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REVIEW ARTICLE

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LAPAROSCOPIC OVARIAN DRILLING (LOD) AS AN ALTERNATIVE MEDICAL THERAPY IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME ETHNIC MELANISIA AT JAYAPURA-PAPUA INDONESIA

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ABSTRACT

Surgery in patients with polycystic ovary syndrome are "Laparoscopic Ovarian Drilling". The Indicated, that has been conducted in patients with infertility due to PCOS who do not respond to stimulation hormonal. Result satisfactory improve ovulatory cycle after action operation. If lower pregnancy rates after surgery gonadotropin hormone can be given with low-dose protocol.

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is an endocrine disorder characterized by hyperandrogenaemia , anovulatoar , hirsutism and prevalence of infertility in the population between 5-10 % (1) . According to Qin (2) , of 121 PCOS subjects population of 128 subjects with genotype - 71G variant , then distribution by ethnicity was 48.8 % Caucasian , 39.7 % African - American , 7.4 % Asian , 3.3 % Hispanic , 0.8 % from other ethnicities , while the control group 55.4 % Caucasian , 38.8 % African - American , 5.84 Asian , 3.3 % Hispanic and 2.5 % of the others . Zawadzki (3) introduce criteria established by the National Institutes of Health (NIH) / NICHD meeting made during 1990. Rotterdam consensus (4.5) last year 2003 antara ESHRE (European Society for Human Reproduction and Embryology) and ASRM (American Society for Reproductive

Medicine) which stipulates that a diagnosis of PCOS should meet at least two of the following three criteria : (1) clinical signs and / or of biochemical hyperandrogenism , (2) Oligo and no ovulation , and (3) a description of PCO. Damage other endokrinopati issued (eg virilizing tumors , congenital adrenal hyperplasia nonclassical , hyperprolactinemia and Cushing syndrome) .

Criteria of the American Society for Reproductive Medicine (ASRM) in 2006 which included all of the above criteria coupled with (6.7), (1) hiperandrogen (hirsutisme and or hiperandrogenemia), (2) ovarian dysfunction (oligo-anovulation and polycystic ovaries or the morphology) and (3) events associated with androgen excess removed. Several heories were proposed to explain the pathogenesis of PCOS (8.9):

- Damage in insulin action and secretion that cause hyperinsulinaemia and insulin resistance.
- Damage caused neuorendocrin primary frequency and amplitude of LH pulses were strong.
- Damage resulting androgen synthesis increased androgen production.
- Changes in cortisol metabolism which can result in increased androgen production.

These factors are respectively the starting point for our understanding of metabolic circuits-pituitary-ovary (ovarian-pituitary-metabolic circuitry) are closely related.

