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Two Systematic Reviews Of Treatment Efficacy On Patient Important Outcomes In Children X-linked Hypophosphatemia

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Objective: We sought to examine the highest certainty evidence on managing X-linked hypophosphatemia (XLH) in children, aiming to inform treatment recommendations of XLH international guidelines. **Data Sources:** We searched Embase, MEDLINE, Web of Science, and Cochrane Central from inception to March 2023. We also reviewed reference lists of eligible studies and pertinent review articles. **Study eligibility criteria:** Eligible studies included randomized controlled trials (RCTs) and observational studies enrolling individuals younger than 18 years old with XLH diagnosed on clinical grounds or with a confirmed pathogenic variant in *PHEX*. Articles were selected according to specific criteria evaluating the effectiveness of burosumab compared to either no treatment or conventional therapy (phosphate salts and active vitamin D) or evaluating conventional therapy compared to no treatment. **Methods:** Two reviewers independently determined eligibility, conducted data extraction, and assessed the risk of bias (RoB) in eligible articles. We employed the GRADE methodology to evaluate the certainty of the evidence. **Results:** After removing duplicates from 7,043 citations, we screened 4,114 records and assessed 254 full texts, of which in the systematic review (SR) addressing burosumab one RCT and one post-Hoc study proved eligible. Being open-label design, the RoB was high, with certainty of evidence on individual outcomes ranging from moderate to very low. Burosumab, compared to conventional therapy, probably prevents lower limb deformity, and improves physical health quality of life (QoL) (moderate certainty). It might also increase height and possibly improve the burden of symptoms related to chronic hypophosphatemia (low certainty). Conversely, burosumab probably increases Treatment-Emergent adverse events after the first administration (moderate certainty), and it may increase dental abscesses (low certainty). In the second SR, one observational study assessing conventional therapy versus no treatment was at high RoB providing very low certainty of evidence regarding the impact of conventional therapy compared to no treatment on final height. **Conclusion:** Our review indicates that burosumab likely offers benefits in preventing lower limb deformity and improving physical health QoL, while potentially increasing height and improving the burden of symptoms related to chronic hypophosphatemia (low certainty). However, it may also increase adverse events, including dental abscesses. Additionally, our review found limited evidence regarding the impact of conventional therapy compared to no treatment on final height in children. These findings highlight the need for further research to better understand the long-term impact of conventional therapy and burosumab in children.

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