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Case Report

DUTCH (Dried Urine Test for Comprehensive Hormones) as a method for detecting disease-related to hormone function

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ABSTRACT

Hormones released and absorbed by the human body in a balanced state will affect the balance and health, while a change in hormone levels can cause various severe and chronic health problems. Hormone testing is a method of measuring hormone levels in the body that can be used to diagnose and treat disease, monitor a patient's overall health, or prevent the development of specific health problems. This study may provide information about the functional hormone test (DUTCH). This study presents the case of a 47-year-old woman with a history of chronic dysmenorrhea. Functional hormone testing was performed on days 19-22 of the menstrual cycle in women with regular 28-day periods. The results of the DUTCH test in this patient are 2-OH dominant, so they are safe from symptoms of estrogen dominance and low 4-OH production. The methylation process is smooth, reducing the risk of cancer-related to estrogen dominance syndrome. Hormone examination through urine is intended to see metabolites (metabolic wastes) of hormones released through urine. How dangerous it is for a person to have Estrogen Domination Syndrome can be determined by looking at estrogen and progesterone metabolites.



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INTRODUCTION

Hormonal tests are mainly performed for disease epidemiology, clinical research, and patient care. Hormone tests can be assessed by their levels in serum or plasma. It can also be seen from the saliva or metabolites found in the urine. The testing technique is carried out using serum samples (Direito et al., 2013). Although serum samples are universally accepted, they have limitations, which are not available in all regions. In addition, a type of cortisol hormone cannot be checked throughout the day. Thus, urine sampling was developed to facilitate the sampling process and shorten the process (Roos et al., 2015).

DUTCH is a functional hormone test performed by taking a dry urine specimen. It was carried out by the Precision Analytical (USA) laboratory. Hormone tests through urine are intended to see metabolites (metabolic wastes) of hormones released through urine. Looking at the metabolites of estrogen & progesterone can help determine how much a person is at risk of developing Estrogen Dominant Syndrome (Rezvanpour & Don-Wauchope, 2017). The NETHERLANDS can check sex hormones (estrogen, progesterone), adrenal hormones (cortisol), and androgen hormones (DHEA, Testosterone) (Newman et al., 2019).

Analysis of dry urine samples on filter paper by gas chromatography with tandem mass spectrometry (GC-MS/MS) gave similar results to serum analyzed by radioimmunoassay (Stanczyk & Clarke, 2010). Likewise, a collection of four samples during the day (4-place method) can be substituted for a 24-hour collection. Urine analysis from a dry sample is equivalent to a liquid urine sample (Newman & Curran, 2021). Urine sample testing is superior to saliva because it loses a significant portion of the patient's HPA Axis function with saliva testing when

measuring cortisol metabolites (Shackleton, 2010). To properly view a patient's cortisol status, free and metabolized cortisol should be measured to avoid misleading results when cortisol clearance is abnormally high or low as in the sex hormones. Measuring estrogen and androgen hormones can provide a complete picture of a more precise clinical diagnosis of hormonal imbalance and HRT monitoring (Krone et al., 2010)

Sex steroid hormone production can be assessed by levels in serum or plasma as well as from metabolites in urine. This makes it easier to take samples, especially for hormones that have daily, circadian, and monthly cycles that need to be checked regularly (Bédard et al., 2000). In Indonesia, the treatment of diseases related to hormonal imbalances such as endometriosis, irregular menstrual cycles, premenstrual syndrome, polycystic ovary syndrome, fibroids, fertility problems, osteoporosis, and hormone-sensitive cancers with medication or surgery. The use of prevention methods with a complete picture of hormonal health, the balance of estrogen metabolism, the balance of androgen metabolism, stress hormones cortisol, DHEA, and other markers with DUTCH examination is still rarely used. The Netherlands also analyzed its importance for reproductive health, bone health, reproductive function, cancer prevention, mood and motivation, and antioxidant defense with free radicals. This report presents the result of the active hormone on a 47-year-old woman with a history of chronic dysmenorrhea and a regular period of 28 days.

CASE REPORT

We report the case of a 47-year-old woman with a history of chronic dysmenorrhea, a health condition associated with hormonal imbalance. Functional hormone testing was performed on days 19-22 of the menstrual cycle in women with regular 28-day periods. The test is carried out by dipping a special paper into



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a urine specimen and drying it. Sampling was done by collecting the urine at certain times, namely at 17.00, before going to bed at 10.00, when waking up, and 2 hours after waking up. All specialty papers that have been soaked in urine are dried and plasticized and sent for

analysis by the Precision Analytical (US) Lab. The hormones assessed and analyzed in this DUTCH are as follows: Estrogen hormone, in three important forms, namely: 2-OH Estrone, 4-OH Estrone & 16-OH Estrone, as shown in the table below.