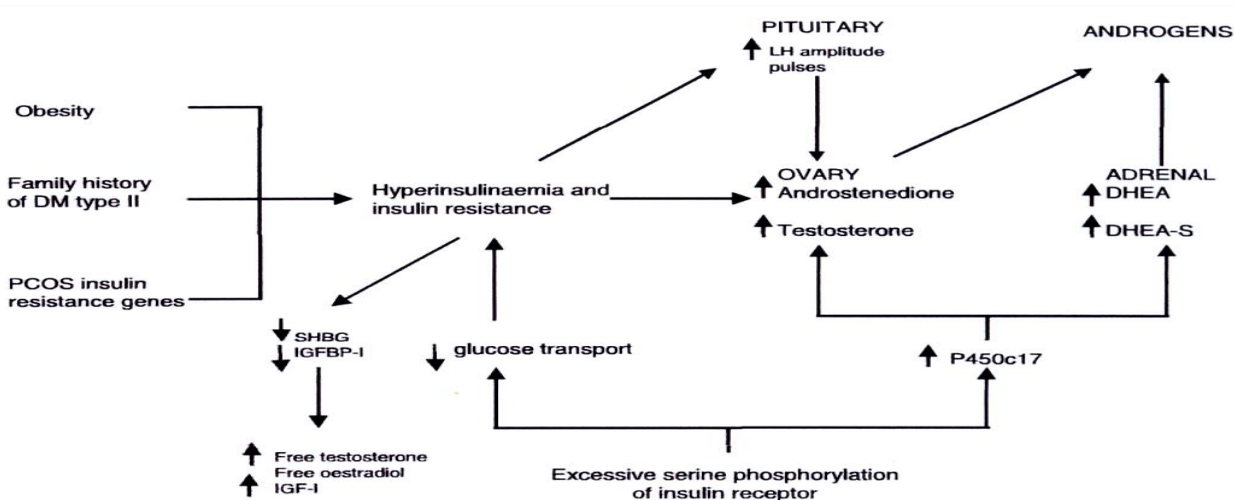


Figure 1. The role of androgen in the PCO, (10)

At first , the reaction cross- insulin with IGF -I receptor - a structure similar to insulin receptors - on the ovarian theca cells was proposed as a possible mechanism of hyperandrogenism - insulin -mediated . Light of the actions that have been known of IGF - 1 in augmenting the theca androgen response to LH (11) , IGF - 1 receptor activation by insulin can lead to increased androgen production in theca cells . However , insulin has been shown to bind to the IGF - 1 affinity 50-500 times much lower than the affinity of IGF - 1 . The influence of insulin with IGF receptor type- 1 therefore an important consideration in high insulin concentrations . The existence of hybrid and atypical insulin / IGF - 1 - which consists of a receptor - has also been described . These receptors can bind to insulin and IGF - 1 with the same affinity . Interestingly , Franks

(12) , using anti - insulin receptor antibody and antibody anti - IGF receptor type I , not only shows that the effect of insulin on steroidogenesis of human granulosa cells in vitro must be mediated through its receptor , but also issued a hybrid insulin receptor / IGF type IGF - I or type - 1 receptor as a receptor -mediated action of insulin that may be .

There are two other important insulin action helped cause of hyperandrogenism in PCOS cases : (1) barriers between serum hepatic synthesis of sex hormone - binding globulin (SHBG) , which allows the androgen and estrogen -free , (2) obstacles hepatic production of IGFBP - 1 , which allow increased circulating levels of IGF - 1 and greater local activity LH levels are believed to increase due in part to the increasing sensitivity of under - stimulation of the brain (pituitary) to GnRH , which materialized due to an increase in LH pulse

amplitude and frequency, but especially the amplitude (high LH and low to normal FSH) may also be caused by increased frequency pulses of GnRH secretion, which is associated with a reduction in hypothalamic opioid hurdle because there is no progesterone old. This increased activity may occur in the hypothalamic and pituitary. This is consistent with the diurnal pattern of LH secretion abnormalities have been reported in children teenage girl living with PCOS which focuses on the patterns of pulsatile LH secretion as an indicator of changing hypothalamic secretion of GnRH. Although pulsatile GnRH stimulus is required to maintain the synthesis and secretion of gonadotropins, it is believed that the

frequency and amplitude of GnRH pulses determine gonadotrophin subunit gene expression and secretion of LH and FSH in the pituitary. So, in the ovulation cycle, increased frequency of GnRH during the follicular phase synthesis of LH support before the LH surge, while the next ovulation, luteal steroid clear slowing of GnRH pulses favor FSH synthesis. In PCOS, LH pulse / continuous rapid GnRH and LH synthesis support, hiperandrogenaemia, and poor follicular maturation. Administration of progesterone in women living with PCOS anovulatif can slow down the secretion of GnRH pulses, supporting FSH secretion and cause follicular maturation.

