www.abiosci.com

REVIEW ARTICLE

Annals of Biological Sciences
2013, 1 (1):23-27

ISSN: 2348-1927

Diagnostic importance of URINALYSIS in endocrinology- A review

Olooto, Wasiu Eniola

Department of Chemical Pathology and Immunology, Olabisi Onabanjo University, Ago-Iwoye. Ogun State, Nigeria

ABSTRACT

Managing endocrine disease conditions by the clinicians involves marrying important health information from the history and clinical findings with results of laboratory investigations. The diagnostic power of endocrine tests depends on the choice of sample, type of tests, the preparation of the patients, the quality of the measurements, and the appropriateness of the reference data. Hence, there is the need for total agreement between the clinicians and the laboratory to take wise clinical decisions for optimal patient care. This review therefore focused on the diagnostic importance of 'simple test' like urinalysis in playing a major role in detecting abnormalities of endocrine origin. Despite the limitations of urinalysis which include the inconvenience and delays of collecting a 24-hr specimen, uncertainty of the collection completeness and the dependency of urinary hormone values on hepatic and renal functions, its importance as a diagnostic tool in endocrinology could not be underemphasized. These deficiencies are well taken care of by measurement of urinary creatinine level concentrations which helps in monitoring collection completeness.

Key words: Urinalysis, endocrine disease, clinicians, creatinine, 24-hr specimen.

INTRODUCTION

Urine is a clear, amber or straw-coloured fluid excreted from the body through the kidneys. The colour varies with diet, drug, diseases of the kidney, systemic diseases and components of the urine. The more concentrated the urine, the more yellow and darker it becomes [5]. It may have no particular smell, or a slight aroma that may alter as a result of disease, urine concentration or time of storage in the bladder. The normal composition of urine includes water, urea, creatinine, sodium, potassium, organic acids, protein, small traces of glucose and protein, and cellular components all responsible for its slightly acidic pH (approximately 5-6).

The normal urine volume in 24 hours is between 650-1500mls. This varies with fluid intake, loss of fluid from the body (diarrhea, profuse vomiting), physical activities (strenuous activities, exercise), environmental temperature and renal status. Urine volume less than 400mls is termed oliguria while anuria is urine volume lesser than 100mls.

Measurement and evaluation of biochemical markers as indicator of normal biological, pathologic processes, or pharmacologic responses play an important role in accurate diagnosis, and adopting appropriate therapeutic methods that improves clinical outcomes. Clinically, urinalysis is of importance in the diagnosis and management of various diseases that are of either metabolic or systemic origin. It is usually done using methods based on the physicochemical properties of the urine and chemical methods. Many disorders can be diagnosed in their early stages by detecting abnormalities in the urine. These abnormalities include increased concentrations of constituents that are not usually found in significant quantities in the urine such as glucose, protein, red blood cells, white blood

cells, crystals and bacteria. Such substances may be present due to high plasma concentration, ineffective filtering due to renal pathology or because of infection.

Urine samples should be collected using 'clean-catch' midstream sampling, which ensures that bacteria present in the urethra are washed away in the first portion of urine [7] or a complete 24-hr urine collection depending on the purpose of use.

Urine as specimen of choice

The choice of urine for diagnosing endocrine abnormalities is based on the presence of original hormones and their metabolites either with or without biological activity. Those with biological activities (e.g. urinary free cortisol) are usually secreted in free unbound form while those without biologic activity are conjugated to carrier proteins and so excreted in the urine.

Traditionally, a 24- hr urine specimen has been used, but 12-hour and 2-hour collections have been validated by researchers [1]. The 24-hr urine specimen is usually used for many endocrine tests because it has the advantages of better analytic sensitivity for some hormones [4, 8]. The use of the first-morning or second-morning urine may be a more convenient alternative for some analytes because most hormones have biologic variation, including circadian, ultradian, diurnal, menstrual and seasonal variations as described by various researchers [10, 18]. Measurement of urinary creatinine concentrations helps in monitoring collection completeness, especially when it is compared with the muscle mass of the patient.

Urine in diagnosing diabetes mellitus

Detection of glucose in urine sample is suggestive of diabetes mellitus. Microalbuminuria is present in nearly between 20% and 40% of patients with either diabetes mellitus [15] and 40% of patients with hypertension [12] in which it progresses to proteinuria reflecting renal involvement in those disease conditions. Albuminuria is not normally seen with urinalysis but with progressive renal involvement albumin is detected in the urine. Microalbuminuria is diagnosed either from a spot urine sample (30-300 mg/L) or a 24-hr urine (between 30 to 300 mg/24 hours) measured on at least two to three occasions over a period of two to three months, in order to confirm the diagnosis or by determining albumin to creatinine ratio in random urine [3]. Value of between 30 and 300 mg/g of creatinine is confirmatory of microalbuminuria while any value higher is described as proteinuria.

