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Benzodiazepine Study for Analgesia and other Clinical Effects

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1. Introduction

Benzodiazepines have come under immense scrutiny within primary care and specialty clinics the past few years. Many pharmacies will not fill scripts; nor carry many of the benzodiazepines. Pain clinics studied have shown an 85% decrement of ER visits and subsequent hospitalizations. The concerns are that the drug as a sedative hypnotic used for varying conditions is dangerous, can lead to OD consequences, addiction, and studies have suggested that in combination with other medications can lead to adverse consequences. Benzodiazepines have been used perioperatively successfully for years under general, regional, and sedation anesthesia for a multimodal approach for medical conditions/treatments of pain, amnesia, tolerance to procedures, and allaying anxiety. Outpatient treatments include short- and long-term oral use for pain control (Clonazepam), anxiety, restless leg syndrome, addiction treatments, seizure control, panic disorder, muscle spasms, tremors, and sleep. Since studies have suggested that benzodiazepines are additive with other sedative hypnotic drugs, they should be severely limited or discontinued. Combinations of muscle relaxants, narcotics, psychiatric drugs, and benzodiazepines within the literature retrospectively have been tied to OD, deaths, and other adverse consequences. The variables within these anecdotal and studies are such that dosages, concomitant therapies, medical conditions (OSA), age, tolerance, palliative care concerns, and many other factors enter patient profiles prior to pinpointing the benzodiazepine as the culprit within a complex interplay of medical risk factors. Benzodiazepines molecularly work by binding of the inhibitory transmitter GABA at various GABA A receptors throughout the CNS (Chloride anions enter the neuron, hyperpolarizes, and inhibits the neuron). Benzodiazepines neuromodulate GABA A receptors conformationally – allowing drug effect. Benzodiazepines orally are short, medium, and long-acting – with varying effects on humans based on a multiplicity of factors (age, absorption, polydrug use, decay, medical conditions (liver/renal capacity)). The benzodiazepines chemically have been shown to displace binding of 3 H diprenorphine- an opiate radioligand from Kappa receptors. Additionally, benzodiazepines have been shown to be agonists at delta opioid receptors (partial pain control). Dopamine and other neurotransmitters surge with benzodiazepine use. Human and animal studies have shown analgesic effects within intrathecal injections. Few clinicians prescribe benzodiazepines for pain control; and the literature is replete with endless clinical benzodiazepine warnings. Should we clinically utilize benzodiazepine drugs within a primary care or pain specialty clinic?

The author is a hybrid anesthesiologist with boards in FP, Anesthesia and Pain Management. One surgical day I administered 7 general anesthetics for pelvic and abdominal surgeries with a boarded gynecologic oncologist who preferred no local anesthetic blocks, spinals, or other interventions due to time/habit/perceived non-need. PACU nurses in recovery noted historical high narcotic requirements for this surgeon's patients. I administered upon awakening 2 mg Midazolam (Benzodiazepine IV 5x the strength of Valium IV). Recovery nurses noted low VAS pain scores upon arrival and during the 90-minute recovery period. Limited to no analgesics (IV narcotics, IV Tylenol, IV methocarbamol) were needed. The sedation in PACU was minor. This was a dramatic

change noted by the PACU RNs. Thus, I reasoned that there was substantial analgesia with benzodiazepines and felt the need to study the phenomenon within our outpatient pain clinic. The author highly respects the issues with polypharmacy regarding the recent concerns of outpatient benzodiazepine oral use. The need to modulate the dose of these valuable drugs within the context of medical conditions and overall chronic analgesia is highly clinician/patient dependent. Most of the medical management for palliative pain control with patients having up to 10 spine surgeries, metastatic cancers, trauma with CRPS, polyneuropathy, etc. involves a combination of varying strength analgesics, psychiatric meds, low dose benzodiazepines, and muscle relaxants is highly patient dependent. Our clinic maintains high standards of care regarding drug testing and compliance. We have been impressed that the selective use of benzodiazepines by themselves or in careful combinations can be quite helpful in many difficult chronic pain/palliative care conditions. All patients within the study have varying combinations of multi-modal treatment with counseling, physical therapy, manual medicine, medications management, injections, alternative medical treatments (Acupuncture), and occasionally surgery. The study design, results, and conclusions of our study with 50 pain management patients with complex conditions and virtually all on controlled low dose benzodiazepines and adjunctive analgesics (including narcotics and non-narcotics) are below.

