Endometrial cancer and hormonal contraceptives

Paula Cortiñas Sardi*

“I have heard what the talkers were
talking, the talk of the,
beginning and the end,,
but I do not talk for the beginning
or the end”.

Walt Whitman. Leaves of Grass.

Endometrial cancer is a disease in the majority of cases related to a hormonal imbalance, having the endometrial hyperplasia as a precursor lesion. The etiopathogenic theory of this neoplasm, involving estrogen influence on the endometrium unopposed by progestogen, has been demonstrated in other studies, highlighting pioneering the PEPI study (Postmenopausal Estrogen / Progestin Intervention Trial), which showed that the use of estrogen therapy without the progesterational counterbalance generated endometrial hyperplasia¹. Known endometrial cancer risk factors include obesity, anovulation, infertility and conditions related to a rise in estrogen and a decrease in progesterone production. The estrogen influence induces an increase in the rate of mitosis giving augmentation of cellular proliferation in endometrial glandular tissue. After ovulation the progestin produced by the corpus luteum has several effects at the level of the endometrial cell: decreases estrogen receptors, increases enzyme 17 β Hydroxysteroid, dehydrogenase that inactive estradiol. On the other hand the progestogen induces apoptosis, cellular differentiation, and the arrest of the cell cycle, compensating the proliferative effect of estrogen².

There is during the climacteric, by increasing the frequency of anovulatory cycles, a hormonal imbalance which could put at risk the patient of developing endometrial hyperplasia or

www.intervalolibre.wordpress.com
September 12, 2015.
endometrial cancer if it is not treated effectively with hormone therapy containing progestogens. In addition, patients with oligoamenorrhea, especially patients with polycystic ovary syndrome, are at risk for this disease due to a lower frequency of production of progestogens in the ovary because a lack of ovulation.

The use of oral contraceptives (OC), due to its antiproliferative effect on endometrial level, has been associated with a decrease in the risk of endometrial cancer, as we have discussed in other articles on this blog. There are several epidemiological studies that have been conducted confirming this association, however, there are no studies with a good level of evidence evaluating if this effect is maintained once ceases the use of the drug and for how long.

In August 2015, is published in the journal *Lancet Oncology* a meta-analysis of 36 studies included 27,276 patients with endometrial cancer and 115,743 without endometrial cancer in North America, Western Europe and Australasia. Of patients with endometrial cancer, 9,459 (35%) used CO and 45,629 (39%) of the patients without endometrial cancer used CO. Taking into account all the patients, in general, the risk of endometrial cancer was significantly lower in the patients who took CO ever compared to those that never did, with a RR 0.69 i.e. a 31% lower incidence. In addition, longer OC consuming is associated with a lower risk of endometrial cancer, with a 48% reduction (RR: 0.52) in patients who used CO between 10 and 15 years. An important finding is that the reduction is greater in women in which endometrial cancer diagnosis was carried out before the age of 60 (28%) than in women diagnosed after age 60 (21%). In the stratified analysis there was no variation in the association with respect to the rate of body mass, parity, use of hormone replacement therapy, menopausal status, smoking, age of menarche, ethnic origin or alcohol consumption. The most recent use of OC was associated with a greater risk reduction, but the protective effect of OCs is maintained for at least 30 years. With every 5 years of use, there is a reduction of 24% (p < 0.0001). No differences were observed between the incidence of endometrial cancer and the dose of estrogen contained in birth control, by which even in low doses of estrogen the protective effect remained, probably associated with the progestin in the formulation. The authors also found that the OC effect varies according to the histological type, with a higher reduction of risk with type I (32%) and less with type II (25%), being the reduction of risk of sarcoma much lower, only 17%; this finding must be related to hormonal etiology more associated to type I than with the two other histological types. In conclusion, the authors assert that thanks to contraceptives, from 1965 until 2014 have been avoided approximately 400,000 cases of endometrial cancer in the regions where the studied patients come from.

Several considerations of these results are derived. Firstly, the importance of the use of CO is anchored in polycystic ovary syndrome, not only for the control of manifestations of hyperandrogenism or menstrual disorders, but for the prevention of the endometrial cancer in this group of patients. Second, based on the results of this meta-analysis, the advantage of using CO in perimenopausal women without contraindication is reinforced in patients with need of contraception or menstrual disorders because the additional benefit of preventing the development of endometrial cancer in a period of increased susceptibility.
This new study reaffirms the concept that the ACO, in addition to prevention by 50% in ovarian cancer, also are positioned firmly in the prevention of endometrial cancer. Its use in well selected patients at risk for suffering from this neoplasia would prevent many cases of endometrial cancer. Hormonal contraception has proven over time to be a treatment with many therapeutic and preventive applications, whenever used under strict selection criteria.

*Gynecologist. Instituto de Oncología Luis Razetti, Salud Chacao y Clinica Santa Sofia, Caracas, Venezuela.

New York, September 11 2015.