In clinical practice detection of microalbuminuria is a critical prognostic indicator that is imperative to aggressive control of diabetes and hypertension.

Also, urinary sediment examination is an integral part in evaluating hypertensive patients. Microscopic hematuria is sometimes seen in hypertention and this may be suggestive of sub-clinical kidney damage at diagnosis [16].

Urine in diagnosing cortisol related abnormalities

Cortisol urine test measures the amount of cortisol hormone in the urine. Cortisol is a steroid hormone released from the adrenal gland in response to adrenocorticotrophic hormone (ACTH), a hormone from the anterior pituitary gland in the brain. A 24-hour urinary free cortisol (UFC) is usually measured to determine increased or decreased cortisol production as it occurs in different diseases such as Cushing's disease and Addison's disease [20]. Increased urinary levels of cortisol may indicate severe depression, adrenal gland tumor, cortisol producing tumor somewhere else in the body or Cushing's disease while decreased urine levels may indicate Addison's disease, hypopituitarism or congenital adrenal hyperplasia.

Urine in diagnosing catecholamine secreting tumors

Diagnosis of tumors can be easily done or predicted by urinalysis. Notable amongst tumors diagnosed are pheochromocytoma, ganglioblastoma, ganglioneuroma, and neuroblastoma [23]. In these conditions, urinary metabolites of catecholamines are usually measured. The major catecholamines (dopamine, norepinephrine and epinephrine) that are produced in excess amount during these conditions are metabolized into other measurable inactive substances (notably homovanillic acid, normetanephrine ,vanillylmandelic acid and metanephrine), which are measured in the urine.

In diagnosing pheochromocytoma, the 24-hr urinary excretion rates of catecholamines and their metabolites are the tests of choice [22]. Clinically, if the suspicion is high, screening with a combination of catecholamines,

metanephrines, and vanillylmandelic acid measurement is recommended. In the case of low clinical suspicion, only measurement of metanephrines is needed for the initial screening but if the metanephrines are increased, the urinary catecholamine and vanillylmandelic acid levels are performed. Patients with pheochromocytomas generally have a twofold increase in epinephrine or norepinephrine excretion rates or an increased urinary metanephrine concentration [19]. However, in patients with advanced or end stage renal disease, measurement of urinary catecholamines may not be valid [21]. In addition to the above, measurement of urinary creatinine is recommended in both low and high clinical suspension state to ensure completeness of 24 hr collection. Urinary creatinine is a product of endogenous metabolism and that the creatinine output for any given individual is relatively constant from day to day especially when it is compared with the muscle mass of the patient. The urine to be used for catecholamine and metanephrine determination is usually collected into bottles with acid preservative because they both deteriorate without a preservative.

False positive elevations in metanephrine levels can be the result of sympathomimetics, tricyclic antidepressants, phenoxybenzamine and calcium channel blockers while selective alpha1-blockers (e.g. doxazosin, prazosin, terazosin), beta-blockers, angiotensin-converting enzyme inhibitors (ACE-I), angiotensin II receptor blockers, and diuretics do not interfere. Urine test for catecholamines may also be used to monitor those who are receiving treatment for these conditions.

Urine in diagnosing hyperaldosteronism

A 24-hr urine specimen is of diagnostic importance in hyperaldosteronism. To achieve this, a 24-hr urine is collected after 3 days of loading with potassium supplementation. Spironolactone and angiotensin-converting enzyme inhibitor medications should be replaced with other drugs before test and thereafter, the urinary concentration of aldosterone, sodium, and potassium is measured. Excretion of greater than 200 mEq of sodium in 24 hr assures adequate sodium load while urinary aldosterone excretions greater than 12 mg in 24 hr confirms hyperaldosteronism. A 24-hr urinary calcium measurement and excretory urograms are often helpful for characterizing patients with PTH-mediated hypercalcemia. A low 24-hr urinary calcium concentration (<100 mg/24 hr) may suggest familial hypocalciuric hypercalcemia [11]. Patients with a positive result of a screening test for primary aldosteronism should undergo confirmation testing. The confirmatory test in primary aldosteronism involves measurement of plasma renin activity (PRA) and plasma aldosterone concentration (PAC) [23]. A ratio of PAC to PRA >20 is a positive screening result. The PAC is typically greater than 200 ng/L (>20 ng/dL), while the PRA is typically low. Secondary cause of hyperaldosteronism is to be considered If PAC and PRA concentrations are increased and the ratio is ≤10. Low concentration of both PRA and PAC requires consideration of adrenal and other metabolic disorders as a cause.

