Weak acid and pepsin reflux induce laryngopharyngeal mucosal barrier injury: a rabbit-model-based study

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Objective

LPRD is linked to severe laryngeal diseases. Current therapy focuses on strong- acid reflux; effects of weakly- acidic reflux and pepsin remain unclear.

- Establish a reproducible rabbit LPRD model
- Explore synergistic injury of weak acid + pepsin to mucosal barrier
- Evaluate transient LP- MI as a diagnostic candidate
- Assess molecular & ultrastructural barrier changes

Methods

- 30 male New Zealand white rabbits (2.5- 3.5 kg).
- Nasopharyngeal catheter to hypopharynx; twice- daily spray (1 mL/kg, 3 min) for 8 weeks.
- 6 groups: pH3 acid / pH5 weak acid / pH7 saline, ± pepsin.
- Assessments: RFS, LP- MI, HE, E- cadherin IHC, lanthanum- nitrate- traced TEM.
- Statistics: t- test, Kruskal- Wallis, Spearman correlation; $p<0.05$ significant.

Key Results

1. RFS scores increased after 8 weeks; pepsin- exposed groups scored higher, positively correlated with acid intensity ($p<0.05$).
2. LP- MI showed no pre- post difference (1903±132 vs 2051±176, $p=0.50$); laryngeal mucus interferes with measurement.
3. E- cadherin was down- regulated, positively correlated with acid- exposure strength ($p<0.05$).
4. All intervention groups showed widened intercellular spaces with lanthanum tracer penetration.
5. Pepsin is an independent factor for mucosal damage.

Ethics

Animal experiment approved by Animal Ethics Committee of Fujian Medical University.

Conclusions

- Acid, weak acid and pepsin all disrupt laryngopharyngeal mucosal barrier.
- Pepsin serves as a key effector, indicating that non- acid reflux is not physiologically inert.
- Mucosal barrier impairment shows dose- dependence on acid intensity and pepsin exposure.
- Epithelial cell- junction disruption is central; transient LP- MI cannot be directly used for diagnosis due to mucus interference.
- LPRD diagnosis should move beyond acid- centric paradigms.

Significance & Implications

- Weak- acid & pepsin- mediated reflux injure mucosa in refractory LPRD patients.
- E- cadherin and barrier integrity may serve as new biomarkers.
- Challenges exclusive pH- monitoring for LPRD diagnosis.
- Informs pepsin- and weak- acid- targeted therapies.
- Provides a reliable rabbit model for LPRD research.