Investigating the Etiology of Primary Failure of Eruption (PFE): A Phenotypic and Genetic Analysis

E-Handout

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I. Purpose and PFE Significance

II. Functional Study

III. *In Silico* Study

IV. Conclusions
Primary Failure of Eruption (PFE): Definition

When a tooth fails to erupt in the absence of a mechanical obstruction, it is called “Primary Failure of Eruption” and indicates a defect in the eruption mechanism itself.

Proffit and Vig, AJO, 1981
Two Types of PFE

- **Type 1:** Progressive anterior-posterior lateral/posterior openbite, beginning from the most mesially affected tooth

- **Type 2:** Variable amounts of infraocclusion from the anterior-posterior, beginning from the most mesially affected tooth

Either type can affect the maxilla, mandible, or both. PFE can be unilateral or bilateral.
Type I PFE

Frazier-Bowers et al., AJO-DO, 2007
Type II PFE

Frazier-Bowers et al., AJO-DO, 2007
Clinical Presentation

- Lateral/posterior openbite
- At least one, infraoccluded permanent 1st molar
- Lack of a mechanical obstruction to tooth eruption
- Higher proportion of patients with CIII skeletal relationship
- May be accompanied by lateral tongue position
- Potential Family History
Purpose and Hypothesis

Purpose: This study was undertaken to observe the effects of a $PTH1R$ gene mutation on protein function. The mutations used in this study were found in PFE-patients.

Hypothesis: $PTH1R$ mutations result in loss of function due to altered protein structure.
Clinical Significance

- Primary Failure of Eruption (PFE)
  - One of many different types of eruption failure

- Proper Identification and Treatment is Imperative, but Not Always Easy

- Applying orthodontic force to PFE affected teeth with a continuous archwire results in an ankylosed tooth and lateral openbite.

- The more that we understand normal and altered eruption patterns, the ability to manipulate tooth movements will increase.
Results of using a continuous archwire with a tooth affected with PFE.....

Frazier-Bowers, et al. 2007
Scientific Significance

- Parathyroid Hormone Receptor-1 (PTH1R) is found all throughout the body.

- PFE is the only PTH1R- anomaly (out of 5) that does not carry high mortality and morbidity rates, in addition to the fact that it only affects the dental units.

- PFE presents a good potential model to investigate normal and altered eruption controls.
Functional Study

• Transfection of COS-7 cells with Wildtype (normal) and Mutant PTH1R
  • Inserted desired copy of PTH1R inside cells, and allowed to grow

• Immunofluorescence assay (IFA) of both COS-7 cell populations
  • Used fluorescent antibiotic markers to show the location of PTH1R protein inside of the cells
**In Silico Study**

- Performed *in silico* analysis on Wildtype PTH1R and four functional mutations
  - Used a computer system to predict the protein structures, based off of a database

- Obtained 3-dimensional structural image

- Used information to better understand the eruption process from a molecular level
In Silico Analysis: WT PTH1R
Conclusions

- There is an appreciable change in protein behavior, function, and structure when comparing Wildtype vs Mutant DNA.

- Specific alterations in two individuals point to the potential expansion of how we view PFE.

- The more we elucidate the genetic patterns of eruption, the possibilities of rendering ideal care increase.