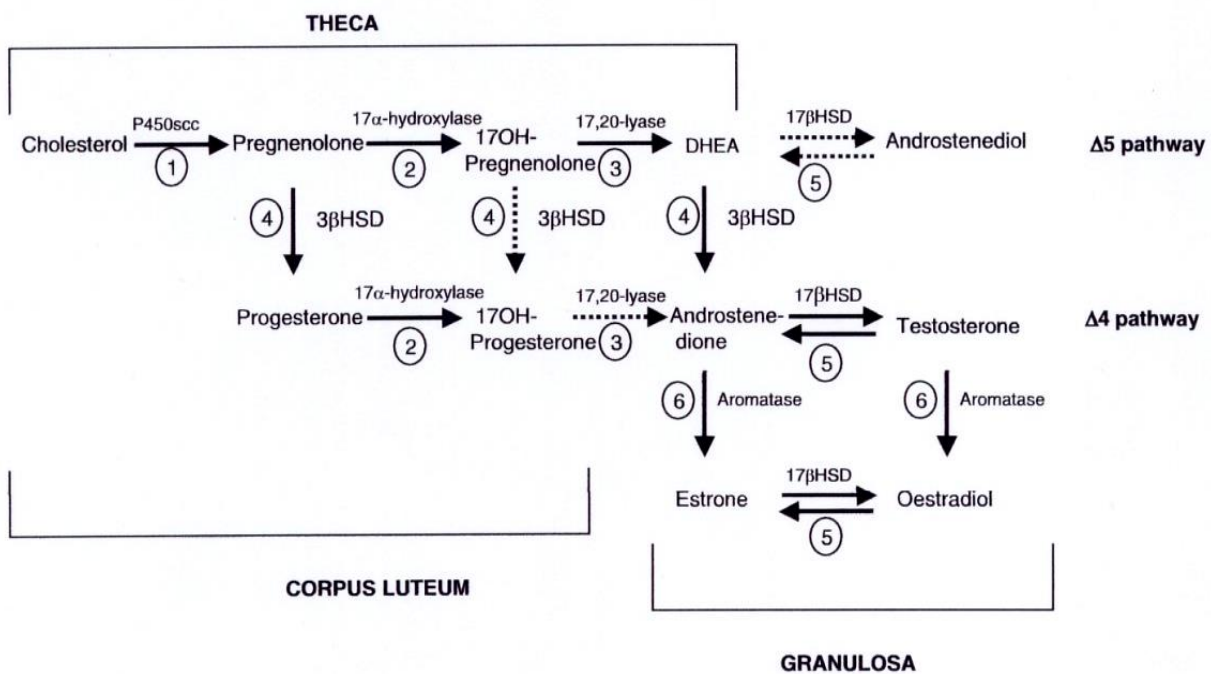


Figure 2. Ovarian steroid biosynthesis, (10)

These data indicate that the increase in plasma LH and pulsatile secretion of GnRH / LH in PCOS is not only a consequence of low progesterone levels caused by anovulation, but reflect insensitivity is the cause of the hypothalamic GnRH pulse obstacles estrogen / progesteron. Meskipun many hypotheses proposed LH hypersecretion dihipofisa to etiology, none of which explain the neuroendocrine abnormalities that lead to excessive LH pulse frequency. On the other hand, it is also clear that increasing concentrations of LH is not always due to dysregulation of the ovary (13,14,15,16). In fact, LH hypersecretion occurs only in about one-third of women with PCOS, especially in non-obese patients. In future studies, not only found that serum LH

concentrations much higher after ovulation induction with GnRH in this group of patients compared with patients with normal ovarian hypogonadism in ultrasonography, but also found that this difference existed before the changes oestradiol levels were observed. This suggests that the primary lesion in the ovary in PCOS, with hypersecretion of LH in the pituitary that is secondary to feedback tagging variants terganggu. The researchers propose an alternative model of PCOS as a form hiperandrogenisme gonadotropin-dependent ovarian where the primary abnormality is the increased concentration of androgen intraovarium. Changing mechanism 5 α -R and / or 11 β HSD activity in women with PCOS is still not known with certainty. Although more

