TWO-YEAR EXPERIENCE OF BUROSUMAB THERAPY IN PEDIATRIC XLH PATIENTS IN SAUDI ARABIA

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INTRODUCTION

X-linked hypophosphatemia (XLH) is a rare, hereditary, progressive and lifelong phosphate wasting disorder characterized by pathological elevations in fibroblast growth factor (FGF) 23 concentration and activity.[1,2]

Conventional therapy for the treatment and management of XLH usually involves the combination of oral phosphate and active vitamin D analogues.[2] 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.[2] Research indicates linear growth failure in approximately 25-40% of the patients with well-controlled XLH.[3] 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.[5-7]

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 phosphatase (ALP) and tubular maximum re-absorption of phosphate to glomerular filtration rate (TmP/GFR) were collected at diagnosis; 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

Patient #	Laboratory parameter	Washout	Burosumab therapy (1 year)						Burosumab therapy (2 years)			
			1M	2M	3M	6M	9M	12M	15M	18M	21M	24M
1	Serum phosphate (mmol/L)	0.82	1.24	1.15	1.03	1.16	1.14	1.19	1.04	1.12	1.15	1.13
	ALP (IU/L)	545	591	558	580	499	555	471	471	528	513	453
	TmP/GFR (mmol/L)	0.83	1.34	1.21	1.00	2.36	0.90	1.13	0.89	NA	1.02	0.73
2	Serum phosphate (mmol/L)	0.63	1.27	1.26	1.08	1.04	1.00	1.13	0.96	0.77	1.06	0.95
	ALP (IU/L)	206	NA	168	149	120	130	108	88	96	126	108
	TmP/GFR (mmol/L)	0.75	1.47	1.33	1.24	1.28	1.32	1.23	1.04	0.71	NA	1.21
3	Serum phosphate (mmol/L)	0.71	1.35	1.25	1.12	1.15	1.05	1.09	1.31	0.77	1.07	0.74
	ALP (IU/L)	472	367	358	321	338	331	325	331	321	359	439
	TmP/GFR (mmol/L)	0.60	1.50	1.31	1.21	1.31	0.87	NA	1.60	0.64	0.90	NA
4	Serum phosphate (mmol.L)	0.63	0.93	1.23	0.98	1.13	1.16	1.37	1.12	0.62	1.13	0.64
	ALP (IU/L)	344	294	292	339	376	343	299	331	337	291	304
	TmP/GFR (mmol/L)	0.78	1.06	1.38	1.03	1.27	1.00	NA	1.35	0.52	0.96	NA
5	Serum phosphate (mmol.L)	0.65	0.91	1.00	0.98	1.00	0.94	0.95	1.08	0.98	0.97	1.04
	ALP (IU/L)	NA	568	458	405	512	410	388	332	325	325	338
	TmP/GFR (mmol/L)	NA	0.53	0.93	0.95	0.94	0.93	0.94	0.96	0.97	0.94	1.10
6	Serum phosphate (mmol.L)	0.44	0.96	1.00	1.05	0.89	0.94	1.26	0.82	1.06	0.93	0.97
	ALP (IU/L)	233	203	159	151	138	113	119	144	133	109	89
	TmP/GFR (mmol/L)	0.48	0.84	NA	NA	NA	NA	NA	0.6	NA	0.75	0.78

Abbreviations: NA - not available or not performed; ALP alkaline phosphate; TmP /GFR tubular maximum re absorption to glomerular filtration rate

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).

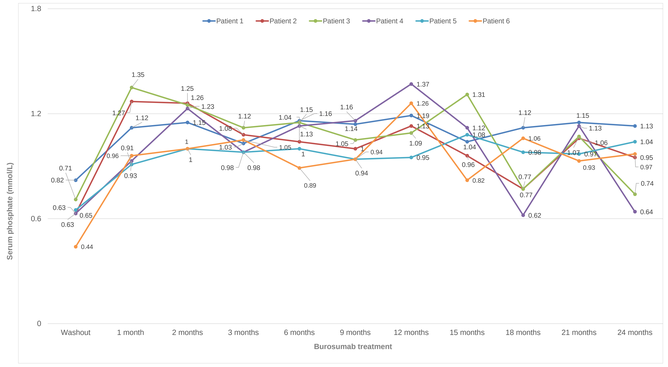

Figure 1: Serum phosphate at 24 months of burosumab treatment

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

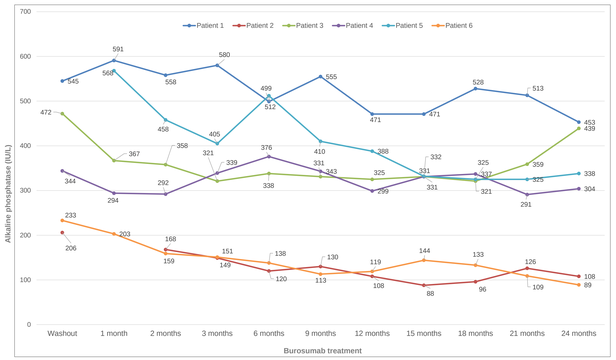

Figure 2: Alkaline phosphatase at 2 years of burosumab treatment

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

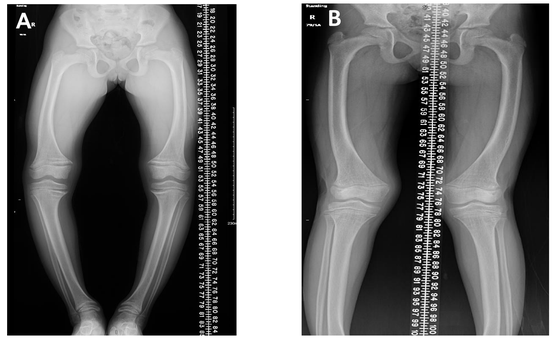

Figure 3: Radiological improvement with burosumab treatment in Patient 2

(A) Baseline lower extremity X-ray at baseline showed bilateral genu varus and and widening and cupping in the medial aspect of the distal femur
(B) Lower extremity X-ray after 2 years of burosumab treatment showed almost healed rickets in the proximal tibia and lateral aspect of the distal femur

Burosumab was well tolerated by all patients and there were no treatment-related adverse events recorded.

CONCLUSIONS

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

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