2. Study Design

Fifty patients were issued a questionnaire requiring 15 minutes. Patient numbers and not names were recorded. The questions involved clinical use of benzodiazepines, VAS pain scores, side effects, combination treatments with respect to narcotic lowering to achieve analgesia, mood effects, work/ADL effects, ER trips for pain control or other needed emergent clinical issues, prior or ongoing addiction treatments, and selective use of one drug for pain control (narcotic, muscle relaxant, psychiatric medication, or benzodiazepine).

3. Results

1) All patients had sole or varying combinations for the chronic and intermittent use of benzodiazepines for pain control, anxiety/panic, restless leg syndrome, addiction disorder, muscle spasticity, sleep, and tremors (100%). 42 patients felt there was substantial analgesia with benzodiazepine use (84%).

2) Benzodiazepines provided ample pain control in drug combinations with medium to low VAS; pain scores in 32 patients (64%) (Previously many patients were VAS 10 scores).

3) Daytime sedation was none in 36 patients (72%). No patients had excessive sedation and a small % incurred mild sedation. No patient required narcotic or benzodiazepine reversal due to drug effect at home or in an ER setting.

4) Use of less narcotic or other analgesics through use of benzodiazepine was recorded by 20 of 50 patients (40%).

5) Mood stabilization with respect to anxiety/depression or other psychiatric condition was 38/50 patients (76%).

6) ADLs were functionally improved at work and home in 37 out of 50 patients with use of benzodiazepines (74%).

7) ER trips over one year for pain, anxiety, or other medically related pain conditions under treatment was zero for 35 out of 50 (70%). One patient had >1 ER visit and the rest had one ER visit (28%).

8) Side Effects of benzodiazepines were mild, not bothersome, and infrequent in all patients – with 24/50 (48%) having zero side effects.

9) Sole Pain control through use of Benzodiazepine medication = 4 of 50 patients (8%).

10) 50 out of 50 patients felt they were not psychologically or physiologically addicted to benzodiazepines; and 50/50 felt they needed the drug (100%).

4. Conclusion

At the molecular and clinical levels benzodiazepines have important analgesic properties. The study reflects the additive/synergistic effect of these drugs on chronic pain patient profiles and VAS scores. Most of our patients have benign pain; yet zero medical or surgical procedures can relieve the neuropathic, nociceptive, or perceived pain itself. Thus, modernly like metastatic cancer, palliative relief is required. Many patients would rather not live than to have to deal with the pain “in-the-wild” without medical treatment and supervision. All patients within the study have subscribed to our clinic for years and acknowledge that medications are just a component of pain control within a multi-modal approach. Our study strongly supports benzodiazepines clinically partially helping with pain control through the simple advantage of improved sleep, allaying anxiety, or functionally/molecularly at receptor sites for analgesia (GABA A, neurotransmitters (dopamine), and opioid kappa and deltoid narcotic CNS receptors). The study supports the partial (uncommonly total) analgesic effect of benzodiazepines on chronic painful conditions. The functional chronic pain patient needs sleep, rest, anxiolysis, muscle spasm and pain control. Combination with other analgesics provided improved pain control (84%) with minimal or zero side effects (48%). Mild side effects noted such as occasional daytime drowsiness were mild, and the trade-off with mood stabilization and pain control favored use of the benzodiazepine drug long term. Use of less drug on a prn basis was encouraged for all patients with mild side effects. In conclusion, benzodiazepines provide substantial, palliative analgesia long term in a highly controlled compliant medical pain clinic for varying chronic painful medical conditions.