

THE ROLE OF RAT HYPOTHALAMUS KISS1, KISS1 RECEPTOR, NEUROKININ AND NEUROKININ RECEPTOR GENES IN THE PROLACTIN-INFERTILITY RELATIONSHIP

Eylül Akbal İŞİK^a, İnanet Nur USLU^a, Gülsevinç AY^a, Nesrin ÇETINEL^a, Gamze CÖMERTPAY^a, Hale ÖKSÜZ^a, Kübra AKILLIOĞLU^c, Ali Kemal TOPALOĞLU^b, Mehmet Bertan YILMAZ^a
^aCukurova University, Faculty of Medicine, Department of Medical Biology and Genetics, ^bDepartment of Paediatric Endocrinology, ^cDepartment of Physiology, Balcali-Adana

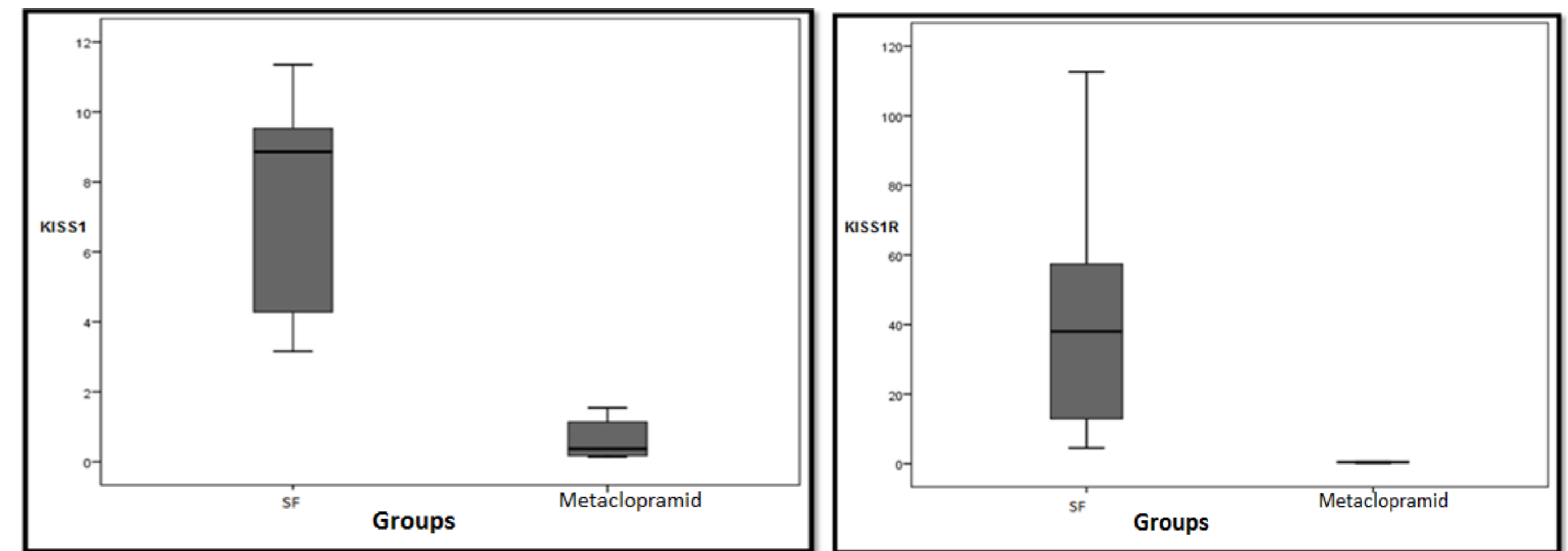
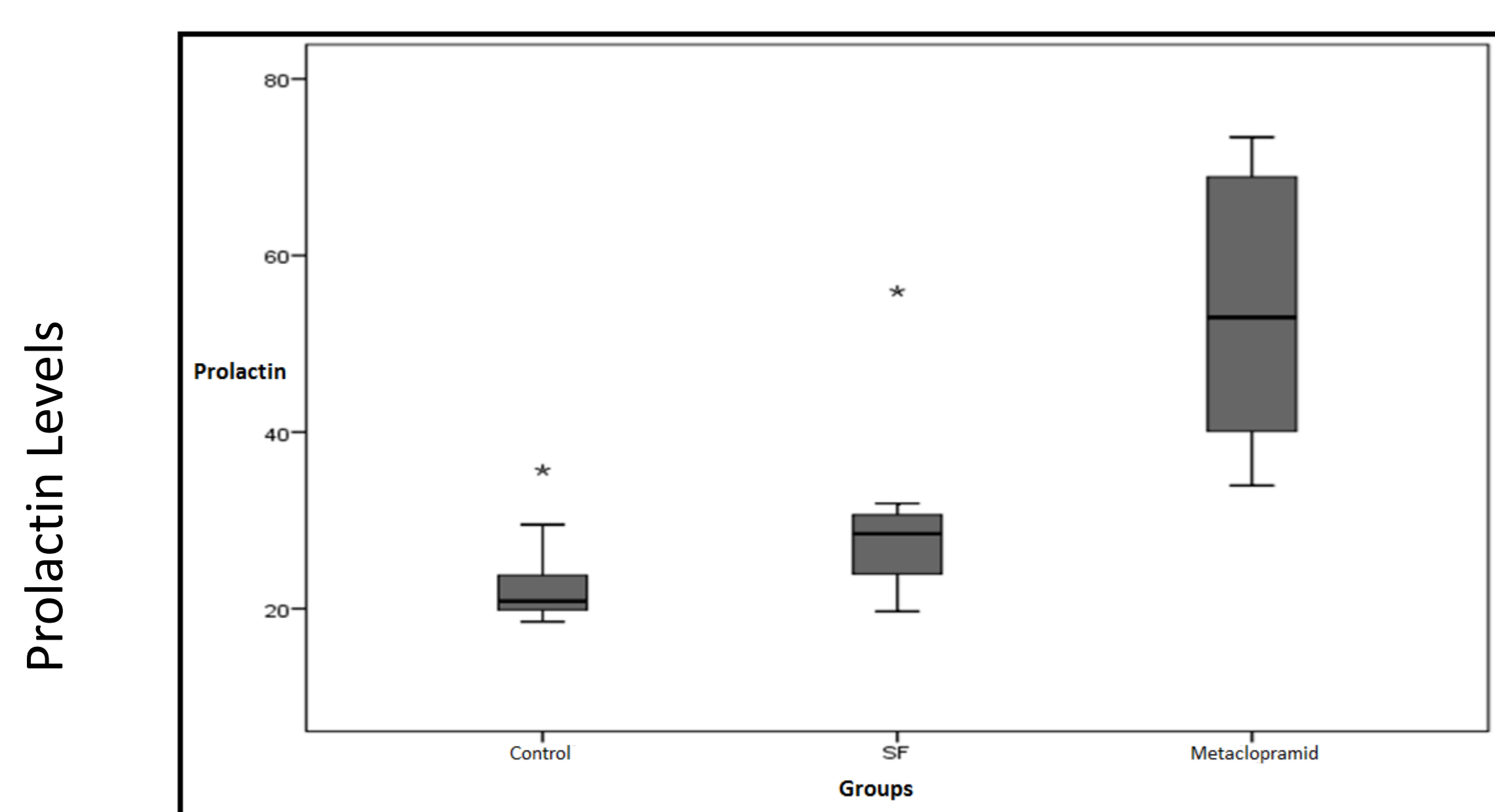
INTRODUCTION