than half of women with SOPKmemiliki overweight, and even obesity can cause abnormalities of cortisol metabolism, this mechanism can not fully explain the abnormal activity of 5 α -R and 11 β HSD in PCOS. Increase 5 α -R activity in PCOS subjects, compared with the control group the same weight. Similarly, changes in the SOP 11 β HSD activity was also confirmed in PCOS

subjects bodied lean. The increased endogenous 11 β HSD1 inhibitor production, as measured in urine, as a mechanism of abnormal cortisol metabolism in other SOPK.Mekanisme proposed is that the high levels of estrogen in PCOS, particularly in the form of oestrone, can inhibit the activity of 11 β HSD1 in the liver. (17.18,19,20)

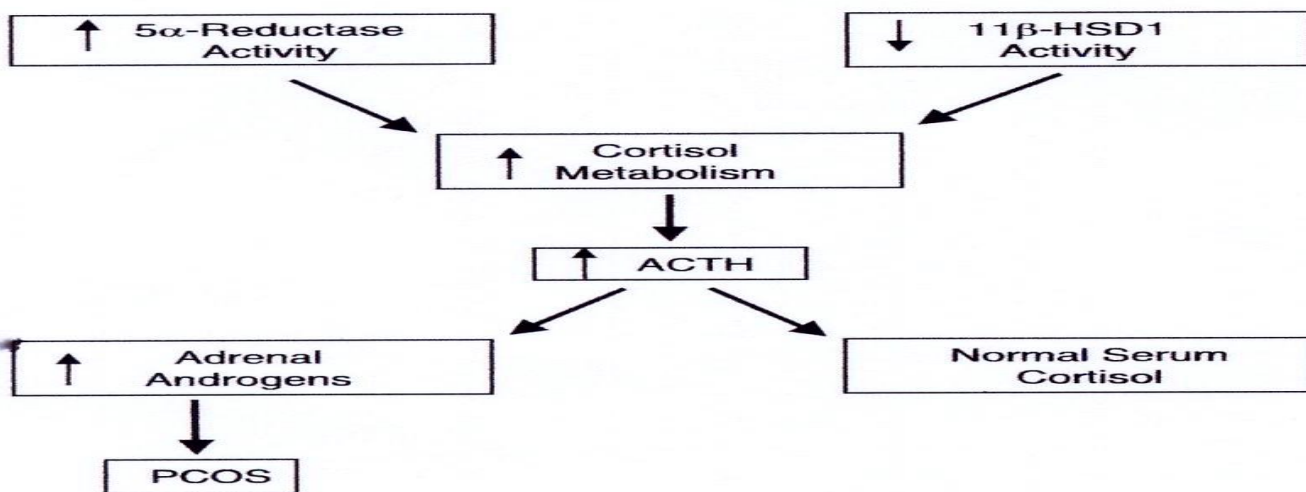


Figure 3. Enhancement cortisol as a peripheral mechanism in the development of PCOS. (10)

The concept of therapy in patients with polycystic ovary syndrome are doing repairs hiperinsulininemia , ovarian stimulation or pengobtan hiperandrogenemia to provide oral contraceptives containing gestagen antiandrogens . Giving metforfin , operative measures may provide improvements spontaneous ovarian cycles . The first invasive procedure in the treatment of polycystic ovary syndrome with wedge resection ovarium.Tehnik do this a lot to do at first , but after the second surgery adhesions found so much going on this operating technique is not used after laparoscopic surgery was introduced .

Technique " Laparoscopic Ovarian Drilling " Laparoscopic action to perform " ovarian drilling " technique replaces ovarian resection was first performed by Gjonnaess in 1984.Tehnik this operation does not regulate the number of holes on the surface of the ovary . Several studies conducted have variations from one hole to forty holes on each surface of the ovary , as well as differences in the instruments used , such as monopolar diathermy , bipolar electrocautery , and incision are simple variations of the laser system . Such as CO2 , argon or Nd : YAG .

