Society for Endocrinology - Media Release

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New hormone treatment shows potential to reverse infertility

Twice weekly injections of the hormone kisspeptin may provide a new treatment to restore fertility in some women. The research is being presented at the Society for Endocrinology BES meeting in Manchester. The findings show that twice-weekly injections of kisspeptin can lead to increases in the levels of sex hormones, which control the menstrual cycle. This is the first study to show this effect can be maintained over the long term and it may lead to new therapies for women whose infertility is due to 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. A team led by Dr Waljit Dhillo of Imperial College London studied women with a condition called hypothalamic amenorrhoea, where a deficiency in sex hormone levels prevents menstruation, resulting in infertility. This affects several thousand women in the UK each year. Previously, Dr Dhillo's group found that a one-off injection of kisspeptin caused an increase in sex hormone production in these women, but further daily administration was not effective as the system stopped responding. The aim of the present study was to examine kisspeptin's potential as a fertility treatment by finding a dose regimen that would maintain sex hormone production over a sustained period of time.

Over eight weeks, a group of 10 women with hypothalamic amenorrhoea were either given twice-weekly injections of kisspeptin (n=5) or twice-weekly injections of saline as a control (n=5). Blood samples were then taken at regular intervals to measure their levels of luteinising hormone (LH) and follicle stimulating hormone (FSH), two sex hormones essential for ovulation and fertility. Women demonstrated a large increase in circulating sex hormones on day 0 (mean maximal LH increase 21.5IU/l), which was halved to 10.0IU/l on day 14. However, after day 14, their responsiveness to the kisspeptin treatment remained steady. On the last day of the trial, women who had been given kisspeptin injections showed a 16-fold increase in their hormonal response, compared to the saline controls.

This is the first long term clinical study to examine the effectiveness of kisspeptin treatment. Twice-weekly injections of kisspeptin, administered over a two month period, can successfully stimulate the release of sex hormones in women with infertility due to hypothalamic amenorrhoea and this treatment does not cause any side-effects. These findings now need to be confirmed in large-scale randomised trials, before any treatments can be brought into clinical practice.

Researcher Dr Waljit Dhillo said:

"Infertility is a highly distressing condition and affects up to one in seven couples in the UK. The results of our study are exciting as they show that kisspeptin may be a novel method for restoring fertility to women with certain types of infertility. Our findings show that an injection of kisspeptin given twice-weekly can reinvigorate the reproductive hormone system in women and raise their levels of luteinising hormone and follicle stimulating hormone, both of which are essential for fertility.

"It is important to emphasise that this is only a small study and we need to carry out further work before our findings can be brought into clinical practice. Our next step is to perform a much bigger clinical study with a larger number of participants to see if kisspeptin administration can enable women with hypothalamic amenorrhoea to regain fertility."

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Notes for editors

This research will be presented as a poster (no. 328) at the Society for Endocrinology BES meeting. The poster will be attended from 12:00-13:30 on 16 March and 12:45-14:15 on 17 March. The abstract for this work is reproduced at: http://www.endocrine-abstracts.org/ea/0021/ea0021P328.htm. This work was funded by the National Institute for Health Research, Medical Research Council and The Wellcome Trust.

The Society for Endocrinology BES 2010 conference is Britain's biggest scientific meeting on hormones, and is taking place at the Manchester Central Convention Complex from 15-18 March 2010. For the full programme, please see http://www.endocrinology.org/meetings/2010/sfebes2010/.

Please mention the Society for Endocrinology BES meeting in any story

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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

Twice-weekly administration of kisspeptin leads to long-term stimulation of reproductive hormone release in infertile women with hypothalamic amenorrhoea

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Background: Hypothalamic amenorrhoea (HA) accounts for over 30% of cases of amenorrhoea in women of reproductive age. Current treatments have limited success rates and side effects. We have recently shown that a single injection of the novel hormone kisspeptin potently stimulates reproductive hormone release in women with HA. However, twice-daily kisspeptin administration to women with HA, results in tachyphylaxis due to desensitisation of the kisspeptin receptor. This suggests that less frequent administration of kisspeptin may lead to sustained reproductive hormone release in women with HA, which would have therapeutic implications.
Aim: To determine if long-term twice-weekly kisspeptin administration chronically stimulates reproductive hormone release in women with HA.
Methods: We performed an ethically approved prospective, randomised, single-blinded, parallel design study. Patients with HA received twice-weekly s.c. injection of either kisspeptin (6.4 nmol/kg) or saline (n=5/group) for 56 days. On days 0, 14, 28, 42 and 56, blood was sampled at regular intervals for 4 h post-injection for measurement of plasma LH and FSH.
Results: Women were more responsive to kisspeptin injection on day 0 than day 14 (mean maximal LH increase in IU/l: day 0, 21.5±10.7; day 14, 10.0±4.3; P<0.001). However there was no further significant drop in responsiveness to kisspeptin beyond day 14 (mean maximal LH increase in IU/l: day 28, 9.0±4.1; day 42, 8.9±3.5; day 56, 7.9±4.5; P>0.05 versus response on day 14). On the last (56th) day, women with HA were still 16 times more response to kisspeptin than saline. No adverse effects following kisspeptin administration were observed during the study.
Conclusion: In this first long-term study of kisspeptin administration to women with HA, we have demonstrated that twice-weekly kisspeptin administration stimulates reproductive hormone release in a sustained manner. Thus kisspeptin may be a future novel therapy for reproductive disorders.