

Simulation-Based Assessment of Awareness in Medical Students and Anesthesia Providers to Race Differences in Propofol Pharmacodynamics

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Background

Racial variability to propofol anesthesia has been described [1,2]. In the context of precision medicine, we hypothesized that patient race would be taken into account, especially when administering a potent drug such as propofol for sedation. We performed 2 simulator-based drug administration studies to evaluate awareness in medical students and in anesthesia providers of racial differences in propofol sensitivity.

Methods

Study 1. Medical Students. We adapted pharmacodynamics data on race and propofol [1,2] to scale the loss and recovery of consciousness (LOC, ROC) thresholds in the Fechner propofol model [3] for different racial groups, based on personal communication from Dr. Fechner that the data were from Caucasian patients. Using Caucasians as the norm (1.0), the mean propofol consumption to achieve similar bispectral index values was set for African Americans at 0.82 and for South Asians (from the Indian subcontinent) at 0.78, and the mean time to eye opening from propofol anesthesia was set for African Americans at 1.6 and for South Asians at 1.9. We did not simulate inter-patient variability within a racial group. With IRB approval and informed consent, a convenience sample of twenty-two 2nd-, 3rd- and 4th-year medical students administered propofol sedation to a mixed reality simulator (male, 32 years old, 66-68 kg) for an upper GI endoscopy. The virtual physical appearance (Figure 1 below) and the programmed pharmacodynamics (PK/PD) were altered to represent 3 different races (South Asian (Indian), Caucasian, African American).

