

<https://doi.org/10.29289/259453942022V32S1005>

## 509 - ASSOCIATION BETWEEN LEVONORGESTREL-RELEASING INTRAUTERINE SYSTEM AND BREAST CANCER

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**Introduction:** The association between the use of hormonal contraception and breast cancer has been debated in the medical community for years. Although older studies have suggested an increase in breast cancer risk with the use of combined oral contraceptive (COC) pills, more recent studies have demonstrated the relative safety of combined contraceptives composed of estrogen and progesterone. Isolated progestagens are usually prescribed to women who have menstrual cycle disturbances; however, literature on the association between the use of isolated progestagens and breast cancer is still controversial. The levonorgestrel intrauterine system (LNG-IUS) device is a long-duration, reversible contraceptive. It has become popular due to its high efficacy as a birth control method and other beneficial effects, such as control of abnormal uterine bleeding and endometrial protection. Nevertheless, its safety regarding breast cancer has is still questioned. Furthermore, it has been debated whether it would be a viable choice for birth control for breast cancer survivors, as well as a tool for endometrial protection among women who use tamoxifen, which leads to endometrial thickening, polyps, and even hyperplasia and endometrial cancer. **Objective:** This study aims to present a literary review of the main articles within the theme of the use of LNG-IUS and its safety for breast cancer survivors and in the general population. **Methods:** A literature review was conducted for articles with this theme, using an electronic library, with predetermined keywords. **Results:** In total, 25 articles were selected that fulfilled the inclusion criteria. Progesterone has a proliferative effect on the breast during the luteal phase of the menstrual cycle, in addition to inducing alveologenesis during puberty and ductal branching during pregnancy. This proliferative effect takes place through the expression of cyclin D1 on nPR-expressing cells. Moreover, it presents a paracrine effect on the adjacent cells that do not express hormone receptors, through the activation of membrane receptors that activate the nuclear factor kappa beta — the receptor activator of NF- $\kappa$ B (RANK). Studies with animals showed that carcinogenesis was accelerated after the administration of progestagens, mediated by RANK ligands (RANKL). It is also known that levonorgestrel has an action on the 17-beta-hydroxysteroid dehydrogenase (17 $\beta$ -HSDs) enzymes on T47D epithelial breast carcinoma cells, increasing the bioactivity of estrogen on these cells. Comparing the use of LNG-IUS with the use of levonorgestrel orally, users of LNG-IUS have significantly lower levonorgestrel serum levels. Some populational studies have evaluated the association of LNG-IUS use and the risk of breast cancer, with discordant results. In some studies, for women who have used LNG-IUS, the risk was up to 73% higher. Regarding its safety for breast cancer survivors using tamoxifen, it has been shown that there is little or no difference in breast cancer recurrence with the use of LNG-IUS. However, other authors claim that there are not enough data to confirm the safety concerning breast cancer recurrence, and its use may lead to irregular bleeding and invasive procedures to assess the endometrial layer. **Conclusion:** In populational studies, the use of LNG-IUS increases breast cancer risk. In breast cancer survivors who use tamoxifen, LNG-IUS seems to protect the endometrium, but more studies are necessary to confirm its safety for breast cancer recurrence.