GONADOTROPIN-RELEASING HORMONE ANALOG TREATMENT IN CHIL DREN WITH IDIOPATHIC CENTRAL PRECOCIOUS PUBERTY: A PHARMACOVIGILANCE STUDY IN A PEDIATRIC POPULATION.

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INTRODUCTION

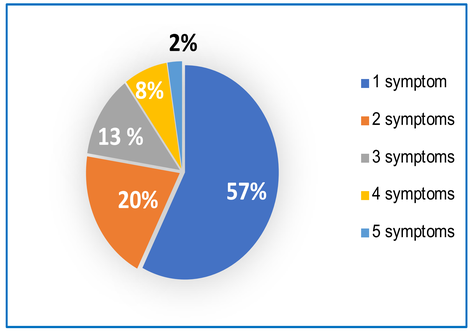
Central precocious puberty (CPP) results from premature activation of hypothalamic-pituitary-gonadal axis. GnRH stimulates the development of secondary sexual features, rapid bone maturation and growth. GnRH agonists (GnRHa) represent the gold-standard therapy in children with CPP. Several pharmaceutical formulations of GnRHa, such as buserelin, histrelin, leuprorelin, triptorelin and goserelin, are available and used clinically. The treatment is generally safe and well tolerated. However, several studies reported side effects, including bruising, pain, injection reactions and sterile abscesses. Furthermore, flushes, headaches, and nausea were observed and are classified as minor menopausal-like side effects.
The aim of our study was to identify which side effects were featured in CPP patients enrolled in this study

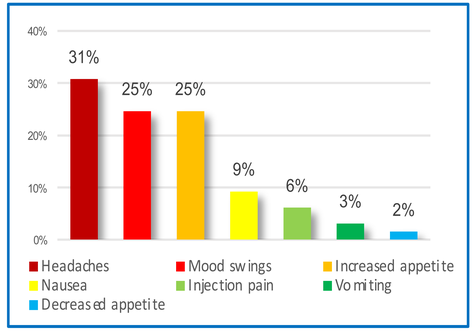
METHODS

Our retrospective study carried out from 2018 to 2020. The enrolled patients were treated with leuprolide (46 patients) or triptorelin (39 patients) and minor menopausal-like side effects appearance during therapy was investigated. Moreover, clinical parameters and radiological changes were monitored to evaluate the possible relationship between **GnRHa** treatment and side effects appearance.

RESULTS

- N=85 patients enrolled (median age 7.35 ± 0,67);
- N=40 symptomatic patients;
- N=23 patients treated with leuprolide and N=17 patients with triporelin reported symptoms (p=0.043);
- The patients treated with triptorelin showed mainly headache (N=13);
- The patients treated with leuprolide showed mainly increased appetite (N= 8) and mood swing (N=8);
- The bone age was significantly lower in symptomatic patients (p=0,004) than in those asymptomatic;
- No significant differences were observed between symptomatic and asymptomatic patients in chronological age (p=0,16), weight (p=0,20) and height (p=0,29) before treatment;
- Symptomatic patients showed a higher ovarian volume and breast growth (BG) than that observed in asymptomatic female (p=0,005);
- No significant differences were detected in peak-stimulated or basal LH,FSH and somatomedin C levels between the two groups of patients.





		Symptomatic patients	Asymptomatic patients	p-value
Clinical evolution	Basal LH (mIU/L)	0.77 ± 0.95	0.53 ± 0.64	0.09
	Basal FSH (mIU/L)	3.58 ± 2.15	2.98 ± 1.57	0.08
	Peak LH stimulated (mIU/L)	13.26 ± 11.07	12.08 ± 14.56	0.14
	Peak FSh stimulated (mIU/L)	14.08 ± 4.97	14.48 ± 0.79	0.36
	Somatomedin C (ng/mL)	263.10 ± 88.75	274.60 ± 117.41	0.23
Radiologic evolution	Uterine lenght (mm)	37.93 ± 7.31	37.53 ± 8.47	0.41
	Ovarian DX volume(cc)	2.70 ± 1.31	2.00 ± 1.22	0.01
	Ovarian SX volume(cc)	2.13 ± 0.88	2.12 ± 1.33	0.24
	Endomatrial rhyme	21	28	0.47

Clinical parameters	Symptomatic patients	Asymptomatic patients	p-value
Chronological Age T0	7.11 ± 0.63	7.39 ± 0.79	0.16
Chronological Age T2	9.89 ± 0.59	10.12 ± 10.12	0.06
Bone Age T0	9.09 ± 1.04	9.70 ± 0.90	0.04
Bone Age T2	11.40 ± 0.88	11.56 ± 0.79	0.23
Initial Body Weigh (Kg)	29.08 ± 6.53	27.98 ± 5.08	0.20
Height T0	126.30 ± 7.00	127.08 ± 5.77	0.29
Height T2	155.63 ± 5.84	155.51 ± 5.99	0.47
Ph1	42.50 %	26.67 %	0.055
Ph2	50.00 %	60.00 %	0.055
Ph3	7.50 %	13.33 %	0.055
B1	2.50 %	11.11%	0.005
B2	57.50 %	71.11%	0.005
B3	40.00%	17.78 %	0.005

CONCLUSIONS

Our results suggest the need of implementing pharmacovigilance activity in pediatric patients treated with GnRH agonists in order to optimize and personalize the treatment.

REFERENCES

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