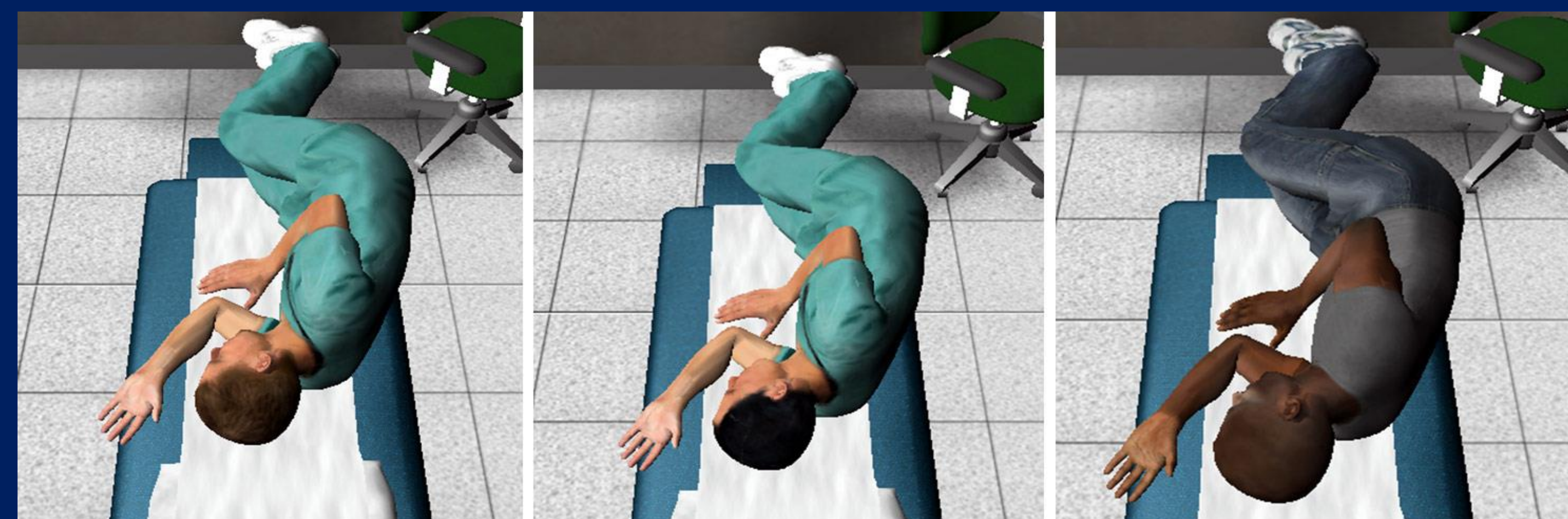


Figure 1. Virtual patients. Left to right: Caucasian, Indian, Black

Study 2. Anesthesia Providers. Using a similar set up (Fig. 2) to Study 1, anesthesia providers interacted with a mannequin (verbal commands, jaw thrusts, trapezius squeeze, mask ventilation, supplemental O₂); the virtual representation (Fig. 2) depicted movement, eyelid closing, breathing, moaning, racial features, and vital signs monitoring (SpO₂, ETCO₂, NIBP, EKG). Based on published data [2,4,5], propofol pharmacodynamics were altered to exhibit increased sensitivity in the following order: Caucasians [4], Blacks [2], and Indians [5] by progressively lowering propofol effect site concentrations for loss of consciousness (LOC, no response to verbal commands). With IRB approval, 37 consented anesthesia providers each administered propofol sedation for upper GI endoscopy to three consecutive simulated male patients (Caucasian, Indian, Black, otherwise similar).



Figure 2. Set-up for study 2 with anesthesia providers

Results

Study 1. Medical Students. LOC duration, as a measure of over-sedation, was significantly higher for the African-American (P=0.003) and Indian (P<0.05) patients compared to Caucasian patients. Patients from races with known sensitivity to propofol were over-sedated (Table 1).

Study 2. Anesthesia Providers. 23 males and 14 females participated (13 faculty, 10 residents, 8 nurse anesthetists, 3 fellows, 3 anesthesiology assistants). Results are reported as range, mean ± sd. Age: 28-68, 38.6 ± 10.1 years; experience delivering propofol sedation: 1-20, 6.8 ± 5.8 years. Loading doses of propofol were Caucasian, 0.27-1.71, 0.77 ± 0.31 mg/kg; Indian, 0.29–1.71, 0.80 ± 0.32 mg/kg; and Black, 0.25-1.71, 0.79 ± 0.28 mg/kg. Time durations of over-sedation (LOC) were Caucasian, 0-318, 147 ± 85 s; Indian, 26–338, 207 ± 68 s; and Black, 0-367, 191 ± 81 s. Between patient races, there was no significant difference in loading doses (p = 0.58) or significant differences in LOC duration (p = 0.014). On average, Caucasians spent significantly less time over-sedated than Blacks (p = 0.0003) or Indians (p = 0.005), Table 2

Race	Time Duration of Loss of Consciousness (s); Mean ± SD
Caucasian	81.72 ± 130.12
African American	289.54 ± 188.0
Asian	313.81 ± 166.49

Table 1. Results: Medical students as study participants

	Loading dose (mg/kg; range, mean ± SD)	Total propofol administered (mg/kg; range, mean ± SD)	LOC duration (s; range, mean ± SD)	Time to recovery (s; range, mean ± SD)
Caucasian	0.27 - 1.71 0.77 ± 0.31	1.16 - 2.77 1.95 ± 0.41	0 - 318 147 ± 85	269 - 701 444 ± 101
Black	0.25 - 1.71 0.79 ± 0.28	1.08 - 3.1 1.59 ± 0.41	0 - 367 191 ± 81	260 - 1090 538 ± 177
Indian	0.29 - 1.71 0.80 ± 0.32	1.51 - 2.6 1.63 ± 0.42	26 - 338 207 ± 68	338 - 1115 522 ± 154

