

Pengaruh Vitamin D3 terhadap Pertumbuhan Folikel dan Kadar Hormon Anti Müller Serum pada Sindrom Ovarium Polikistik Melalui Pengaturan Reseptor Insulin dan Reseptor Vitamin D Darah = The Effect of Vitamin D3 on Follicle Growth and Serum Anti-Müllerian Hormone Level in Polycystic Ovary Syndrome Through Regulation of Blood Insulin and Vitamin D Receptors

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Abstrak

Ketimpangan antara kadar vitamin D25(OH) rendah dan keadaan resistensi insulin pada penderita SOPK dengan anovulasi kronik menarik untuk digali lebih jauh. Anovulasi kronik pada SOPK diyakini disebabkan terhentinya pertumbuhan folikel di ovarium. Pada resistensi insulin, vitamin D diperkirakan berperan di sel sasaran dengan menambah substrat reseptor insulin. Perlu diungkap pengaruh vitamin D terhadap pertumbuhan folikel ovarium dengan mengukur kadar AMH, kemudian diperbandingkan antara penderita SOPK-RI dan SOPK-nir-RI berdasarkan perubahan kadar reseptor insulin darah. Penelitian ini bertujuan menentukan pengaruh pemberian vitamin D3 terhadap pertumbuhan folikel ovarium dan penurunan kadar AMH melalui jalur reseptor insulin dan reseptor vitamin D darah. Penelitian dua tahap dilakukan dari 14 Agustus 2018 hingga 25 Februari 2019 terhadap 35 subjek SOPK-RI dan 35 subjek SOPK-nir-RI di Poliklinik Infertilitas dan Endokrinologi Departemen Obstetri dan Ginekologi RSPAD Gatot Soebroto (RSGS), Jakarta. Tahap pertama adalah iris-silang antara SOPK-RI dan nir-RI untuk membandingkan kadar vitamin D25(OH), AMH, reseptor insulin dan reseptor vitamin D darah. Tahap kedua adalah uji kuasi-eksperimental untuk mengetahui pengaruh pemberian vitamin D3 12.000 IU per minggu selama tiga bulan terhadap pertumbuhan folikel dengan peman-tauan USG-transvaginal atau transrektal sebulan sekali dan kadar AMH pada SOPK-RI dan nir-RI. Kadar glukosa puasa, insulin puasa, vitamin D25(OH), AMH diukur dari darah. Reseptor vitamin D darah dan reseptor insulin darah diperiksa dari sel mononukleus darah tepi (SMDT). Hasil penelitian memperlihatkan bahwa: (1) prapemberian vitamin D3 nilai yang berbeda bermakna antara SOPK-RI dan SOPK-nir-RI adalah kadar glukosa puasa (84 vs. 78 mg/dL; $p = 0,016$), insulin puasa (20,3 vs. 7,49 IU/mL; $p < 0,001$) (2) pascapemberian vitamin D3 yang berbeda bermakna adalah kadar glukosa puasa (82 vs. 79 mg/dL; $p = 0,049$), insulin puasa (23,19 vs. 10,54; $p < 0,001$), reseptor insulin lebih tinggi pada SOPK-RI dibandingkan SOPK-nir-RI (18,80 vs. 14,78 ng/mL; $p = 0,020$), reseptor vitamin D pada SOPK-nir-RI menurun bermakna (63,29%); (3) pascapemberian vitamin D3 ditemukan: (a) delta perubahan kadar vitamin D25(OH) pasca (8,38 ng/mL (63,4%) [SD 4,06] SOPK-RI vs. 12,31 ng/mL (10,29%) SOPK-nir-RI, $p < 0,001$); (b) delta perubahan penurunan kadar AMH pasca SOPK RI 10,29 vs. SOPK-nir-RI 14,61%; $p = 0,492$); (c) delta peningkatan diameter folikel antara dua kelompok SPOK meningkat pada bulan pertama (14,3% vs. 50%), kedua (33,3% vs. 66,7%), dan ketiga (50% vs. 66,7%), tetapi yang berbeda bermakna ($p < 0,05$) hanya pada bulan pertama, yaitu lebih besar pada SOPK-nir-RI. Disimpulkan bahwa vitamin D3 menurunkan kadar AMH pada SOPK-RI dan SOPK-nir-RI, serta meningkatkan pertumbuhan folikel pada kededua kelompok SOPK, pada bulan pertama perubahan diameter folikel lebih besar pada SOPK nir-RI. Prapemberian vitamin D3 tidak ditemukan perbedaan kadar reseptor insulin dan reseptor vitamin D pada kededua kelompok SOPK, sedangkan pascapemberian vitamin D3

terdapat penurunan kadar reseptor vitamin D pada SOPK-nir-RI.