Prolactin hormone, which is secreted from the hypophysis, plays a role in milk production. Prolactin also functions in metabolism and reproductivity. Increase in prolactin blood level leads to various disorders. The most important disorders of these are anovulation and amenore/galactore. Anovulation is a critical problem and gives rise to infertility. The ovulation can be controlled by hormones and biological substances called neuropeptide. It has been considered that kisspeptin and neurokinins are involved in the control of ovulation. Kisspeptins, encoded by Kiss1 gene separately expressed in neuronal populations of hypothalamus, are classified in neuropeptide family. They play crucial roles in timing of puberty and fertility. Furthermore, the other prominent neuropeptide, which has been thought to be effective in these situations, is Neurokinin B (NKB). In recent neuroanatomic studies, it has been shown that NKB is synthesized in particularly hypothalamic neurons and arcuate nucleus in response to sexual steroids. So it has been suggested that NKB indirectly affects KISS1 synthesis since NKB and kisspeptin reside together in this region. It has been long thought that NKB and KISS1 interact with hormones involved in puberty and reproductivity. In this regard our aim was to delineate the interaction between them.

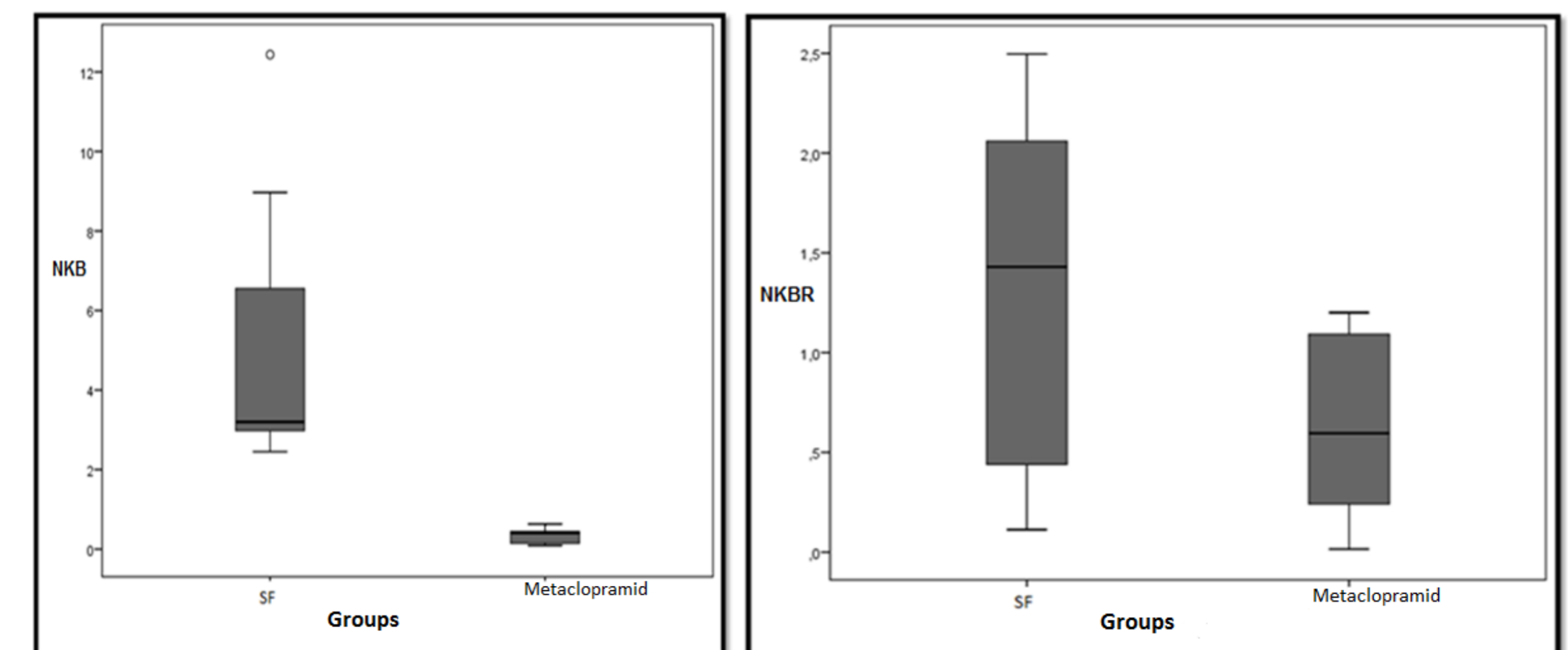
METHODS

In this study, 40 female 12-16 weeks old Wistar Albino rats were used. 3 groups were included; control group (10), physiological saline (SF) group (10), and metoclopramide group (20). Blood prolactin levels of rats belonging to all groups after two weeks of metoclopramide administration period prolactin was measured using ELISA immunoassay kit. Expression levels of Kiss1, Kiss1 Receptor, Neurokinin, Neurokinin Receptor genes were analyzed along with blood PRL levels of all rats.

RESULTS



Graph showing Kiss1, Kiss1R expression values in metoclopramide and SF groups



Graph showing NKB, NKBR expression values in metoclopramide and SF groups

CONCLUSION

This study investigated the relationship between prolactin and infertility in terms of kisspeptin and NKB. Therefore, in our study we investigated association between Kiss1, Kiss1 receptor, neurokinin and neurokinin receptor and infertility in face of increased in blood prolactin levels in rats.

We found that Rats with high prolactin levels had lower Kiss1, Kiss1 Receptor and neurokinin gene expression compared to control group ($p < 0,001$).

As a result, we believe that neuropeptides mediate adverse effects of increased prolactin on reproduction and our study may shed light on infertility problems caused by high prolactin levels.

- 1.Greenhall E, Vessey M. The prevalence of subfertility: our view of the current confusion and a report of two new studies. *Fertil. Steril*, 1990; 54: 978–983.
- 2.Biller BM, Luciano A, Crosignani PG, Molitch M, Olive D, Rebar R, Sanfilippo J, Webster J, Zacur H. Guidelines for the diagnosis and treatment of hyperprolactinemia. *J Reprod Med* 1999; 44(12):1075–1084.
3. Terasawa E, Fernandez DL. Neurobiological mechanisms of the onset of puberty in primates. *Endocr Rev*, 2001; 22: 111–151.
4. Cheng G, Coolen LM, Padmanabhan V, Goodman RL, Lehman MN. The kisspeptin/neurokinin B/dynorphin (KNDy) cell population of the arcuate nucleus: sex differences and effects of prenatal testosterone in sheep, *Endocrinology*, 2010;151(1):301-11.

Funding: Supported by Cukurova University Department of Scientific Research Projects . Project Number: TF2014YL3

Conflict of interest: There is no conflict of interest between authors