

Neurocognitive performance and self-reported sedation following administration of lorazepam

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Introduction

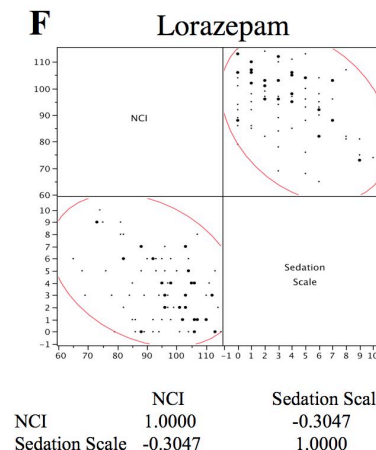
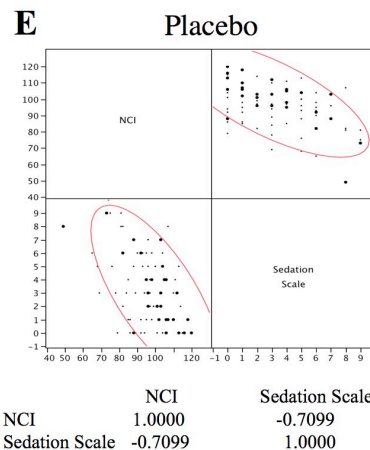
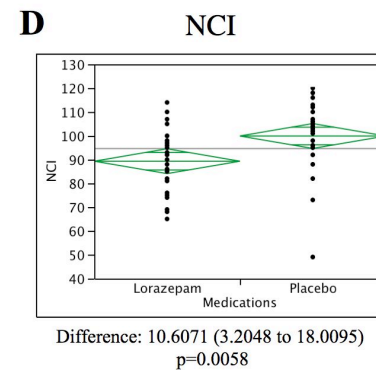
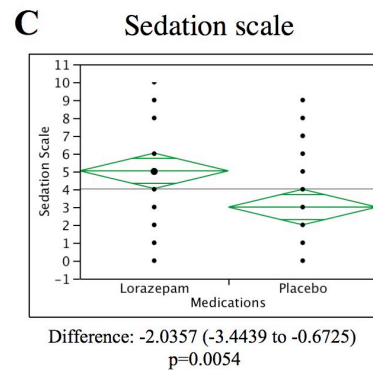
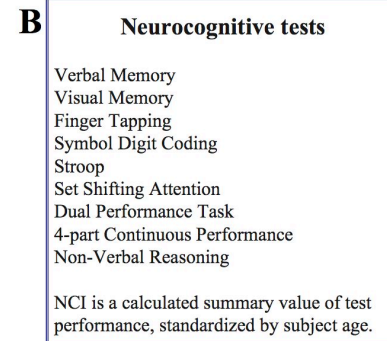
Lorazepam, like other benzodiazepines, is frequently used to treat anxiety disorders, agitation, and insomnia. Cognitive impairment is a commonly reported adverse effect of lorazepam use (1, 2, 3). However, optimal and effective mechanisms for measuring the effects of lorazepam on cognition have not been established. In this two-period, cross-over study, subjects were given a battery of computerized neurocognitive tests at baseline (4). They were subsequently administered a one-time dose of lorazepam 2mg orally or placebo. At all study visits subjects were asked to rank their sedation level on a 0-10 linear scale (Fig. A) and were tested with the computerized battery (Fig. B). Test performance with lorazepam was compared to placebo using a summary score, Neurocognitive Index (NCI; mean=100, std. dev=15).

Methods

Study design: Randomized, double-blind, cross-over design, placebo controlled

Subject population: 28 healthy volunteers. Exclusion criteria included 1) prior or current drug or alcohol abuse, 2) use of concomitant medications that are known to interact with lorazepam, 3) IQ ≤ 70 , 4) Mini Mental Status Exam ≤ 26 , 5) Hopkins Verbal Learning Test < 2 standard deviations below the age norm, 6) Center for Epidemiological Studies Depression Scale ≤ 16 , or 7) presence of clinically significant cardiovascular, endocrine, hematopoietic, hepatic, neurologic, psychiatric or renal disease.

Disclosures: AF Boyd is CEO of CNS Vital Signs and a developer of the battery.



Discussion & Results

Currently, many studies use subject-rated sedation scales to measure lorazepam-induced cognitive impairment (1, 2, 3). These measurements are subject to error. This study is an acute assessment after single doses, as such it would be less likely to show differences between objective and subjective measures. However, in chronic treatment situations, perception of cognition is more related to mood than objective performance(5). Results using the two measures were similar. The lorazepam group self-reported increased sedation, and their neurocognitive performance was decreased. The mean change in sedation score between the lorazepam and the placebo group was 2 points on a 10 point scale (p=0.005) (Fig. C), while the mean change in NCI was 10 points (p=0.006) (Fig. D). NCI and sedation score correlated at -0.71 (p<0.001) for the placebo group (Fig. E). However, NCI and sedation only correlated at -0.30 (p=0.11) for the drug group (Fig. F).

Conclusions

Using an objective neurocognitive performance measure concurrently with a subjective sedation scale measure in a population sedated with lorazepam, yielded similar results. A computerized battery such as the one used in this study may offer a sensitive and easily administered measure of sedation.

References

- Rush, CR, Higgins, ST, Bickel, WK, and Hughes, JR. Acute effects of triazolam and lorazepam on human learning, performance and subject ratings. *J Pharmacol Exp Ther.* 1993; 264(3): 1218-26.
- Mintzer, MZ, Frey, JM, Yingling, JE, and Griffiths, RR. Triazolam and zolpidem: a comparison of their psychomotor, cognitive, and subjective effects in healthy volunteers. *Behav Pharmacol.* 1997; 8(6-7): 561-74.
- Pomara, N, Tun, H, DaSilva, D, Hernando, R, Deptula, D, and Greenblatt, DJ. The acute and chronic performance effects of alprazolam and lorazepam in the elderly: relationship to duration of treatment and self-rated sedation. *Psychopharmacol Bull.* 1998; 34(2): 139-53.
- Gualtieri, CT and Johnson, LG. Reliability and validity of a computerized neurocognitive test battery. *CNS Vital Signs. Arch Clin Neuropsychol.* 2006; 21(7): 623-43.
- Marino SE, Meador KJ, Loring DW, Okun MS, Fernandez HH, Fessler AJ, Garvan CS, Kustra RP, Miller JM, Ray PG, Roy A, Schoenberg MR, Vahle VJ, Werz MA. Subjective perception of cognition is related to mood and not performance. *Epilepsy and Behavior* 2009;14(3):459-64.