Pharmacokinetics, safety and tolerability of inhaled epinephrine from Cyclops™ in healthy volunteers

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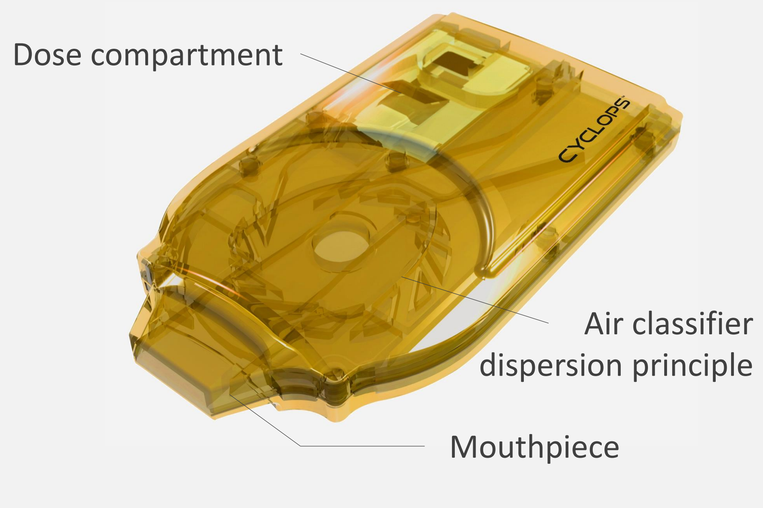
Introduction

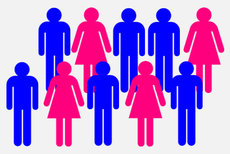
- Intramuscular administration of epinephrine by autoinjectors is prone to errors and associated with a high barrier to use.[1-3]
- This puts patients at risk of untimely treatment of allergic reactions, which increases the chance of anaphylaxis.[1-3]
- Epinephrine dry powder inhalation offers a more convenient, low-barrier alternative to autoinjectors, thereby preventing the occurrence of anaphylaxis due to untimely treatment.

Aim

To study the systemic exposure, safety and tolerability of inhaled epinephrine from Cyclops™ dry powder inhaler[4] in healthy volunteers.



Methods



10 healthy volunteers

Epinephrine Cyclops™
- Placebo (3 x n = 3)
- 0.35 mg (n = 7)
- 0.65 mg (n = 7)
- 1.3 mg (n = 7)

EpiPen®
- 0.3 mg (n = 10)

Tests ≤180 min post-dose:
- Blood sampling
- Heart rate
- Blood pressure
- General adverse events
- Local irritation
- Lung function (FEV1)

Results and discussion

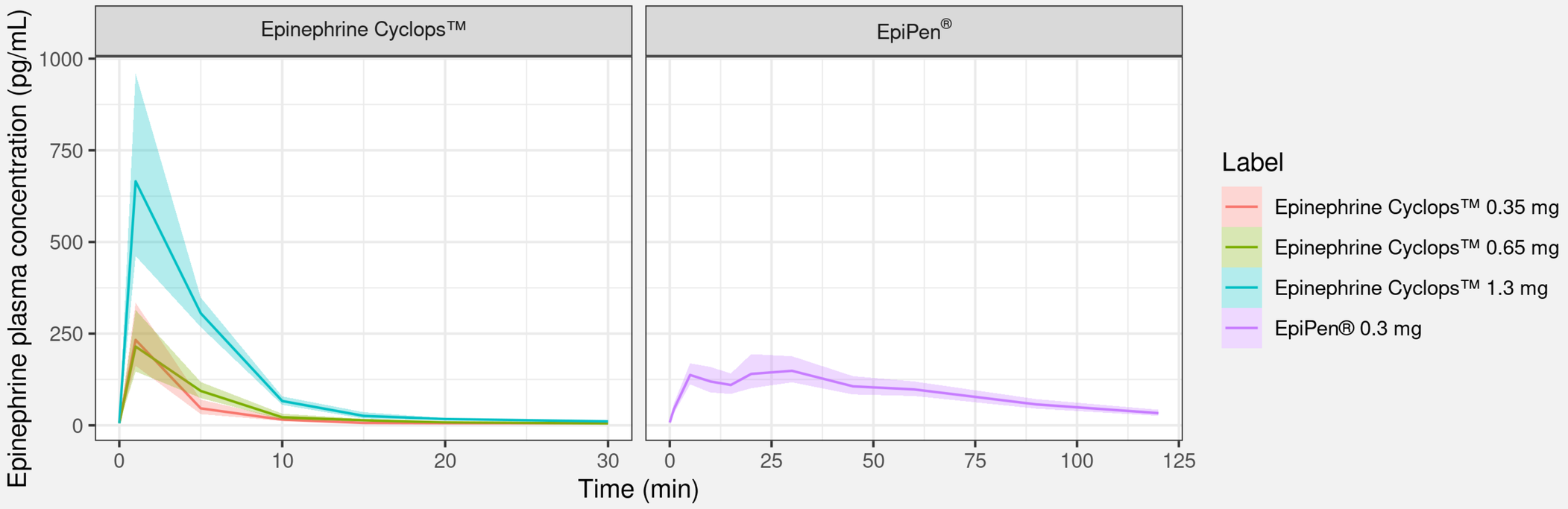


Figure 1: plasma epinephrine concentration profiles following inhalation (Cyclops™) and intramuscular injection (Epipen®).

- No adverse reactions were observed following inhalation of epinephrine with Cyclops™.
- Fast epinephrine absorption following inhalation and low barrier to use may lead to earlier intervention.
- Lack of dose proportionality due to intersubject variability and small population size.
  - Strongest responders at 0.35 and 1.3 mg were in the placebo arm for the 0.65 mg dose.
- Does the shorter exposure duration following Epinephrine Cyclops™ lead to symptom relapse? If so: repeat dosing may solve this issue.
  - On the contrary, a less advanced allergic reaction due to earlier intervention may require a lower epinephrine exposure.
- Patients that are at risk of severe reactions likely need to carry an epinephrine autoinjector as a backup.

Table 1: Pharmacokinetic results; geom. mean (geom. Cv).

	t_{max} (min)	C_{max} (pg/mL)	$AUC_{0\text{-}30min}$ (pg*h/mL)
0.35 mg inh.	1.8	240 (130%)	24.3 (66.1%)
0.65 mg inh.	1.8	247 (111%)	34.0 (47.4%)
1.3 mg inh.	2.4	712 (113%)	78.9 (58.6%)
EpiPen®	33,6	270 (76%)	78.7 (79.5%)

Conclusions

- Epinephrine from Cyclops™ is well-tolerated and systemically absorbed within a few minutes, which demonstrates its potential as a first-line rescue treatment.
- The short exposure allows for repeated treatment without dose stacking.
- This offers the potential for a more convenient alternative to autoinjectors with a lower barrier to use (i.e. non-invasive, easy and convenient to handle, fast onset of action).
- This may ultimately reduce the occurrence of anaphylaxis due to untimely treatment.

References

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