unable to complete their test after the first and second treatment week, respectively, because of serious performance impairment. The results indicate that buspirone and diazepam were equally effective in reducing overall anxiety symptoms. Buspirone also reduced concomitant depressive symptoms and symptoms of interpersonal sensitivity and anger-hostility. Diazepam was slightly more effective in reducing somatic symptoms and relieving sleep disturbances. Moreover, abrupt discontinuation of diazepam resulted in a relapse of psychic anxiety symptoms and a partial relapse of somatic anxiety symptoms to the placebo-baseline level. Buspirone had no effects on driving performance. In contrast, diazepam caused serious impairment during the first three weeks of treatment. Impairment was still apparent but no longer significant in the fourth week and the group's performance recovered to baseline at the end of placebo-washout.