

Are Expired EpiPens Still Viable?

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Practice Options from Beyond Our Pages focuses on identifying, critiquing, and placing into context research studies published in other journals that have the potential to change our clinical practices. It is written by Allergy-Immunology Fellows partnered with faculty members, and does not require an invitation for submission. This feature is coordinated by Editorial Board members Matthew Rank, MD and Julie Wang, MD.

REFERENCE

Cantrell FL, Cantrell P, Wen A, Gerona R. Epinephrine concentrations in EpiPens after the expiration date. *Ann Intern Med* 2017;166:918-9.

BACKGROUND

Epinephrine is a potentially life-saving first-line treatment for patients experiencing anaphylaxis. Epinephrine autoinjectors, including EpiPen products, provide a readily available premeasured dose of medication, allowing for immediate treatment of anaphylaxis by patients and lay people. These devices are routinely prescribed to patients at risk for anaphylaxis, as delayed treatment with epinephrine is associated with most cases of fatal anaphylaxis.¹ However, the increasing cost of these autoinjectors has raised serious concerns about access to this important medication. According to a 2016 *Lancet* article, the cost of the EpiPen device increased to more than \$600 over a relatively short amount of time.² Additionally, EpiPens expire after 12 to 18 months and need to be replaced on a continual basis. Given recent concerns regarding cost and availability, alternatives to EpiPens or other autoinjectors have been suggested by some. These alternatives include prefilled epinephrine syringes. However, prefilled syringes are less user-friendly than autoinjectors: they require more training, are subject to mishandling/dosage errors, must be protected from ultraviolet light and temperature extremes, and must be replaced every 2 to 3 months.³ Thus, epinephrine autoinjectors, including EpiPen, remain the preferred means by which patients can self-administer

epinephrine in an emergency. This article examines the potency of epinephrine in EpiPen autoinjectors past their expiration date.

METHODS

Expired, unused EpiPens were collected from patients and providers at a community clinic. Expiration dates and color changes were noted. Epinephrine concentrations were determined by liquid chromatography-tandem mass spectrometry.

RESULTS

Thirty-one EpiPens (0.3 mg dose) and 9 EpiPen Jrs (0.15 mg) were collected for analysis, which ranged from 1 to 50 months beyond the expiration date. No discoloration was noted on any device. At least 90% of the labeled epinephrine dose was found in 19 of 31 (65%) EpiPens and in 5 of 9 (56%) EpiPen Jrs. The lowest percentage of available dose was 84% in 2 EpiPens and 81% in 1 EpiPen Jr. Of note, the 6 EpiPens that were 49 to 50 months beyond their expiration dates contained 84% to 88% of the labeled epinephrine dose.

CRITICAL APPRAISAL

This study attempts to answer the practical question of advising patients who cannot afford to replace their EpiPen autoinjectors on the use of outdated devices. It suggests that many outdated EpiPens retain a substantial, and likely therapeutic, amount of epinephrine up to 50 months past the expiration date. A study published in 2000 demonstrated declining epinephrine dose with time beyond the expiration date.⁴ This study evaluated 28 EpiPen and 6 EpiPen Jr devices 1 to 90 months past expiration. Compared with the current study, their findings demonstrated lower percentages of available epinephrine, with a mean 79% (range, 51% to 100%) for EpiPens and 72% (range, 55% to 93%) for EpiPen Jr. They also found a rate of decline in percentage of epinephrine over time, with an inverse correlation of 0.63 between the content and number of months past expiration. However, therapeutic doses are likely still maintained for some time after the expiration date. A similar study from 2015 showed that EpiPens that were less than or equal to 24 months past their expiration date contained at least 90% of their labeled epinephrine dose.⁵

A limitation of this current study is its small sample size, with inclusion of very few EpiPen Jrs. In addition, the other commercially available epinephrine autoinjectors were not included in this analysis, which limits generalizability of the results. Analysis of additional outdated EpiPens and EpiPen Jrs are needed to determine the timeframe during which a useful concentration of

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No funding was received for this work.

Conflicts of interest: D. D. Patadia declares no relevant conflicts of interest. D. R. Stukus is an unpaid member of the Asthma and Allergy Foundation of America Board of Directors; and has received consultancy fees from Aimmune Therapeutics.

Received for publication June 2, 2017; revised June 22, 2017; accepted for publication June 26, 2017.

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2213-2198

<http://dx.doi.org/10.1016/j.jaip.2017.06.026>

epinephrine is delivered by the device. Additionally, clinical applicability cannot be determined from this study, nor can the safety of outdated EpiPen products. The authors of the current study contend that even with a decline in epinephrine concentrations <90%, delivery within the recommended dose range would still likely occur. However, the study by Simons et al in 2000 identified variable and significantly decreased bioavailability of epinephrine from expired autoinjectors compared with nonexpired devices, as measured by blood samples from rabbits at various time points after injection. It remains unknown whether this would have clinical implications in the treatment of someone experiencing anaphylaxis. Ultimately, additional studies to address questions surrounding bioavailability and how this correlates with measurement of epinephrine by mass spectrometry are needed to influence, and potentially extend, the labeling of expiration dates on EpiPen devices, which would benefit patients by reducing cost from annual prescription refills.

RECOMMENDATION

Patients should still be encouraged to maintain access to non-expired epinephrine autoinjectors to ensure delivery of the best

possible dosage in case of an anaphylactic reaction. However, should treatment with epinephrine be necessary when an expired autoinjector is the only available option, then patients should also be counseled to still use their device; it may very well offer benefit and will not likely cause any harm. This is an important message for patients to understand as they may be reluctant to use an expired autoinjector due to concerns of potential harm, and therefore delay administration of this essential treatment.

REFERENCES

1. Bock SA, Munoz-Furlong A, Sampson HA. Further fatalities caused by anaphylactic reactions to food, 2001-2006. *J Allergy Clin Immunol* 2007;119:1016-8.
2. Rubin R. EpiPen price hike comes under scrutiny. *Lancet* 2016;388:1266.
3. Pepper AN, Westermann-Clark E, Lockey RF. The high cost of epinephrine autoinjectors and possible alternatives. *J Allergy Clin Immunol Pract* 2017;5:665-8.e1.
4. Simons FE, Gu X, Simons KJ. Outdated EpiPen and EpiPen Jr autoinjectors: past their prime? *J Allergy Clin Immunol* 2000;105:1025-30.
5. Rachid O, Simons FE, Wein MB, Rawas-Qalaji M, Simons KJ. Epinephrine doses contained in outdated epinephrine auto-injectors collected in a Florida allergy practice. *Ann Allergy Asthma Immunol* 2015;114:354-6.e1.

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