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DRUG POINTS

Slipped capital femoral epiphyses associated with the withdrawal of a gonadotrophin releasing hormone

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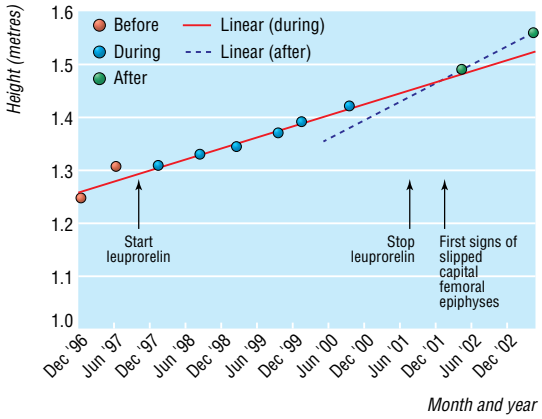
Leuprorelin, buserelin, and triptorelin belong to the group of gonadotrophin releasing hormone (GnRH) analogues. Kempers and Noordam previously reported an association between slipped capital femoral epiphysis during treatment with buserelin and triptorelin, or shortly after discontinuation of these drugs.[1]

The Netherlands Pharmacovigilance Centre Lareb received a report concerning an 11 year old girl who had been using leuprorelin 3.75 mg once monthly over four years, for precocious puberty. Seven months after the last injection she experienced pain in her right leg. An ultrasound showed a slight excess of synovial fluid in the hip. The pain increased, and in addition the patient complained about pain in her left hip. Two months later an x ray film showed bilateral slipped capital femoral epiphyses of both hips. The patient recovered fully after treatment with a dynamic hip screw. The initial symptoms coincided with the increase in growth velocity shortly after treatment with leuprorelin was stopped (figure).



Patient's growth curve before, during, and after the use of leuprorelin; linear trend lines during and after use

Slipped capital femoral epiphyses occur mainly in boys in late childhood or adolescence and are associated with delayed skeletal maturation, overweight, high growth velocity, and tall stature.[1 2] The incidence is reported to vary between 0.71/100 000 and 61/100 000.[1] None of the patients described in literature met the typical risk factors, and neither did our patient. Four out of five events of slipped capital femoral epiphyses associated with GnRH agonist reported in the literature, as well as in our patient, occurred shortly after the drug had been discontinued. The assumption had been that during treatment with a GnRH agonist low oestrogen concentrations decrease epiphyseal activity and weaken the epiphyseal plate.[1] The increase in growth velocity after stopping GnRH agonist, subsequently results in a reduction of the shearing force needed for the displacement of the epiphysis.[1] A similar mechanism may be involved in children treated with growth hormone, who were more likely to develop slipped capital femoral epiphyses than children with idiopathic short stature who were not treated.[3] We suggest that cessation of GnRH agonists be added to the list of known risk factors for slipped capital femoral epiphysis.

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