Acute and chronic effects of kisspeptin-54 administration on GH, prolactin and TSH secretion in healthy women

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Introduction

- Kisspeptin (KP-54) is a hypothalamic neuropeptide acting on the KISS1R at GnRH neurons to secrete GnRH into the portal circulation (1,2,3).
- GnRH then acts on pituitary gonadotrophs to secrete gonadotrophins.
- Inactivating mutations of KISS1R lead to pubertal failure (4,5).
- KISS1R are found in various tissues including the pituitary (6).
- KP-54 is being used in various clinical trials, including as the trigger for oocyte maturation in IVF.
- There is an ongoing debate due to conflicting animal studies as to whether KP-54 stimulates non-reproductive pituitary hormones.
- There have been no human studies to date looking at the effects of kisspeptin on non-reproductive pituitary hormones.

Aim

To establish whether kisspeptin-54 stimulates non-reproductive pituitary hormones in healthy female volunteers.

Methods

- Post hoc analysis of a prospective, single blinded, placebo controlled, one way cross over study (6).
- 5 healthy women (aged 24-37).
- Month 1 – self administered subcutaneous injections of 0.9% saline twice daily from day 7-14 of the menstrual cycle.
- Month 2 – self administered subcutaneous injections of kisspeptin-54 twice daily from day 7-14 of the menstrual cycle (6.4 nmol/kg).
- Study 1 – acute effects of kisspeptin for 4 hours after 1st injection.
- Study 2 – GH pulsatility 4 days after starting injections. 8 hours of regular blood sampling to review GH pulsatility.
- Study 3 – Chronic effects of kisspeptin at day 14 compared with hormone levels on day 7 (first and last day of injections).

Conclusion

- For the first time in humans we have investigated the effects of kisspeptin on non-reproductive pituitary hormones.
- We observed no significant change in GH, TSH or PRL after kisspeptin administration, either acutely or after 7 days.
- It is important to recognise that we cannot exclude that kisspeptin has subtle effects on the secretion of these hormones.
- As kisspeptin is emerging as a possible treatment for certain infertility disorders, our data importantly suggests that at the dose tested, kisspeptin does not cause stimulation of other pituitary hormones.

Results – Acute effects

- Time profile of Kisspeptin-IR after injection, (A) GH, (B) PRL and (D) TSH hormone levels presented as AUC. No significant difference in hormone levels between groups.

Results – GH pulsatility

- Mean amplitude of the GH pulses collated for the five participants.

Results – Chronic effects

- Chronic effects of kisspeptin-54 on GH pulsatility.
- Grouped mean GH results for each time point of the 8 hour study following 4 days of twice daily injections of kisspeptin-54 (month 2).
- Collated results from all participants and shown for (A) GH, (B) PRL and (C) TSH. No statistical difference in hormone levels between the vehicle and kisspeptin groups or between the day 7 and 14 results.

References