



Letter to the Editor

Is transdermal iontophoretic delivery of naloxone sufficient for the management of intoxication in opioid-overdosed patients?

Dear Sir,

The paper "In vitro and in vivo transdermal iontophoretic delivery of naloxone, an opioid antagonist" by R. Yamamoto et al., that has recently appeared in the *International Journal of Pharmaceutics* (Yamamoto et al., 2012), gave me some reason for concern. Based on an interesting experimental study, the authors suggested that the anodal iontophoretic patch system for naloxone with constant current supply could attain sustainable therapeutic blood levels of naloxone in opioid-overdosed patients; therefore, this transdermal delivery rates of naloxone is sufficient for the management of intoxication in opioid-overdosed patients. As you know, naloxone is well absorbed by all parenteral routes of administration, including the subcutaneous, intramuscular, endotracheal, intranasal, and inhalational routes (Howland and Nelson, 2011). Although this is an interesting paper pointing out to the potential benefits of controllable naloxone delivery by iontophoresis, in emergency situations such as the time when the healthcare providers are encountered with an opioid-intoxicated patient suffering from severe ventilatory depression and in desperate need of emergent management and direct administration of the naloxone into the systemic circulation, one would certainly not want to use such an approach. I think, therefore, this system cannot be recommended as the first-line treatment in such situation. In this case, administration of naloxone by intravenous or most of the abovementioned routes will easily and rapidly reverse the respiratory depressant effects of the opioids (Howland and Nelson, 2011). Furthermore, although needleless delivery is clearly advantageous, it seems that there is

little role for in-hospital use of the suggested anodal iontophoresis patches for naloxone. Because, it is not clear whether upward or downward titration can easily be enough accomplished to both maintain adequate ventilation and avoid withdrawal in the patients dependent upon opioid agonist, evaluation for the re-development of respiratory depression requires nearly continuous monitoring and titration of naloxone doses and not sustainable blood levels of naloxone.

Declaration of interest

The author reports no conflicts of interest. The author alone is responsible for the content and writing of the paper.

References

- Howland, M.A., Nelson, L.S., 2011. Opioid antagonists. In: Nelson, L.S., Lewin, N.A., Howland, M.A., Hoffman, R.S., Goldfrank, L.R., Flomenbaum, N.E. (Eds.), *Goldfrank's Toxicologic Emergencies*, 9th ed. McGraw-Hill, New York, NY, pp. 579–585.
- Yamamoto, R., Takasuga, S., Yoshida, Y., Mafune, S., Kominami, K., Sutoh, C., Kato, Y., Yamauchi, M., Ito, M., Kanamura, K., Kinoshita, M., 2012. In vitro and in vivo transdermal iontophoretic delivery of naloxone, an opioid antagonist. *Int. J. Pharm.* 422, 132–138.

Hossein Sanaei-Zadeh
 Department of Forensic Medicine and Toxicology,
 Tehran University of Medical Sciences, Tehran, Iran
 E-mail address: h-sanaiezadeh@tums.ac.ir

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