Urine in diagnosing cushing syndrome

Cushing syndrome is a rare condition occurring in approximately 10 per millions [14] with hypercortisolism as the main clinical presentation. As a screening test, urinary free cortisol is done only in patients with specific clinical features such as central obesity, osteoporosis, proximal muscle weakness, facial plethora, or striae. Such patients must not be on exogenous glucocorticoids, including topical applications to genital area such as hemorrhoid medications, which could contaminate urine collections. Also, history of chronic alcoholism should be established because this may cause hypercortisolism, which can mimic Cushing syndrome [9]. Alcoholic patients should refrain from drinking alcohol at least 1 month before testing.

A 1-mg overnight dexamethasone test is useful in patients with ambiguous urinary free cortisol values. Due to low diagnostic accuracy, the 24-hr 17-hydroxycorticosteroid test is not recommended as a screening test for Cushing syndrome [24]. Generally, two urinary free cortisol measurements are done to diagnose endogenous hypercortisolism. The paired measurement of ACTH and cortisol determines whether the disease is of adrenal origin.

Urine in diagnosing ketoacidosis

Ketoacidosis is a state of increase levels of ketone bodies (notably acetoacetate and β-hydroxybutyrate) in the body. Ketoacidosis usually occur as a complication of untreated or poorly managed diabetes mellitus in which case there is insulin abnormalities. The diagnosis is suspected with the presence of ketone breath and confirmed by the ketone test which is achieved using the urine sample. The test is done when the blood sugar is higher than 240 mg/dL with associated vomiting, dehydration and unconsciousness. The urine pH, which is a measure of the hydration status of the body, is also measured [6].

Urine in diagnosing infertility

Urinalysis is an important part of the infertility work-up, because it may reveal unsuspected, fertility-impairing disorders such as kidney disease or diabetes mellitus. Urinalysis can also detect lower urinary tract infections (UTIs) such as urethritis (inflammation of the urethra) and cystitis (inflammation of the bladder); it could detect significant presence of pus cells or increased white blood cells- an indicator of possible infection. Urinalysis will also show the possible presence of sperm in the urine- an indicator of retrograde ejaculation. Retrograde ejaculation occurs when semen pushes backwards into the bladder instead of out of the penis. This is caused by the failure of nerves and muscles in the bladder neck to close during orgasm and results in difficulties in delivering sperm to the vagina during intercourse. Retrograde ejaculation can be caused by previous surgery, medications or diseases affecting the nervous system. Signs of this condition may include cloudy urine after ejaculation and diminished or "dry ejaculation" with orgasm. The presence of sperm in urine is common in both fertile and infertile men but more prevalent among infertile men (98.7%) in whom it comprised about 46% of the total sperm count [2].

Some infertile men may achieve orgasm without much ejaculate (dry ejaculation) or have cloudy urine after ejaculation. In such individuals, urinalysis immediately after ejaculation may help to diagnose retrograde ejaculation. A post-ejaculatory urinalysis should be performed in patients with ejaculate volumes of less than 1 ml, except in patients with bilateral vasal agenesis or clinical signs of hypogonadism.

Urine in diagnosing pregnancy

In addition to symptomatic presentations associated with pregnancy, urinalysis is of great usefulness in diagnosing pregnancy. The test depends on the detection of large quantities of human chorionic gonadotrophin (hCG), a gonadotrophic hormone produced by the trophoblast. Urine of pregnant women contains hCG soon after implantation and this combine with anti-hCG in solution when added together. The presence of anti-hCG in the mixture is tested for with a suitable indicator.

Higher levels of hCG is observed in choriocarcinoma, thus monitoring levels of this hormone is used to determine responses to chemotherapy and prognosis.

Urine in diagnosing Pre-Eclampsia

Preeclampsia is diagnosed in a pregnant woman with characteristic new onset of hypertension (systolic and diastolic blood pressure of $\geq$ 140 and 90 mm Hg, respectively, on two occasions, at least 6 hours apart) and proteinuria (protein excretion of $\geq$ 300 mg in a 24-hr urine collection) that develop after 20 weeks of gestation in previously normotensive women [17]. A 24-hr urine collection dipstick test of $\geq$ ++, or a random urine collection dipstick test of $\geq$ + in a previously normotensive woman after 20 weeks of pregnancy suggests preeclampsia complicating the pregnancy.