Table 1. This technique differences

Author	Study design	No. of patients	Ovulation rate	Pregnancy rate spontaneous	Live birth rate	No. of holes	Technique
Gjonnæss (21)	Prospective uncontrolled	62	92%	69%	n.a.	3-8	Unipolar electrocautery, 200-300 W
Abdel Gadir et al.(22)	Randomised LOD versus HMG versus FSH	29	71.4 %	34.5 %	27.5 %		Unipolar electrocautery

Author	Study design	No. of patients	Ovulation rate	Pregnancy rate spontaneous	Live birth rate	No. of holes	Technique
Keckstein et al. ⁽²³⁾	Prospective uncontrolled	19 CO ₂ laser	71.4 %	36.8 %	n.a.	10–30	CO ₂ : 20–30 W continuous mode
		11 Nd:YAG	55%	27.2 %			Nd:YAG : 45–70 W defocussed laser beam
Armar et al. ⁽²⁴⁾	Prospective uncontrolled	21	80.9 %	52.3 %	38.1 %	4–8	Unipolar diathermy
Kovacs et al. ⁽²⁵⁾	Prospective uncontrolled	10	70%	30%	20%	10	Unipolar electrocautery
Gürgan et al. ⁽²⁶⁾	Prospective uncontrolled	7 electrocautery	71%	57%	n.a	20–30	Unipolar electrocautery 70 W
		10 Nd:YAG	70%	40%		20–25	Nd:YAG laser 30–60 W
Gürgan et al. ⁽²⁷⁾	Prospective uncontrolled	40	70%	50%	45%	20–25	Nd:YAG laser 50 W
Armar and Lachelin ⁽²⁸⁾	Prospective uncontrolled	50	86%	66%	n.a. after LOD only	4	Unipolar diathermy
Greenblatt and Casper ⁽²⁹⁾	Prospective uncontrolled	8	100 %	87.5 %	62.5 %	8–10	Unipolar cautery
Naether et al. ⁽³⁰⁾	Prospective uncontrolled	133	55%	43%	34.5 %	5–20	Unipolar electroca

Author	Study design	No. of patients	Ovulation rate	Pregnancy rate spontaneous	Live birth rate	No. of holes	Technique
	trolled						utery 400 W/s
Balen and Jacobs ⁽³¹⁾	Randomised controlled	4 unilateral	75%	0	0	4	Unipolar diathermy 40 W
		6 bilateral	33%				
Heylen et al. ⁽³²⁾	Prospective two-laser techniques	22 vaporisation	82%	55% (total)	47.2 % incl. clomiphene	15–40	Argon, continuous 8–12 W
		22 perforation	77.3 %	72.7 % (total incl. clomiphene)			
Liguori et al. ⁽³³⁾	Prospective uncontrolled	97	90%	81%	n.d.	5–20	Unipolar electrocautery 4 mA
Lazovic et al. ⁽³⁴⁾	Randomised crossover	28 LOD	75%	29%	–	n.a.	Unipolar diathermy and CO ₂ laser
		28 low-dose FSH		60%			
Vegetti ⁽³⁵⁾	Prospective, randomised	16 LOD	81.2 %	25%	12.5 %	20	Electrocauterisation
		13 low-dose FSH	84%	38%	30.7 %		
Muenserman and	Prospective randomised	10 LOD	70%	50%	36%	10–30	CO ₂ laser 10 ⁵ W/cm ²

