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JOURNAL ARTICLE

Comparative effects of two different delivery systems on gonadotropin-releasing hormone (GnRH) antagonist-induced suppression of gonadotropins and testosterone in man

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The Nal-Glu gonadotropin-releasing hormone (GnRH) antagonist, when given in daily subcutaneous (SC) doses of 5 mg or higher, maximally suppresses serum luteinizing hormone (LH) and follicle-stimulating

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hormone (FSH) levels to near undetectable levels and induces azoospermia in normal men; lower doses (1.5 and 3.0 mg) are less effective. Cost and convenience are important considerations in contraceptive development. Studies with GnRH agonists suggest that constant delivery is more effective in suppressing gonadal function than equal doses by single daily injection. In this study, we examined whether the constant infusion (CI) of a submaximal suppressive dose (1.5 mg) of Nal-Glu would be more effective in suppressing the pituitary-gonadal axis than its repeated single daily injections (SDI). This (1.5 mg) dose was selected because the 5 mg dose given once daily SC for 21 days led to maximal suppression of LH, FSH, and testosterone (T) levels, whereas 1.5 mg once daily for 21 days gave only partial suppression. It was felt that if continuous infusion was considerably more effective than intermittent administration of this submaximal dose, then the development of long-acting sustained release delivery systems for contraceptives based on GnRH antagonist analogs would allow both reduced cost and enhanced convenience. One and a half mg of Nal-Glu was administered SC either as a SDI or CI over 24 hours for 21 days to two groups of five normal men. Three measurements of serum LH, FSH, and T were performed before antagonist injection and 1, 2, 4, 8, 12, 16, and 24 hours after Nal-Glu injection on days 0, 1, 7, 21. (ABSTRACT TRUNCATED AT 250 WORDS)

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