Abstract #:

Dental abnormalities in children with X-linked hypophosphatemia

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BACKGROUND

X-linked hypophosphatemia (XLH) is an inherited metabolic disorder caused by mutations in the PHEX (phosphate regulating endopeptidase X-linked) gene. These mutations result in a significant increase in FGF23 protein activity. FGF23 inhibits renal phosphate reabsorption in the proximal tubule of the kidney, which results in increased phosphate excretion out of the body. It also inhibits 1-alpha hydroxylase, which results in a decrease in 1,25-$(OH)_2$ vitamin D production and therefore decreased intestinal absorption of phosphate and calcium. XLH is usually diagnosed in infancy-childhood with symptoms typically appearing within the first 2 years of life. Patients diagnosed with XLH present with defects in skeletal mineralization such as rickets. XLH also manifests dental abnormalities, including enlarged pulp chambers, blunted roots, and spontaneous abscess formation in non-carious primary teeth. XLH is conventionally treated with high dose oral phosphate and calcitriol, or active vitamin D. Crysvita (burosumab-twza) is an FDA-approved FGF23-blocking antibody that binds to FGF23 protein, which subsequently inhibits its biological activity and allows for normal renal phosphate reabsorption and serum vitamin D levels. When phosphate homeostasis is restored with therapeutic interventions, it may be possible to see differences in the manifestation and progression of XLH.

OBJECTIVE

To determine if there is a difference in occurrence of dental abnormalities in children diagnosed with X-linked hypophosphatemia (XLH) after starting FGF23-blocking antibody Crysvita compared to conventional therapy.

MATERIALS AND METHODS

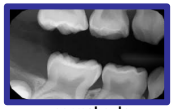
A retrospective chart review was conducted on patients of record diagnosed with XLH and seen at Texas Scottish Rite Hospital (TSRH) dental clinic between 1/1/16 to 10/31/22. Information collected: patient age, medication history, dental radiographs, and Epic medical and dental progress notes. This study was approved by TSR IRB. Approval number STU-2022-1002

Criteria for Inclusion of Subjects:

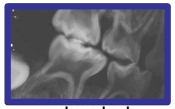
1. Children diagnosed with X-linked hypophosphatemia
2. Patients aged 6 months to 18 years
3. Patients that are of record with TSRH dental clinic in the time frame of study

Criteria for Exclusion of Subjects:

1. Children diagnosed with XLH that are NOT patients of record of TSRH dental clinic
2. Patients with a history of craniofacial trauma noted in the records (could cause tooth defects)
3. Patients with history of medication use that is known to cause dental abnormalities

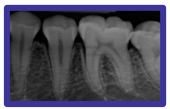


normal pulp

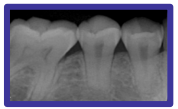


enlarged pulp

Pulp chambers were considered enlarged if the chamber appeared rectangular in shape and had pulp horns extending toward the dentin-enamel junction.



normal root



blunted root

The presence of root blunting was determined using a binary visual scale:

Yes: none to minimal root blunting
No: >2mm abnormal root blunting

RESULTS

Medication Regimen	# of Patients	Abscess (# patients)	Blunted root (# patients)	Enlarged chamber (# patients)
Calcitriol/Vitamin D Only	21	7	4	4
Transitioned to Burosumab	13	5	2	3
Neither Medication	4	2	0	2
Age of Transition to Burosumab	**# of Patients**	**Abscess after starting Burosumab**	**Blunted root (# patients)**	**Enlarged chamber (# patients)**
1 - 3 years old	1	1	0	0
3 - 5 years old	3	1	1	0
5 - 8 years old	2	1	0	2
9+ years old	7	2	1	1
Duration of Time on Burosumab (In years)	**# of Patients**	**Abscess after starting Burosumab**	**Blunted root (# patients**	**Enlarged chamber (# patients)**
Between 0 - 1	5	1	0	1
Between 1 - 2	4	2	1	2
Between 2 - 3	2	1	1	0
Between 3 - 4	2	1	0	0

RESULTS (cont'd) & DISCUSSION

38 patients met the inclusion criteria for this study. There was no statistically significant association (p-value 0.467) found between the presence of dental abnormalities and the type of medication regimen (calcitriol vs. burosumab) used. While there is a clinically significant difference in that at least 50% of patients not taking any medication presented with abscesses compared to 33% in the calcitriol group and 38% in the burosumab group, it is not of true statistical significance given the small sample size of this pilot study. The was also no statistically significant association found between the age of transition to burosumab or the duration of time on burosumab and the presence of dental abnormalities studied.
Significant limitations in the data were presented. Given the hospital's transition to electronic health records (Epic) in 2016, it was not possible to retrieve patient data regarding the start date of the calcitriol regimen for patients who were put on calcitriol prior to 2016. Several potential confounders were also recognized. Although the presence of enlarged pulp chambers is a possible finding in patients with XLH, taurodontism is also a noted feature seen in several other disorders that would need to be ruled out. Root blunting is another finding that has several other possible etiologies such as undiagnosed trauma or grinding habits. A future, large-scale longitudinal cohort study could consider conducting a clinical exam to rule out wear facets of teeth that would indicate a grinding habit.

CONCLUSIONS

- While there appears to be a clinically significant difference showing fewer abnormalities in both medication groups compared to the non-medication group, caution should be taken due to the small number of samples.
- This pilot study would benefit from the merits of a large-scale longitudinal cohort study with a larger sample size in order to have statistically meaningful data.
- Almost half of the patients in this study showed at least one of the three investigated abnormalities– dentists should be aware of such radiographic findings and monitor for the development of any incidental findings at recalls.

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