



Hormone offers promise as fertility treatment

New research suggests the hormone kisspeptin shows promise as a potential new treatment for infertility. The research is being presented at the annual Society for Endocrinology BES meeting in Harrogate. Scientists led by Dr Waljit Dhillon from Imperial College London, have shown that giving kisspeptin to women with infertility can activate the release of sex hormones which control the menstrual cycle. This research could lead to a new fertility therapy for women with low sex hormone levels.

Kisspeptin is a product of the KISS-1 gene and is a key regulator of reproductive function. Animals and humans lacking kisspeptin function do not go through puberty and remain sexually immature. In a previous study, Dr Waljit Dhillon and colleagues showed that kisspeptin treatment leads to the production of sex hormones in fertile women; they have now extended their research to look at the effects of kisspeptin in women whose periods have stopped due to a hormone imbalance.

In this study, funded by the Medical Research Council, The Wellcome Trust and National Institute for Health Research, a group of ten women who were not menstruating and infertile, were injected with either kisspeptin (n=5) or saline (control, n=5). Blood samples were then taken to measure their levels of luteinising hormone (LH) and follicle stimulating hormone (FSH), two sex hormones essential for ovulation and fertility. Kisspeptin led to a 48-fold increase in LH and 16-fold increase in FSH, when compared to the control treatment.

This is the first study to show that kisspeptin can stimulate sex hormones in women with infertility and presents kisspeptin as a potential new therapy for human infertility.

Researcher Dr Waljit Dhillon from the Department of Investigative Medicine at Imperial College London said:

"Infertility is a devastating condition that affects millions of couples worldwide. This research shows that kisspeptin offers huge promise as a treatment for infertility. From our previous results, we know that kisspeptin can stimulate release of reproductive hormones in healthy women. We have now extended this research to show that kisspeptin treatment has the same effect in women with infertility. In fact, our current data show that kisspeptin causes a greater increase in luteinising hormone production in non-menstruating women, than that in fertile women in the previous study. This is a very exciting result and suggests that kisspeptin treatment could restore reproductive function in women with low sex hormone levels. Our

future research will focus on determining the best protocol for repeated kisspeptin administration with the hope of developing a new therapy for infertility.”

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Notes for editors

The paper will be presented at the Society for Endocrinology BES meeting at 16:15 on Monday 16 March 2009. The abstract for this work is reproduced below: see <http://www.endocrine-abstracts.org/ea/0019/ea0019oc4.htm>. This work was funded by the National Institute for Health Research, Medical Research Council and The Wellcome Trust.

The Society for Endocrinology BES 2009 is Britain's biggest scientific meeting on hormones, and is taking place at the Harrogate International Centre, Harrogate, from 16-19 March 2009. For the full programme, please see <http://www.endocrinology.org/meetings/2009/sfebes2009/prog/prog.aspx>

Please mention the Society for Endocrinology BES meeting in any story

For more information: please contact the Society for Endocrinology press office

Rebecca Ramsden

Public & Media Relations Assistant

Mobile: +44 (0)7531 945 676

Tel: +44 (0)1454 642 252

Email: rebecca.ramsden@endocrinology.org

Jennie Evans

Public & Media Relations Officer

Mobile: +44 (0)7773 797 501

Tel: +44 (0)1454 642 230

Email: jennie.evans@endocrinology.org

The Society for Endocrinology is Britain's national organisation promoting endocrinology and hormone awareness. For general information, please visit our website: <http://www.endocrinology.org>

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ABSTRACT

Kisspeptin Potently Increases Reproductive Hormone Release in women with hypothalamic amenorrhoea – a potential novel therapy for infertility

CN Jayasena¹, OB Chaudhri¹, GK Nijher¹, KG Murphy¹, A Ranger¹, A Lim², D Patel², A Mehta², C Todd², R Ramachandran¹, V Salem¹, GW Stamp³, M Donaldson⁴, MA Ghatei¹, SR Bloom¹, WS Dhillon¹

¹Dept of Investigative Medicine, Imperial College London, Hammersmith Hospital, United Kingdom,

²Dept of Imaging, Imperial College Healthcare NHS Trust, Charing Cross Hospital, United Kingdom,

BACKGROUND: Kisspeptin is a critical regulator of normal reproductive function. In humans inactivating mutations of the kisspeptin receptor GPR54 cause hypogonadotropic hypogonadism and pubertal failure. Activating mutations of GPR54 cause precocious puberty. Hypothalamic amenorrhoea (HA) accounts for over 30 percent of cases of amenorrhoea in women of reproductive age. Current treatments have limited success rates and side effects. In rodent models of HA hypothalamic KISS1 expression is reduced, and kisspeptin administration restores reproductive function. We recently demonstrated that subcutaneous (sc) kisspeptin injection (6.4nmol/kg) stimulates reproductive hormone release in human females with normal menstrual cycles. The effects of kisspeptin administration in patients with infertility have not been investigated previously.

AIM: To determine the effects of kisspeptin administration on gonadotrophin release in infertile women with HA.

METHODS: We performed an ethically approved prospective, randomised, double-blinded study. Patients with HA received a sc bolus injection of either kisspeptin-54 (6.4nmol/kg) or 0.9% saline (n=5 per group). Blood was sampled at regular intervals for 4 hours post-injection for measurement of plasma gonadotrophins.

RESULTS: Kisspeptin potently increased mean luteinising hormone (LH) 48-fold and follicle stimulating hormone (FSH) 16-fold when compared to saline injection (mean change over 4 hours post-injection compared to baseline: LH (IU/l); saline 0.5 ± 0.6 , kisspeptin 24.0 ± 3.5 , ($P < 0.001$). FSH (IU/l); saline 0.6 ± 0.7 , kisspeptin 10.2 ± 3.5 , ($P < 0.001$). Subjects with HA were over 4-fold more responsive to kisspeptin injection than previously studied healthy females in the follicular phase of the menstrual cycle (mean area under curve LH increase: HA 40.2 h.iU, healthy females in follicular phase 9.8 h.iU, $P < 0.01$).

CONCLUSION: In this first study of kisspeptin administration within a human model of infertility, we demonstrate that exogenous administration of kisspeptin in women with HA potently stimulates LH and FSH release. Our data shows that kisspeptin is a potential novel therapy for human infertility.