.....Discrepancy between low-level vitamin 25(OH)D and insulin resistance in PCOS patients with chronic anovulation required to be further explored. Chronic anovulation in PCOS is believed to be caused by the follicular arrest in the ovary. In insulin resistance the vitamin D is thought to play a role in target cell by adding the insulin receptor substrate. It is necessary to elucidate the effect of vitamin D on the ovarian folliculogenesis by measuring the AMH levels, which are then compared between patients with IR-PCOS and non-IR-PCOS based on the changes in blood insulin receptor levels. The aim of this study is to determine the effect of vitamin D3 administration on ovarian follicular growth and reduction of AMH through insulin receptor and blood vitamin D receptor pathways. The two stages study was carried out from 14th August 2018 to 25th February 2019 on 35 IR-PCOS and 35 non-IR-PCOS subjects at the Infertility and Endo-crinology Out-patient Clinic, Department of Obstetrics and Gynecology, Gatot Soebroto Central Army Hospital (RSGS), Jakarta. The first stage was a cross-section study between IR-PCOS and non-IR-PCOS to compare levels of vitamin 25(OH)D, AMH, blood insulin receptors and vitamin D receptors; the second is a quasi-experimental test to determine the effect of 12,000 IU vitamin D3 administration per week for 3 months on follicular growth with transvaginal or transrectal ultrasound monthly and AMH levels on IR-PCOS and non-IR-PCOS. Fasting glucose, fasting insulin, vitamin D25(OH), AMH levels are measured from the blood. Blood vitamin D receptor and insulin receptor were measured from the peripheral blood mononuclear cells (PBMC). The results of the study demonstrated that: (1) before administration of vitamin D3, there were differences in fasting glucose (84 vs. 78 mg/dL; $p = 0.016$) and fasting insulin (20.3 vs. 7.49 IU/mL; $p < 0.001$) between the two groups; (2) after vitamin D3 administration, significant differences were found between the two groups for the levels of fasting glucose (82 vs. 79 mg / dL; $p = 0.049$), fasting insulin (23.19 vs. 10.54; $p < 0.001$); higher insulin receptors was found in IR-PCOS compared to non-IR-PCOS (18.80 vs. 14.78 ng / mL; $p = 0.020$), the vitamin D receptors in non-IR-PCOS decreased significantly (63.29%); (3) vitamin 25(OH)D levels before vitamin D3 administration were not significantly different in the two groups (13.84 vs. 10.97 ng/mL; $p = 0.327$), while after vitamin D3 administration the levels increased significantly (8.38 ng/mL (63.4%) [SD 4.06] in IR-PCOS vs. 12.31 ng/mL (10.29%) in non-IR-PCOS, $p < 0.001$); (4) AMH levels decreased in the both groups after vitamin D3 administration but the ratio of the decrease was not significantly different (10.29 vs. 14.61%; $p = 0.492$); (5) follicular diameter between the two groups increased in the first month (14.3% vs. 50%), the second month (33.3% vs. 66.7%), and the third month (50% vs. 66.7%) after vitamin D3 administration, but the significant difference (< 0.05) was demonstrated only in the first month, which was greater in non-IR-PCOS than that in the IR-PCOS. It is concluded that vitamin D3 decreases AMH levels in both IR-PCOS and non-IR-PCOS. It increases folliculogenesis in both PCOS groups; in the first month, the changes in follicular diameter are greater in non-IR-PCOS. Before vitamin D3 administration, there is no difference in the levels of insulin receptors and vitamin D receptors between the two groups, whereas after vitamin D3 administration there is a decrease in the levels of vitamin D receptors in non-IR-PCOS. Keywords: AMH, IR-PCOS, non-IR-PCOS, PBMC, vitamin D receptor, insulin receptor, vitamin D25(OH).