

Preclinical testing of expired antivenoms and its uses in real-world experience: a systematic review

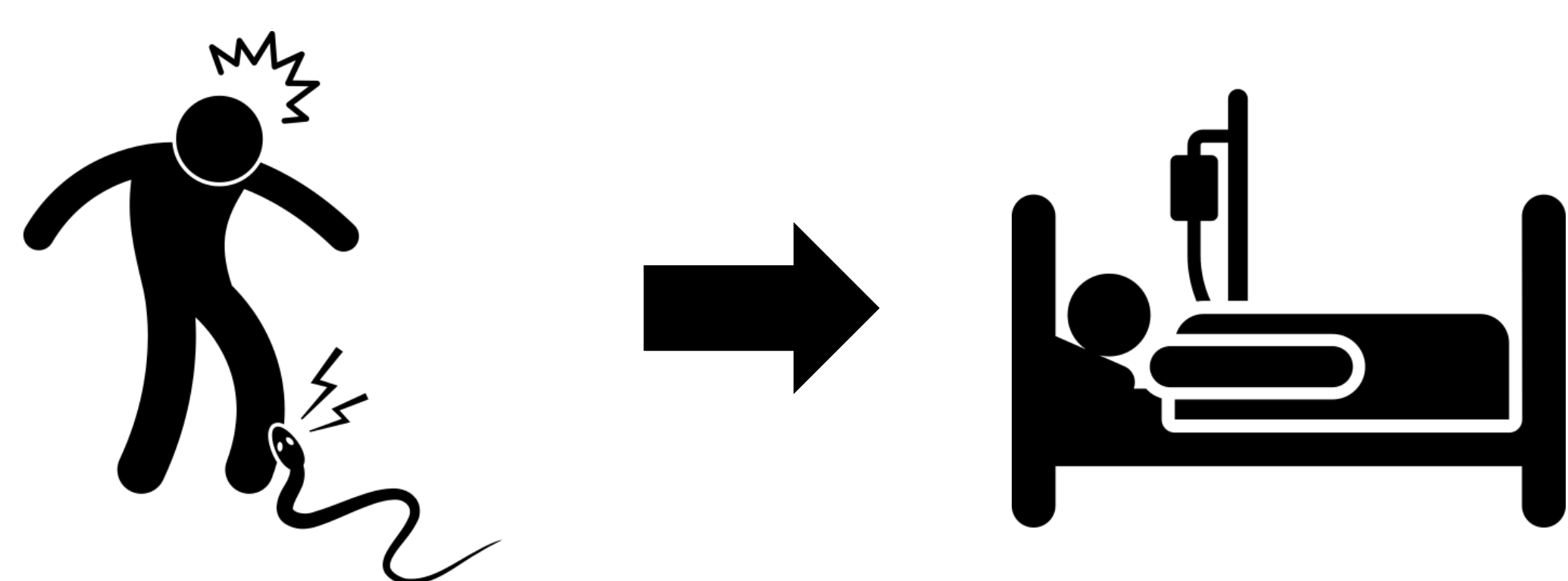
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HPR167

Introduction

- Limited access to antivenoms is a global challenge in treating snakebite envenoming.
- In emergency situations where non-expired antivenoms are not readily available, expired antivenoms may be used to save lives with the risk of deteriorating quality, efficacy, and safety.



Objective

To systematically review and summarize the sparse preclinical evidence of neutralizing efficacy of expired antivenoms and real-world experience of using expired antivenoms in humans.

Methods

We searched for articles published until 1 March 2023 in PubMed, Scopus, Web of Science, and Embase. Studies demonstrating the preclinical studies evaluating expired antivenoms or studies describing the real-world experience of using expired antivenoms were included. Narrative synthesis was applied to summarize the evidence of expired antivenoms.

Results

- Fifteen studies were included. Ten were preclinical studies, and five were real-world experiences of using expired antivenoms in humans.¹⁻¹⁵
- The expired duration of antivenoms in the included studies ranged from two months to 20 years.

Quality

- The standard quality control of expired antivenoms was evaluated in one study.¹
- After 12 years of their production, the expired antivenoms passed the standard quality control tests including insoluble foreign matter, pH, protein content, sterility, pyrogen, appearance, osmolality, dissolution time, and moisture content.
- The quality of expired antivenoms was comparable to non-expired antivenoms.

Safety

- The safety profile of using expired antivenoms was reported in two included studies.^{2, 3}
- However, it was inconclusive due to limited information.

Efficacy

Table 1 Efficacy of expired antivenoms

| Efficacy of expired antivenoms | Duration of expiration | | |
|--------------------------------|------------------------|-----------------------|-----------------------|
| | < 5 years | 5 – 10 years | > 10 years |
| Preclinical efficacy | | | |
| Immunoglobulin concentration | ✓ ^{4, 5} | ✓ ^{4, 5} | ✓ ^{4, 5} |
| Venom binding activity | ✓ ⁴⁻⁹ | ✓ ⁴⁻⁹ | ✓ ⁴⁻⁹ |
| In vitro neutralizing efficacy | ✓ ^{1, 7-10} | ✓ ^{1, 7-10} | ✓ ^{1, 7-10} |
| In vivo neutralizing efficacy | ✓ ^{9, 10} | No data reported | ✓ ^{9, 10} |
| Real-world experiences | | | |
| Case reports or Case series | ✓ ^{2, 11-13} | ✓ ^{2, 11-13} | ✓ ^{2, 11-13} |

✓: Comparable to non-expired antivenoms, however, could be gradually declined after expiration

Conclusion

Expired antivenoms may be feasible as a short-term solution to save severely envenoming victims' lives when non-expired antivenoms are inaccessible. Therefore, further investigations may be needed to support the extension of antivenoms' expiration date according to their potential efficacy after expiration. However, when expired antivenoms are inevitably used, a risk-benefit assessment should be conducted before administration, and close monitoring is required.



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