REPRODUCTIVE ENDOCRINOLOGY

Kisspeptin treatment for infertility?

Hyperprolactinaemia is associated with decreased levels of gonadotrophic-releasing hormone (GnRH) and is a major cause of anovulatory infertility. Findings of a new study in mice suggest that kisspeptin is a potential therapy for infertility in women with hyperprolactinaemia.

GnRH replacement therapy rescues fertility induced by hyperprolactinaemia in humans, but prolactin might not suppress gonadotrophin release by acting directly on GnRH neurons. A team of researchers led by Nadine Binart of Université Paris-Sud set out to test the theory that prolactin acts on kisspeptin neurons upstream of GnRH neurons.

The investigators inserted prolactin-releasing minipumps into mice to generate a model of hyperprolactinaemia. These mice did not have regular oestrous cycles, had impaired ovulation and reduced serum levels of luteinizing hormone and follicle-stimulating hormone, and had reduced expression of kisspeptin in areas of the

brain involved in sex steroid feedback. However, daily injections of kisspeptin restored cyclicity and ovulation rate.

Additionally, *in vitro* studies using mouse hypothalamic explants showed that GnRH release was inhibited by treatment with prolactin. However, administration of kisspeptin restored GnRH secretion.

“High levels of prolactin block expression of kisspeptin, a hormone that induces secretion of GnRH,” explains Binart. “By administering kisspeptin we restored ovulation in mice with high levels of serum prolactin. Clinical trials are in progress in our hospital to investigate the efficacy of kisspeptin as a treatment for infertility induced by hyperprolactinaemia.”

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Original article Sonigo, C. *et al.* Hyperprolactinemia-induced ovarian acyclicity is reversed by kisspeptin administration. *J. Clin. Invest.* **122**, 3791–3795 (2012)