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Editorial

Fertility sparing treatment for early stage endometrial cancer: current situation and new strategy

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▸ See the article "Long-term outcomes of progestin plus metformin as a fertility-sparing treatment for atypical endometrial hyperplasia and endometrial cancer patients" in volume 30, e90.

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The incidence of endometrial cancer is strikingly increasing. As the increasing of patients, the young patients who wish to conceive are also increasing. Fertility sparing treatment by progestin for endometrial intraepithelial hyperplasia (EIH) or atypical endometrial hyperplasia (AEH), and grade 1 endometrioid carcinoma (EC) without myometrial invasion were introduced since 1990's. A multicenter prospective study or many retrospective studies were reported [1,2]. Currently it has been recognized as an optional treatment listed in several treatment guidelines [3]. Many facilities have the women who bore baby after successfully treated by progestin. Medroxyprogesterone acetate (MPA) or megestrol acetate (MA) are the most frequently used for this treatment. Although fertility sparing treatment by progestin showed relatively high remission rate, it showed low pregnancy rate, and high relapse rate. Gallos et al. [2] reported 40.6% of relapse rate, and even in successfully treated women pregnancy rate was only 28.1%.

Metformin is one of the most widely used biguanide for type 2 diabetes mellitus overcoming insulin resistance. It also has some function for anti-neoplastic effect, and reduce the risk of cancer in diabetes patients [4]. Metformin plus MA showed higher remission rate than MA monotherapy [5]. Mitsuhashi et al. [6] reported the promising result of phase II trial combination treatment by MPA plus metformin for 38 patients. This combination showed 81% of complete remission (CR) rate within 36 weeks treatment, and only 10% of patients relapsed.

In this issue, Mitsuhashi et al. [7] reported the long-term outcome of 63 patients (42 with EC, 21 with AEH) who were treated by MPA 400 mg/day and metformin (750–2,250 mg/day). It resulted 97% CR rate within 18 months, and only 13% of patients relapsed during 57 months of median follow up period. MPA plus metformin cohort had surprisingly better outcome than their MPA alone treatment cohort outcome as a historical control. A multicenter retrospective study treatment by progestin showed 30% recurrence rate, and also obese women (body mass index [BMI] >25 kg/m^2) patients had high risk for recurrence [8]. On the contrary, this report showed significantly better prognosis for obese women. It might be related to suppress the secretion of adipokines by metformin. Because there were no severe adverse effects, this study has no upper limit of BMI in eligibility criteria. It may be good news for obese young women with endometrial cancer.

The present study has some limitation, which was a retrospective study from single institution. Nevertheless, they are planning to start the prospective multicenter large phase II trial of MPA plus metformin as fertility sparing treatment from this September. The result of this new trial should be noted.

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