INTRODUCTION

X-linked hypophosphatemia (XLH) is a rare, hereditary, progressive and fatal phosphate wasting disorder characterized by pathological elevations in fibroblast growth factor (FGF) 23 concentration and activity.1-3

Conventional therapy for the treatment and management of XLH usually involves the combination of oral phosphate and active vitamin D analogues.4 However, this therapy only targets phosphate and vitamin D deficiencies and not the disease-causing excess of FGF23. Furthermore, it is known to be associated with high failure rates, long-term adverse events and worsening of XLH complications when used over a longer period.4 Research indicates linear growth failure in approximately 25–40% of the patients with well-controlled XLH.5 Additionally, compliance and tolerability has been a major concern with conventional therapy as patients usually suffer from gastrointestinal symptoms due to the multiple doses needed to achieve therapeutic response.4

Burosumab is a fully human IgG1 monoclonal anti-FGF23 antibody that addresses the underlying pathophysiology of XLH and demonstrates significant clinical improvement in related symptoms. It was approved by the FDA in 2018 and is indicated for the treatment of XLH in adult and pediatric patients 6 months of age and older.6

AIM

The aim of this study was to evaluate the effect of burosumab treatment in Saudi pediatric XLH patients previously on conventional therapy.

METHODS

The study analyzed the data of six pediatric XLH patients (median age of 8.8 years) collected from three centers [National Guard Hospital (Riyadh), King Faisal Specialist Hospital (Riyadh) and National Guard Hospital (Jeddah)] from 2018-2020. Biochemical parameters including serum phosphate, alkaline phosphate (ALP) and tubular maximum re-absorption of phosphate to glomerular filtration rate (TmP/GFR) were collected at diagnostic, every month until three months, and every three months until 24 months into burosumab treatment. Burosumab was administered at a starting dose of 0.8 mg/kg and the dosing was increased at three months to 1.14 mg/kg and 1.07 mg/kg in two patients and at six months to 1.03 mg/kg in one patient.

RESULTS

All patients had improved biochemical parameters at two years of burosumab treatment (Table 1).

Table 1: Effect of burosumab in Saudi pediatric XLH patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Laboratory parameter</th>
<th>Washout</th>
<th>Burosumab therapy (1 year)</th>
<th>Burosumab therapy (2 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1M</td>
<td>Serum phosphate</td>
<td>1.05</td>
<td>1.03</td>
<td>1.01</td>
</tr>
<tr>
<td>2M</td>
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<tr>
<td>18M</td>
<td>Serum phosphate</td>
<td>0.91</td>
<td>1.03</td>
<td>1.03</td>
</tr>
</tbody>
</table>

The improvement in ALP levels was consistent for all patients throughout the burosumab treatment duration (Figure 2).

All patients had increased serum phosphate and reduced ALP levels in the first year of treatment. Burosumab also led to improved TmP/GFR levels at 12 months in the five patients for which data was available.

Four patients reported continuous improvement in the serum phosphate levels in the second year of burosumab treatment. Two patients reported initial serum phosphate improvement but presented with reduced levels after 21 months due to treatment compliance issues with episodic discontinuations related to the COVID-19 pandemic (Figure 1).

The x-ray evaluation indicated marked improvements in rickets (Figure 3).

Figure 1: Serum phosphate at 24 months of burosumab treatment

The x-ray evaluation indicated marked improvements in rickets (Figure 3).

Figure 2: Alkaline phosphatase at 2 years of burosumab treatment

The improvement in ALP levels was consistent for all patients throughout the burosumab treatment duration (Figure 2).

CONCLUSIONS

The two-year experience demonstrated that treatment with burosumab led to marked radiological and biochemical improvement in pediatric XLH patients in Saudi Arabia.

REFERENCES


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