

Original Articles

Reproductive Biology Section

Very unusual symptoms consistent with a possible migraine immediately following the injection of recombinant follitropin beta

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Summary

Purpose: To present a new side effect of follitropin beta not shared with highly purified urinary follicle stimulating hormone (FSH). **Materials and Methods:** Follitropin beta was administered for preparation of in vitro fertilization-embryo transfer (IVF-ET). **Results:** Within a few minutes of injection of subcutaneously of follitropin beta, a 27-year-old woman developed a feeling of fever, headache, nausea, vomiting dizziness, and a visual aura consistent with migraine syndrome. These side effects did not occur when switched to highly purified urinary FSH. **Conclusions:** Since this reaction did not occur when injected with FSH not made with recombinant DNA technology, it is concluded that recombinant FSH (at least with follitropin beta) can produce an immediate migraine-like syndrome.

Key words: Recombinant FSH; Follitropin beta; Migraine headaches; High purified urinary FSH.

Introduction

It is important to make the public and medical field aware of side effects from medications even if extremely rare. It is even more important if an alternative equally effective therapy can be recommended to avoid these side effects. A case is reported of an usual constellation of symptoms that immediately followed the injection of recombinant follicle stimulating hormone (FSH) (follitropin beta). However, these side effects were not seen following injection of highly purified urinary FSH.

Case Report

A 27-year-old woman was treated with recombinant FSH (follitropin beta). Immediately after her first injection she felt feverish although her temperature was only 37.2°C. This was associated with visual hallucinations in the form of colored zigzag lines on the wall that looked like neon lights. She also experienced headaches, dizziness and nausea. The symptoms dissipated spontaneously two hours after the subcutaneous injection of 150 IU. She thought that these symptoms were coincidental, so she took a second injection the next day. Though the same symptoms occurred, they disappeared again about an hour later, she tried it one more time the next day. However, the same

symptomatology occurred and she consulted our office. The present authors advised her to seek the opinion of a neurologist before proceeding with any more gonadotropin injections.

The neurologist ascertained that she had no history of migraine headaches or hypertension. Her only reaction to medication was to oxycodone and other analgesics which caused severe nausea and vomiting. Occasionally wine would give her a headache.

Her complete neurological examination was negative. The woman was further evaluated by electroencephalogram (EEG) and an electrocardiogram (EKG). Both the EEG and EKG were normal. She asked the neurologist if she could recommend some type of treatment that could counteract the adverse reaction to FSH injections. The neurologist had no suggestions nor any explanations for these symptoms other than somehow the injection of follitropin beta may have cause a migraine headache with visual aura.

Since the patient wanted to proceed with in vitro fertilization (IVF) because of unexplained infertility, having failed to conceive despite luteal phase support with progesterone and intrauterine insemination. She consented to try FSH injections again. However, this time she was switched to highly purified urinary FSH. She has had no reaction at all to highly purified urinary FSH despite generation of supra-normal sera estradiol levels.

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Discussion

Something in the manufacturing process for recombinant FSH (at least follitropin beta) can induce a very unusual migraine-like syndrome. The reaction is too quick to consider it was related to a sudden increase in estradiol. Most likely it is an allergic reaction to some ingredient needed to form recombinant FSH. It could be specific to the manufacturing of just follitropin beta. However, follitropin alpha was never tried.

The fact that there was no reaction to high purified urinary FSH suggests that the reaction was specific to some

chemical used to prepare FSH using recombinant DNA technology rather than what is used for highly purified urinary FSH.

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