Table 1. Results of the estrogen hormone test

No	Estrogen Hormone Test	Result	Patient's Percentage	Expected Percentage
1	2-OH Estrone	The patient's body produces enough 2-OH during the initial phase of metabolism, which protects her from EDS symptoms.	84%	60-80%
2	4-OH Estrone	Estrogen positively influences the patient's body since it shields the patient from the symptoms of Estrogen Dominance Syndrome (EDS). The patient's body creates enough 2-OH during the first phase of metabolism to keep EDS symptoms at bay.	7%	7.5-11%
3	16-OH Estrone	The patient's body produces very little 16-OH. It provides an overview that the risk of EDS symptoms is relatively low due to the much higher level of 2-OH.	9%	13-30%

Table 2. Results of the testosterone hormone test

No	Testosterone Hormone test	Result	Normal Range
1	Testosterone	4.7 ng/mg	2.3 – 14 ng/mg
2	5a-DHT	3.3 ng/mg	0 - 6.6 ng/mg
3	5a-Androstane diol	18.4 ng/mg	12 – 30 ng/mg
4	5b-Androstane diol	58.0 ng/mg	20 – 75 ng/mg
5	Epi-Testosterone	9.6 ng/mg	2.3 – 14 ng/mg



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Another hormone analyzed was progesterone. The sample results show that the production of progesterone is very high. High progesterone can occur naturally but also due to stress or synthetic progesterone hormones such as those found in hormonal birth control drugs.

Testosterone was also tested. Women and men both produce testosterone, but normal testosterone levels in women are generally lower than in men. It can be seen that the testosterone levels produced by the sample are still within normal limits, and the levels of testosterone metabolites (5a/5b-androstenediol) are also within the normal range.

A hormone that was tested was androgen. It seems that the results of normal DHEA

hormone production. This indicates that the function of the adrenal glands produces sufficient DHEA. In addition, free cortisol (cortisol circulating in the arteries) and cortisol metabolites (the product of cortisol metabolism) were still within normal limits. This indicates the optimal function of the HPA (Hypothalamus-Pituitary-Adrenal Axis) axis.

Another marker that was analyzed was the Organic Acid Test (OATs). The following are some of the organic acid markers assessed in the Netherlands: Methylmalonate Acid (MMA), Xanthurenate & Kynurenate, Pyroglutamate, Homovanillate (HVA), Venilmandelate (VMA), melatonin, 8-OHdG, which act as markers of DNA damage.

Table 3. Results of the DHEA, Cortisol test

No	Total of DHEA Production	
	Age	Range
1	20 - 39	1300 – 3000
2	40 - 60	750 - 2000
3	>60	500 - 1200
4	20 - 39	1300 – 3000

Table 4. Result of some organic acid markers that were assessed in the DUTCH.

No	Organic Acid Markers	Result	Normal range
1	Methylmalonate (MMA)	0.8 ug/mg	0-2.2 ug/mg
2	Xanthurenate	0.4 ug/mg	0-1.4 ug/mg
3	Kynurenate	2.6 ug/mg	0-7.3 ug/mg
4	Pyroglutamate	56.3 ug/mg	32-60 ug/mg



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DISCUSSION

Hormone or metabolite analysis is useful for dealing with patients with many nonspecific symptoms to diagnose and screen for various diseases (Sansone et al., 2019). Steroid hormones measured from urine samples are essential in diagnosing hormone-related diseases (de Jong et al., 2017). The hormones assessed and analyzed at DUTCH are as follows: Estrogen, in three essential forms: 2-OH Estrone, 4-OH Estrone, and 16-OH Estrone. These three hormones have their respective functions and can describe abnormalities in estrogen metabolism (Newman & Curran, 2021).

The first type of estrogen hormone is 2-OH, which can be categorized as a type of estrogen with a very positive effect on our bodies; it protects us from the symptoms of diseases caused by Estrogen Domination Syndrome (EDS). The production of 2-OH in the first phase of metabolism from the samples taken was relatively high. Thus, protecting them from EDS symptoms (Newman & Curran, 2021).

The second estrogen hormone is 4-OH, which can damage cell DNA and undergo mutations, making it very susceptible to developing into cancer. If the level of 4-OH is excessive, and in phase II, it cannot be metabolized entirely through the methylation process, the risk of cancer will increase significantly. The production of 4-OH in this sample was not high, and the methylation process was smooth. The cancer risk associated with estrogen dominance syndrome is low because it is still protected by optimal metabolism. This condition can be maintained by consuming vegetables from the cabbage group such as cabbage, cauliflower, broccoli, broccoli sprouts, Brussel sprouts, broccoli sprouts every day (Sampson et al., 2017).

