Q&A column

Editor: Frederick L. Kiechle, MD, PhD

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Q. After naloxone is administered, are opiates still detectable in the body? If so, for how long and in what quantities?

A.Naloxone has no effect on the concentration of opioids in the body. Opioids, such as fentanyl and morphine, act by triggering the opioid receptors in the brain (primarily the mu-opioid receptors), causing analgesia and, in sufficient dosage, anesthesia. Respiratory depression is a potentially fatal dose-related side effect, especially after illicit opioid use. Naloxone has been widely used in emergency departments for decades as a reversing agent to treat opioid overdoses and, more recently, as a take-home treatment in the form of a nasal spray.

Naloxone works by binding to the same opioid receptors but without triggering the receptors and, therefore, does not cause analgesia or respiratory depression. It competitively blocks the access of opioids to the mu-opioid receptors in the brain and displaces the opioids already bound, but it does not destroy them or change their overall concentration in the body.

A disadvantage of naloxone is that its half-life is shorter than that of most opioids. It has a half-life of about 0.3 to 1.3 hours, whereas fentanyl has a half-life of two to six hours and methadone of 15 to 36 hours. Therefore, opioid-intoxicated patients need to be closely observed after naloxone administration, even if they are awake and alert. They may need to receive additional doses, depending on the severity of the opioid intoxication and type of opioid. An opioid that is still in the body after naloxone administration could cause a relapse into a coma once the naloxone has metabolized and its blood concentration decreased.

The potential need for repeat or continued administration of naloxone is illustrated in a case report from 2019 in which a 22-month-old girl ingested methadone syrup and developed marked somnolence. Her mother administered naloxone nasal spray, which initially reversed the somnolence, and the child was transported to the local emergency department. Her vital signs were very good initially, but four hours after the first dose of naloxone she developed somnolence, respiratory depression, and pinpoint pupils. She was administered one intravenous dose of naloxone without significant improvement, followed by a second dose that reversed the somnolence. The girl was started on a continuous intravenous infusion of naloxone, which was tapered off after about 36 hours. She recovered completely and was discharged about 48 hours after admission.

This case report demonstrates that multiple doses of naloxone may be required to treat an opioid intoxication, especially one involving an opioid with a long half-life, such as methadone. Naloxone may need to be administered until a sufficient amount of opioid is naturally metabolized and excreted from the body.

Lebin JA, Chen BC, Valento MJ. Reversal of pediatric opioid toxicity with take-home naloxone: a case report. *J Med Toxicol*. 2019;15(2):134–135.

Graham R. Jones, PhD
Forensic Toxicologist, Office of the Chief Medical Examiner
Clinical Professor
Department of Laboratory Medicine and Pathology
University of Alberta

Edmonton, Canada
Member, CAP Toxicology Committee

Q. Why do proficiency testing specimen results for common immunoassay analytes sometimes vary greatly with different instrument manufacturers and their reagents? Does that mean the patient's results for the same specimen could vary greatly based on the instrument used? If so, is this acceptable? Wouldn't the variation in results confuse the clinician and patient?

A.It is true that results for proficiency testing specimens for common immunoassay analytes sometimes vary with reagents from different manufacturers or even from the same manufacturer for the same analyte if different methods are used. This variability may be attributed to analytical and biological diversity and a lack of analyte harmonization and standardization. The absence of standardization is reflected by the use of diverse units and varying reference intervals.

To explain this observation, I would like to focus on autoimmune disease serologic testing. Heterogeneity in analytes for detecting the same antibody, diversity in immunological methods, and the use of manual versus automated instruments contribute to the variability in some CAP Surveys. Another major contributing factor is the lack of international standards or reagents to calibrate different assays of the same analyte. Lastly, biologic variability in host immune responses may inherently limit commutability between assays based on the type of analytes used. For example, a patient of a certain genetic background may respond to parts of an antigen (i.e. epitopes) that are not present in the immunoassay being used to evaluate that patient, thereby giving a false-negative result. Furthermore, each patient with a specific autoimmune disease may produce polyclonal antibodies that are unique in structure, selectivity, affinity, and avidity to the target antigen, making it difficult to establish a common standard.

It is very likely that a patient may get different results if the same specimen is tested using different immunoassays or instruments from different manufacturers. Lack of consensus in proficiency testing is likely an indirect measure of how variability in test performance characteristics may negatively impact patient results and patient evaluation and management. Comparable test performance implies patients will get the same result irrespective of the assay or method used or where the testing is conducted. It assures that health care providers can reliably evaluate and manage their patients. The clinical significance of discrepant results depends on how results are reported, interpreted, and communicated to the health care provider and used in the diagnosis and management of the patient.

It is very likely that discrepant results between immunoassays from different laboratories would confuse clinicians and patients. Understanding these limitations may help minimize confusion and potential harm to patients. Such scenarios are a major reason why there are several initiatives to harmonize or standardize laboratory tests at a global level. There are also a number of laboratory guidance documents and recommendations on how to validate, interpret, and communicate test results so that health care providers are familiar with these challenges and can act appropriately to avoid patient harm.

Jacobs JFM, Bossuyt X. Standardization and harmonization of autoimmune diagnostics. *Clin Chem Lab Med*. 2018;56(10):1563–1567.

Anne E. Tebo, PhD, D(ABMLI)
Co-director
Antibody Immunology Laboratory
Senior Associate Consultant
Division of Clinical Biochemistry and Immunology
Department of Laboratory Medicine and Pathology
Mayo Clinic College of Medicine
Rochester, Minn.