Table 2. Results: Anesthesia providers as study participants

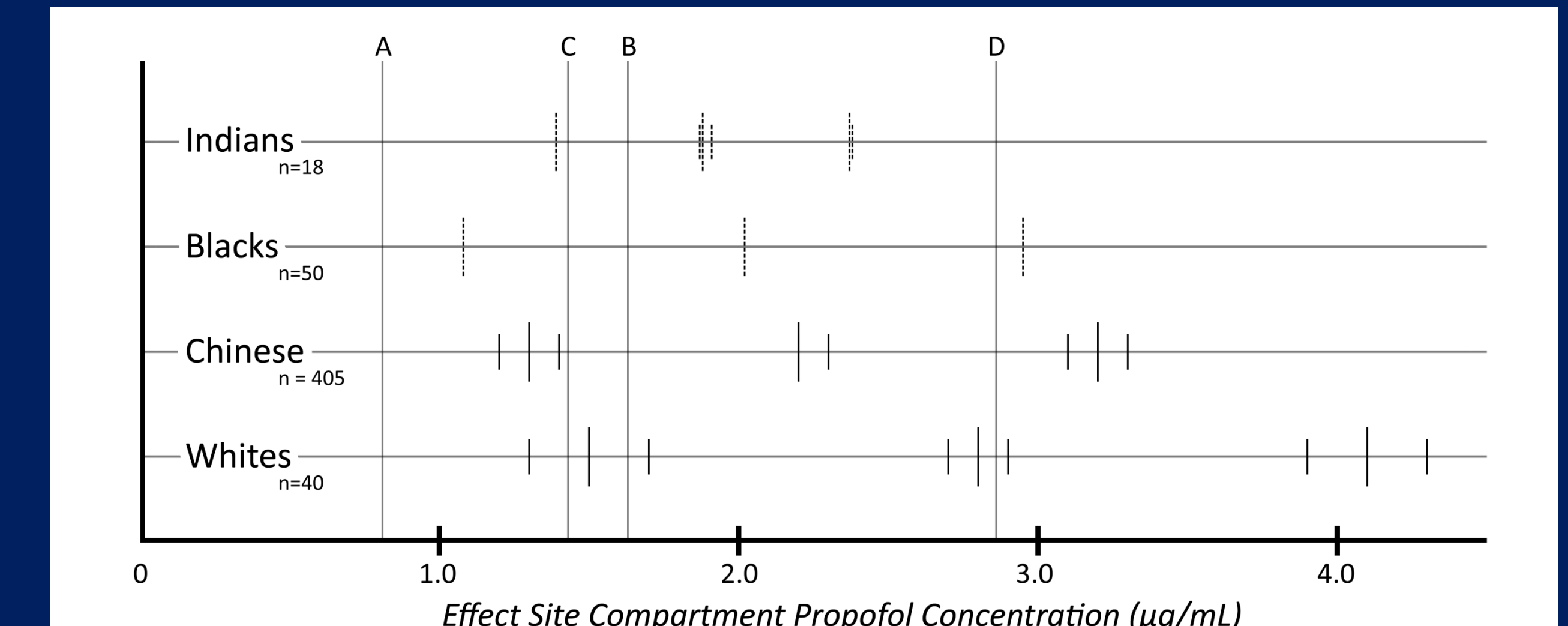


Figure 3. The effect site compartment (ESC) EC05, EC50 and EC95 (L-R along each line corresponding to a race) propofol concentrations at LOC. Lines A, B represent peak ESC concentrations (0.81, 1.63 µg/mL) predicted by the Marsh model (manual mode, non-TCI) for a bolus of 0.5 mg/kg (low end of dosing range for sedation) and 1.0 mg/kg (high end). Lines C, D represent peak ESC concentrations (1.43, 2.86 µg/mL) predicted by the Fresenius (modified Marsh model with faster equilibration between the plasma and effect site compartments) model (manual mode, non-TCI) for a bolus of 0.5 mg/kg and 1.0 mg/kg. Where available or derivable, 95% C.I. is also displayed. The short line in the middle of each set is the EC value with the two shorter lines on each side representing the 95% C.I. [6]

Conclusions

Our data indicate that both study participant groups (medical students and anesthesia providers) lacked awareness of the racial variability in the response to propofol. It suggests a need for education and training in racial variability to drugs and racially adapted PK/PD models that vary based on the race of the simulated patient for pragmatic precision medicine in the form of race-based dosing. We recently developed such a point of care app for race-based propofol dosing that runs on mobile phones and is available at:

<http://vam.anest.ufl.edu/WebSims/propofolsim/mobile/>

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