Author	Study design	No. of patients	Ovulation rate	Pregnancy rate spontaneous	Live birth rate	No. of holes	Technique
Kleinstein ⁽³⁶⁾		8 GnRH-a followed by FSH	67%	63%	29%		
Felemban et al. ⁽³⁷⁾	Retrospective	112	73.2%	72% (cumulative probability after 24 months)	–	10–15	Unipolar electrocautery 40 W
Zullo et al. ⁽³⁸⁾	Randomised	32 minilaparoscopy	81.2%	65.6%	59.3%	10–15	Unipolar electrocautery
	Controlled	30 standard	86.6%	60.0%	56.6%		
Kriplani et al. ⁽³⁹⁾	Prospective uncontrolled	66	81.8%	54.5%	n.a.	n.a.	Monopolar diathermy
Fernandez et al. ⁽⁴⁰⁾	Prospective uncontrolled	13	46.2%	23.1%	23.1%	10–15	Transvaginal hydrolaparoscopy bipolar versapoint device
Amer et al. ⁽⁴¹⁾	Retrospective	116 LOD	n.a.	61%	56%	3–10 (diathermy)	Electric diathermy 30 W
	Longitudinal follow-up	34 control				10–40 (laser)	Argon laser 12–14 W continuous mode
	Prospective	28 LOD	54%	28.6%	21.2%	10	Monopolar

Author	Study design	No. of patients	Ovulation rate	Pregnancy rate spontaneous	Live birth rate	No. of holes	Technique
Farquhar et al. ⁽⁴²⁾	Randomised						electrocautery
		19 patients 3 cycles HMG/FSH	81% per cycle				
Takeuchi et al. ⁽⁴³⁾	Prospective randomised	17 harmonic laser	94%	77%	n.a.	n.a.	Harmonic scalpel laser
		17 Nd:YAG	94%	60%			Neodym YAG laser
Casa et al. ⁽⁴⁴⁾	Prospective	28	66.7%	76% (cumulative after 6 months)	76%	n.a.	Transvaginal hydrolaparoscopy bipolar versapoint electrode
Malkawi et al. ⁽⁴⁵⁾	Prospective	64 metformin	79.7%	64.1%	n.a.	n.a.	n.a.
		97 LOD	83.5%	59.8%			
Bayram et al. ⁽⁴⁶⁾	Randomised controlled trial	83 LOD	63%	37%	34%	5–10	Bipolar needle electrode
		85 FSH					
Fernandez et al. ⁽⁴⁷⁾	Prospective	80	91%	39.7% (drilling alone) 60% (incl. stimulation)	35.6% (total incl. stimulation)	10–15	Transvaginal, coaxial bipolar

Author	Study design	No. of patients	Ovulation rate	Pregnancy rate spontaneous	Live birth rate	No. of holes	Technique
Palomba et al. ⁽⁴⁸⁾	Prospective randomised	54 metformin	54.8 %	18.6 %	59%	3-6	Monopolar 40 W
		55 LOD	53.3 % per cycle	13.4 % per cycle	36% per patients		
Suhartono H. et al (etc)	Prospective RESEARCH	50	25/50 100 %	11/50 100%	11/50 100 %	5-10	Monopolar 40W

Differences laparoscopic ovarian drilling techniques to this day there is no better based on evidence base between electro cautery , CO2 laser , harmonic scalpel and Nd : YAD laser. Fernandes (47) hidrolaparocopi transvaginal action , by inserting " veress needle " through the cavity douglas and put 300 cc saline . Ovarian vaporization used elektosurgical bipolar probe called "VersaPoints".

Pathomechanisme Wedge incision technique was performed while patomekanismenya 2 decades can not be explained. Ovarian drilling will damage the cortex and the ovarian stroma and follicular androgen small irrigation causing intraovarium decrease androgen levels and androgen production . Consequently a decline in estrogen that will hypersecreti increase on in pituitary LH and follicle in the ovary fix .

Ferraret hypothesis (49) will improve the state of hyperinsulinemia and insulin resistance that will affect the levels of LH and FSH . Hipergicemia corrected , an increase in SHBG and leptin levels corrected so that the LH levels , reduced ovarian volume and an increase in ovarian vascularization. Some research data will improve hormonal profiles , ovulation and pregnancy rates

CONCLUSION

"Laparoscopic Ovarian Drilling" is an interesting alternative in the treatment of polycystic ovary syndrome

patients that there is no ovulation. "LOD" can affect hormonal balance and improve ovarian response.

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