EVALUATION OF THE CLINICAL AND MOLECULAR REPERCUSSIONS OF THE USE OF CONTRACEPTIVES THAT CONTAIN ONLY PROGESTOGEN

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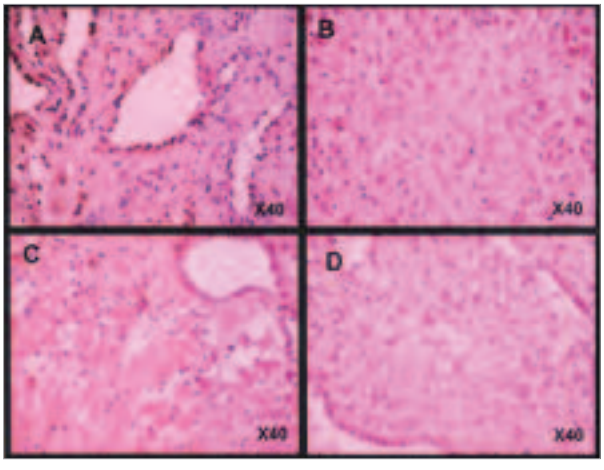

Immunohistochemical localization of chemokines in endometrium exposed to a levonorgestrel–releasing intrauterine system. (A) IL-8 in bleeding group, (B) IL-8 in non- bleeding group, (C) 6CKine in bleeding group, (D) 6CKine in non-bleeding group. IL, interleukin

There has been a trend towards the use of contraceptive methods containing just progestogen, among which implants, emergency contraception and SIU-LNG. With the increase in use, clinical evaluation has become important. This project aims to study aspects of contraceptive implants as endometrial alterations in women with and without bleeding, via metalloproteinase expression and microarray (cDNA). Also the prevalence of persistent ovarian follicles will be evaluated, an observation that is more frequent during the use of such methods. In addition, we will prospectirely evaluate the effect of the implants on bone mass. We have also studied emergency contraception (EC) with levonorgestrel, focusing on the acrosome reaction *in vitro*. We wish to study the calcium influx and the acrosome reaction *in vivo* in spermatozoids obtained from a uterine wash from women after the use of EC. Finally, the project also proposes new studies on the three monthly injectable medroxiprogesteron, byevaluating the function of the FSH isoforms during the use of this method.

SUMMARY OF RESULTS TO DATE AND PERSPECTIVES

Regarding the *in vitro* and *in vivo* influence of LNG upon sperm functions, we showed that the *in vitro* addition of LNG to capacitated human spermatozoa in amounts similar to those observed after the administration of LNG as EC did not affect the acrosomal reaction rate neither the calcium influx or tyrosine phosphorylation. However, when the quantity of LNG was higher and similar to that observed in users of the LNG-IUS, the *in vitro* LNG was able to affect the detection of D-mannose binding sites or pellucid zone (ZP) receptors. We evaluated whether the *in vivo* administration of LNG as EC to women was able to affect acrosomal reaction of sperm recovered from uterus and the expression of glycodelin-A in the endometrium. No effect was observed. These results changed the concept existing during the previous 30 years that the LNG as EC interfered with sperm functions.

In relation to the effects of the progestin-only contraceptives upon the endometrium we evaluated the effect in women with and without breakthrough bleeding (BTB) during use of progestin in order to understand the mechanism that provokes BTB in some women. The most important issue in the determination of BTB was mediated by inflammation. We are at present writing a manuscript about the endometrium of women with and without BTB in which we used the microarray technique. The results corroborated the inflammation as the main factor in BTB.

Regarding the clinical effects of the progestin-only contraceptives, we evaluated the effect on bone mineral density (BMD). We published the first study on BMD among users of the LNG-IUS which showed no deleterious effect when compared to controls. We are currently evaluating the same cohort at 10 years of use. Also, our group was the first to compared BMD in users of two models of subdermal contraceptive implants at baseline, 18 and 36 months of use and these women will be evaluated again at 60 months of use. Additionally, we evaluated the pharmacokinetics of depot medroxyprogesterone acetate (DMPA) among HIV-positive women users and non-users of triple antiretroviral therapy, and the results showed no effect. This observation reinforces the use of this highly effective contraceptive by young women in an unconcerned manner in countries where the prevalence of HIV infection is high. Also, we provide insight about the value of FSH among women on the menopausal transition who used DMPA and are in amenorrhea in order to determine menopausal status.

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