# EP-129
# Effects of Metformin on Sex Steroid Levels in Postmenopausal Type-2 Diabetic Patients

Uğur Ünlütürk[1], Filiz Bakar[2], Yüksel Ürün[3], Serpil Nebioğlu[2], Ali Rıza Uysal[1]

[1]Department of Endocrinology and Metabolism, Faculty of Medicine,
[2]Department of Biochemistry, Faculty of Pharmacy, [3]Department of Medical Oncology, Ankara University, Ankara, Turkey

## OBJECTIVES

Metformin treatment was associated with decreased risk of various cancers including breast cancer. Exposure to sex steroid is related with increased risk of breast cancer. In this study, we aimed to evaluate the effect of metformin treatment on serum levels of sex steroids and sex hormone binding globulin (SHBG) in postmenopausal women with type-2 diabetes mellitus.

## METHODS

Postmenopausal patients with newly diagnosed type-2 diabetes were recruited to the study. Before starting life-style modifications and metformin treatment, anthropometric measurements were taken and fasting blood samples were collected in order to evaluate plasma glucose, HbA1C, serum levels of insulin, sex hormones, and sex hormone binding globulin (SHBG). All of the basal tests were repeated for each subject at the end of 12 weeks.

## RESULTS

At the end of 12 weeks, 36 patients completed the study and were included into the analyses. Five of 36 patients did not use metformin due to gastrointestinal side effects or noncompliance with therapy. Remaining patients used at least 500 mg to maximum 2000 mg/day of metformin treatment. Mean body-weight and body fat mass, fasting insulin, HbA1c levels significantly decreased in patients who used metformin. Patients receiving metformin treatment also showed significant decreases in total and free testosterone, total and free estradiol, estrone levels, and significant increases in dehydroepiandrosterone sulphate and SHBG levels. A borderline significant decrease was seen in androstenedione levels, as well. Fasting plasma glucose and estrone sulphate levels did not change significantly (Table 1). When compared to the patients who did not use metformin therapy, changes in estradiol levels were significant, and changes in estrone and testosterone levels were marginally significant in patients receiving metformin.

Table 1.

| | Basal | 12th week | P-value |
|---|---|---|---|
| Age, y | 55.8± 4.2 (46-64) | - | - |
| Duration of Menopause (SD), y | 10.3± 6.2 | - | - |
| BMI (SD), kg/m2 | 31.4 ± 5.1 | 29.5 ± 4.8 | <0.001 |
| Weight (SD), kg | 76.3 ± 13.6 | 71.4 ± 12.9 | <0.001 |
| Waist circumference (SD), cm | 96.8 ± 10.4 | 91.5 ± 10.3 | <0.001 |
| Fat mass (SD), kg | 31.7 ± 10.1 | 27.7 ± 9.0 | <0.001 |
| Fasting Plasma Glucose , mg/dL | 116 ± 21 | 96 ± 14 | NS |
| Postprandial Glucose, mg/dL | 195 ± 64 | 126± 31 | NS |
| Fasting Insulin, IU/mL | 23.7 ± 12.1 | 14.5± 6.7 | 0.018 |
| HbA1c (IQR), % | 6.8± 1.1 | 6.0 ± 0.5 | <0.001 |
| SHBG, nmol/L | 42.4 ± 12.2 | 42.5 ± 12.3 | 0.004 |
| Estradiol, pg/mL | 37.55 ±19.3 | 30.5 ± 11.2 | <0.001 |
| Free Estradiol, pg/mL | 0.91 ± 0.84 | 0.85 ± 0.76 | <0.001 |
| Estrone, pg/mL | 21.5 ± 8.4 | 19.2 ± 7.4 | 0.010 |
| Estrone Sulphate, pg/mL | 68.53 ± 36.7 | 63.5 ± 29.6 | NS |
| Total Testosterone, ng/dL | 28.7 ± 16.5 | 22.2 ± 16.1 | <0.001 |
| Free Testosterone, ng/dL | 1.84 ± 0.86 | 1.34 ± 0.52 | 0.042 |
| Androstenedion, ng/mL | 0.79 ± 0.20 | 0.43 ± 0.18 | 0.055 |
| DHEAS, ug/dL | 83.5 ± 49.9 | 87.29± 60.3 | <0.001 |

SD: standard deviation; y: year; NS: Not significant

## CONCLUSIONS

Metformin treatment may have favorable effects on breast cancer risk through decreasing androgen and estrogen levels in postmenopausal type-2 diabetic patients.

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