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Propofol in COVID 19 – From basic science to clinical impact



Dear Editor,

We read the case report by Soh et al. [1] and the comments of Sohn [2] with great interest. However, we would like to highlight some of the important actions of propofol and its current application to COVID-19 cases.

Propofol (2,6-diisopropylphenol) a sedative-hypnotic agent is widely used for both induction and maintenance of sedation in critical care units. Earlier it was thought that propofol increases angiotensin-converting enzyme2 (ACE2) expressions in human endothelial cells as mentioned by Sohn [2]. However, recently [3] it was demonstrated that propofol infusion increases ACE2 mediated conversion of angiotensin II to angiotensin, which results in a fall in angiotensin II levels and an elevation of angiotensin 1 to7; and these exhibit protective effects of lungs by way of recovery of endothelial cell function via an up-regulation of ACE2-Ang-Mas axis, subsequent to phosphorylation of endothelial nitric oxide (NO) synthase to generate NO, and regulation of apoptosis-related protein such as bcl-2, caspase9. Moreover, propofol also increases the concentration of cyclic guanosine monophosphate in cultured endothelial cells through a NO dependent mechanism [4]. In addition, propofol exerts its antioxidant property [5,6] as evidenced by the inhibition of lipid peroxidase production in the platelet membrane and a decrease in tissue consumption of glutathione [7].

Interestingly, its ability to inhibit inflammatory response was demonstrated by Taniguchi et al. [8] in the form of a reduction in the cytokine response (TNF-alpha and IL-8) and neutrophil infiltration in the lungs in endotoxemic rats received propofol infusion. Propofol also, prevents the development of metabolic acidosis during endotoxemia [8]. Apart from the anti-inflammatory response, it also has an antithrombotic effect by way of inhibiting the platelet aggregation possibly in combination with the effects of the solvent, intralipid as well as increases leucocyte nitric oxide production, and inhibition of platelet thromboxane synthesis [9]. In view of the multiple protective actions, FDA of USA recently permitted the emergency use of the Fresenius Propoven 2% emulsion to maintain sedation via continuous infusion for COVID-19 patients older than 16 years who require mechanical ventilation [10].

To summarize, propofol a short-acting intravenous sedative-hypnotic agent has multiple actions, including significant antioxidant and anti-inflammatory activities, apart from attenuation of angiotensin II-induced endothelial dysfunction. As the benefits are more, its various actions and applications have to discuss in the regular teaching and learning activities of health science students and residents, and during clinical rounds, so as to broaden its clinical applications in the years to come.

References

- [1] Soh M, Hifumi T, Isokawa S, Shimizu M, Otani N, Ishimatsu S. Neuroleptic malignant syndrome in patients with COVID-19. *Am J Emerg Med*. 2020 May 22. <https://doi.org/10.1016/j.ajem.2020.05.042> (S0735-6757(20)30384-3; Online ahead of print).
- [2] Sohn JT. Propofol and sedation in patients with coronavirus disease. *PLoS One*. 2018 Jul 11;13(7):e0199373. <https://doi.org/10.1371/journal.pone.0199373> eCollection 2018.
- [3] Zhang L, Wang J. Propofol prevents human umbilical vein endothelial cell injury from Ang II-induced apoptosis by activating the ACE2-(1-7)-Mas axis and eNOS phosphorylation. *PLoS ONE*. 2018;13(7).
- [4] Petros AJ, Bogle RG, Pearson AD. Propofol stimulates nitric oxide release from cultured porcine aortic endothelial cells. *Br J Pharmacol*. 1993;109:6-7.
- [5] Murphy PG, Myers DS, Davies MJ, Webster NR, Jones JG. The antioxidant potential of propofol (2,6-diisopropylphenol). *Br J Anaesth*. 1992;68:613-8.
- [6] Mathy-Hartert M, Mouithys-Mickalad A, Kohnen S, Deby-Dupont G, Lamy M, Hans P. Effects of propofol on endothelial cells subjected to a peroxynitrite donor (SIN-1). *Anaesthesia*. 2000;55(11):1066-71.
- [7] Vasileiou I, Xanthos T, Koudouna E, et al. Propofol: a review of its non-anaesthetic effects. *Eur J Pharmacol*. 2009;605(1-3):1-8.
- [8] Taniguchi T, Yamamoto K, Ohmoto N, Ohta K, Kobayashi T. Effects of propofol on hemodynamic and inflammatory responses to endotoxemia in rats. *Crit Care Med*. 2000;28:4.
- [9] De La Cruz JP, Páez MV, Carmona JA, De La Cuesta FS. Antiplatelet effect of the anaesthetic drug propofol: influence of red blood cells and leucocytes. *Br J Pharmacol*. 1999;128(7):1538-44.
- [10] Coronavirus (COVID-19) update: daily roundup. Available at: <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-daily-roundup-may-11-2020>. (Accessed on 22nd June 2020).

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