The third estrogen hormone is 16-OH, a type of proliferative estrogen (supports tissue growth) but rarely causes DNA damage in cancer. The

production of 16-OH in the sample body is low, indicating that the risk of having EDS symptoms is relatively low because 2-OH is much higher (Newman et al., 2019).

The sample results showed very high progesterone production. High progesterone can occur naturally but also due to stress and synthetic progesterone hormones such as those found in hormonal birth control drugs. On the plus side, high progesterone protects against the deleterious effects of estrogen that cause cancer due to EDS. High progesterone can cause symptoms such as bloating or flatulence, fatigue & food cravings, or an urge to eat, especially high-calorie foods. On the other hand, optimal progesterone is an excellent condition if the sample plans to become pregnant. We know that samples produce eggs at ovulation with high progesterone, ready to be fertilized (Groenewoud et al., 2017).

Another hormone analyzed is testosterone. Both women and men produce testosterone, but the normal female testosterone range is generally lower than men's. We can see that the testosterone levels produced by the samples are still within the normal range; testosterone metabolite levels (5a/5b-androstenediol) were also within the normal range (Savkovic et al., 2018). Normal testosterone can prevent symptoms: fatigue (low energy), decreased libido, and lack of motivation. Androgen hormone is the result of average DHEA hormone production, which indicates the function of the adrenal gland to produce sufficient DHEA (Klein et al., 2019).

Free cortisol (cortisol in blood vessels) and metabolites of cortisol (the product of cortisol metabolism) were still within normal limits. This indicates optimal functioning of the HPA (Hypothalamus-Pituitary-Adrenal Axis) (Marcos et al., 2014). Another marker analyzed was Organic Acid tests (OATs). Some of the organic acid markers assessed at DUTCH are as follows.



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JURNAL KEDOKTERAN FKUM SURABAYA

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Methylmalonate Acid (MMA), the sample's MMA levels were still in the normal range of 0.8 ug/mg. This shows that the intake of B12 is sufficient but can be further increased so that its function can be more optimal. Xanthurenate & Kynurenate levels of Xanthurenate & Kynurenate, which are metabolites of vitamin B6, also appeared to be within the normal range. It should be increased a little more, maybe up to 0.8 for Xanthurenate and up to 4 for Kynurenate, so the function can be more optimal (McCann et al., 1996).

Pyroglutamate, Pyroglutamate released in urine samples is at the upper threshold. Pyroglutamate is a metabolite of glutathione, the most vital antioxidant that protects our body. Low levels of glutathione can be caused by the use of drugs (fever reducers, pain medications) and exposure to toxins (e.g., alcohol). This is in line with the history that the sample often used analgesics as pain relievers during dysmenorrhea (Newman & Curran, 2021).

Homovanillate (HVA) is a metabolite of the neurotransmitter Dopamine (nerve hormone). The sample's HVA level was at a lower threshold, indicating little dopamine production or low dopamine levels that can be converted to HVA (Black et al., 2015). Low levels of dopamine, which can be converted to HVA, can be caused by a deficiency of several nutrients. Conversely, low dopamine production can be caused by BH4 deficiency, iron, and tyrosine. Some of the symptoms of low dopamine are addiction (to food or other substances), food cravings, pleasure-seeking, sleepiness, impulsivity, tremors, low motivation, fatigue & flat affect (Blasco et al., 2010).

Venilmandelate (VMA), the sample VMA test results were in the upper threshold; An increase in the threshold can be caused by

physical or psychological stress. Melatonin, the sample's melatonin level, was also on the upper threshold. No studies show that high levels of melatonin can be a problem. However, the problem can be found in chronic fatigue syndrome or depression conditions. Increased melatonin levels can be caused by consuming foods/supplements containing melatonin (Schiffer et al., 2019). The last marker is 8-OHdG, which serves as a marker of DNA damage. The higher the level, the more severe the oxidative stress condition in the body. The sample's 8-OHdG level is still within the normal range.

CONCLUSION

We report a 47-year-old woman with 28-day regular menstruation who underwent the DUTCH test. The results of the DUTCH test in this patient are 2-OH dominant, so they are safe from symptoms of estrogen dominance and low 4-OH production. The methylation process is smooth so that the risk of cancer related to estrogen dominance syndrome is low.

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