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LETTER TO THE EDITOR

Dexmedetomidine-induced contraction in the human umbilical artery

Lee SH[1], Sohn JT[1,2]

Department of Anesthesiology and Pain Medicine, Gyeongsang National University College of Medicine, Gyeongsang National University Hospital, Gyeongsang, Republic of Korea. **jtsohn@gnu.ac.kr**

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Dear Editor

I have read your interesting article entitled, "In vitro vasoactive effects of dexmedetomidine on isolated human umbilical arteries," recently published in Bratisl Med J (1). The alpha-2 adrenoceptor agonist dexmedetomidine is widely used for sedation (2). The following comments should be considered to understand this article (1). First, two cumulative dexmedetomidine dose-response curves were generated in the same human umbilical artery (HUA) before and after treatment with inhibitors. Dexmedetomidine ($2x10^{-5}$ M)-induced maximal contraction was used as the reference value of contraction evoked by dexmedetomidine (1). However, it is important to confirm HUA viability by assessing contractility to KCl or 5-hydroxytryptamine and the value generated can be used as a reference instead of that generated by dexmedetomidine ($2x10^{-5}$ M) in the present experiment (1, 3). Additionally, as the HUA strip produces spontaneous contraction and shows wide variability in vasoreactivity to a vasoconstrictor and inconsistency of vasoreactivity over time in the same HUA, KCl-induced contraction contributes to decreased spontaneous contraction and reduced variability of vasoreactivity and may stabilize the HUA (3,4). Furthermore, two dexmedetomidine dose-response curves generated in the same HUA even without inhibitors may not be identical (1). Thus, a comparison should be performed. It is not clear how it can be verified that dexmedetomidine used in the first dexmedetomidine dose-response curve is completely washed out before the second experiment to generate a dose-response curve in the presence of the inhibitors. Second, the clinically relevant concentration of dexmedetomidine used for sedation in humans approximately corresponds to 10^{-8} M. Third, prazosin ($3x10^{-9}$ M), an alpha-1 adrenoceptor inhibitor, inhibits dexmedetomidine-induced contraction in isolated rat aorta, whereas a very high concentration of prazosin (10^{-5} M) attenuated vasoconstriction induced by all concentrations of dexmedetomidine in the HUA (1, 5). This prazosin-mediated inhibition of dexmedetomidine-induced contraction may be associated with non-specific actions. Fourth, as cumulative dexmedetomidine dose-response curves were evaluated in the reported study, using a line graph appropriate for a cumulative dose-response curve instead of a bar graph in Figures 2 and 3 would be more helpful for readers to understand Figures 1 and 2 (1). In addition, for the comparison of the magnitude of cumulative dexmedetomidine-induced contraction in the presence or absence of inhibitors in the same HUA, it is more reasonable to use a linear mixed effect model or two-way repeated measure analysis of variance followed by Bonferroni's multiple comparison test rather than Wilcoxon rank test, which was used in the reported study (1). p value used in the Wilcoxon rank test in the reported study should be adjusted to about 0.008 ($p = 0.05/6$) to reduce the type 1 error (1). I believe that this study contributes to understanding the mechanism associated with dexmedetomidine-induced contraction in HUA.

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Department of Anesthesiology and Pain Medicine, Gyeongsang National University College of Medicine, Gyeongsang National University Hospital, 15 Jinju-daero 816 beon-gil, Jinju-si, Gyeongsangnam-do 52727, Republic of Korea Institute of Health Sciences, Gyeongsang National University, Jinju-si, 52727, Republic of Korea

Address for correspondence: JT Sohn, Department of Anesthesiology and Pain Medicine, Gyeongsang National University Hospital, 79 Gangnam-ro, Jinju-si, 52727, Republic of Korea.
Phone: +82.55.7508586, Fax: +82.55.7508142

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