Abstract

**BACKGROUND:** Sedation or anesthesia is used to facilitate many cases of an estimated 45 million diagnostic and therapeutic medical procedures in the United States. Preclinical studies have called attention to the possibility that sedative-hypnotic drugs can increase pain perception, but whether this observation holds true in humans and whether pain-modulating effects are agent-specific or characteristic of IV sedation in general remain unclear.

**METHODS:** To study this important clinical question, the authors recruited 86 healthy volunteers and randomly assigned them to receive one of three sedative drugs: midazolam, propofol, or dexmedetomidine. The authors asked participants to rate their pain in response to four experimental pain tasks (i.e., cold, heat, ischemic, or electrical pain) before and during moderate sedation.

**RESULTS:** Midazolam increased cold, heat, and electrical pain perception significantly (10-point pain rating scale change, 0.82 ± 0.29, mean ± SEM). Propofol reduced ischemic pain and dexmedetomidine reduced both cold and ischemic pain significantly (-1.58 ± 0.28, mean ± SEM). The authors observed a gender-by-race interaction for dexmedetomidine. In addition to these drug-specific effects, the authors observed gender effects on pain perception; female subjects rated identical experimental pain stimuli higher than male subjects. The authors also noted race-drug interaction effects for dexmedetomidine, with higher doses of drug needed to sedate Caucasians compared with African Americans.

**CONCLUSIONS:** The results of the authors' study
call attention to the fact that IV sedatives may increase pain perception. The effect of sedation on pain perception is agent- and pain type-specific. Knowledge of these effects provides a rational basis for analgesia and sedation to facilitate medical procedures.

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