Efficacy and Safety of Long-Acting Gonadotropin Releasing Hormone Analogs

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Gonadotropin-releasing hormone analog (GnRHa) therapy is an efficacious treatment for suppressing pubertal progression in young patients with central precocious puberty (CPP), is considered standard-of-care for this indication, and results in improved height and psychosocial outcomes (1). However, usage of GnRHa's in children with early-normal and/or normally-timed but rapid tempo puberty lacks clear-cut efficacy in terms of height preservation/augmentation (2). While there has been concern that GnRHa therapy may be associated with increases in body mass index and decreases in bone mineral density, available long-term data do not support these or other long-term adverse consequences (3). However, there remain conflicting data on the long-term risk of polycystic ovarian syndrome in conjunction with CPP (3). Treatment with injectable GnRHa formulations does not appear to impair gonadal function after treatment cessation, with onset or return of menarche within 1-2 years of treatment cessation, and normal rates of fertility so far in limited long-term follow-up studies (4). Because of these limited available data from females in their late teens to adulthood regarding the impact of GnRHa therapy on fertility, a long-term study investigating fertility, fecundity, and health of offspring would be a valuable addition to our understanding of the safety of this class of drugs. The ability to compare differential results among types of GnRHa therapy used is limited by the depth of the published literature. Physiological effects after treatment discontinuation with histrelin, which has only been available in US to treat children with CPP for ~9 years, have not been fully evaluated, but clearly merit further assessment and we await results from a patient registry investigating long-term follow-up of girls with CPP treated with histrelin, which will evaluate time to menarche or resumption of menses. There are currently no long-term post-treatment follow-up data on 3-monthly depot leuprolide, and such data would also be of great value.

References

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