A test that involves checking patients' urine for podocytes has been proposed based on the detection of these specific cells only in the urine of pre-eclamptic women whilst none was found in women who had a normal pregnancy, or who suffered from pregnancy-induced hypertention [13].

CONCLUSION

The use of urine specimens as a diagnostic tool in endocrinology is fundamentally based on the presence of both the original hormones and the biologically active or inactive metabolites of these hormones in urine. Its use in diagnosing endocrine disorders is because it has the advantages of simpler and better analytic sensitivity for hormones many of which have short half-lives and are thus rapidly cleared from the blood. However, the inconvenience and delay in collecting 24-hr urine specimen and the uncertainty of the collection completeness are grey areas that are corrected by measurement of urinary creatinine concentrations. Blood specimen is also to be considered which have both the time completeness advantage and the limitation of time dependency.

REFERENCES

[1] Abebe J, Eigbefoh J, Isabu P, Okogbenin S, Eifediyi R, Okusanya B. *J Obstet Gynaecol*, **2008**, 28,496-500.
[2] Akanksha Mehta, Jonathan PJ, Pat M, and Mark S., *Androl*, **2012**, 33 (5), 917-920.
[3] American Diabetes Association. Nephropathy in Diabetes. *Diabetes Care*, **2004**, 27:S79-S80.
[4] Demir A, Alfthan H, Stenman UH, Voutilainen R. *Pediatr Res.*, **1994**, 36, 221–226.

[5] Dougherty L, Lister S. The Royal Marsden Hospital Manual of Clinical Nursing Procedures Oxford: Blackwell Publishing, **2004**.
[6] Eisenbarth GS, Polonsky KS, Buse JB. Type 1 Diabetes Mellitus. In: Kronenberg HM, Melmed S, Polonsky KS, Larsen PR. Kronenberg: Williams Textbook of Endocrinology. 11th ed. Philadelphia, Pa: Saunders Elsevier; **2008**, chap 31.
[7] Higgins C. Microbiology testing. In: Understanding Laboratory Investigations. Oxford: Blackwell Science, **2000**.
[8] Hourd P, Edwards R. *Clin Endocrinol* **1994**, 40, 155–170.
[9] Lamberts SW, Klijn JG, de Jong FH, Birkenhager JC. *JAMA* **1979**, 242, 1640-1643.
[10] Maes M, Mommen K, Hendrickx D, Peeters D, D'Hondt P, Ranjan R, et al. *Clin Endocrinol* **1997**, 46, 587–598.
[11] Marx SJ, Spiegel AM, Levine MA. *N Engl J Med*, **1982**, 307, 416-426.
[12] Montalescot G, Collet JP. *Eur Heart J*., **2005**, 26, 2616-2622.
[13] Muller-Deile, J, and Schiffer, M. *Journal of Pregnancy*, Vol. **2011**, 6 pages.
[14] Nieman LK, Cutler GB. Cushing's syndrome. DeGroot LJ eds. Endocrinology, WB Saunders Philadelphia, PA, **1995**, 1741-1769.
[15] Ochodnicky P, Henning RH, van Dokkum RPE, de Zeeuw D. *J Cardiovasc Pharmacol*., **2006**, 47, S151-S162.
[16] Olanrewaju TO, Aderibigbe A. *J. Nephrol*, **2010** Sep-Oct; 23(5), 547-555.
[17] Redman CW, Sargent IL. *Science*, **2005**, 308, 1592–1594.
[18] Sebastian-Gambaro MA, Liron-Hernandez FJ, Fuentes-Arderiu X. *J Clin Chem Clin Biochem*, **1997**, 35, 845–852.
[19] Sheps SG, Jiang N-S, Klee GG. Diagnostic evaluation of pheochromocytoma. Endocrinol Metab Clin North Am, **1988**, 17, 397–414.
[20] Stewart PM, Krone NP. The adrenal cortex. In: Kronenberg HM, Melmed S, Polonsky KS, Larsen PR, eds. Williams Textbook of Endocrinology . 12th ed. Philadelphia, PA: Saunders Elsevier; **2011**, chap 15.
[21] Stumvoll *M*, Radjaipour *M*, Seif *F*. *Am J Nephrol*, **1995**, *15, 147–151*
[22] Young WF Jr. *Eur J Endocrinol*, **1997**, 136, 28–29.
[23] Young WF. Adrenal medulla, catecholamines, and pheochromocytoma. In: Goldman L, Ausiello D, eds. Cecil Medicine. 23rd ed. Philadelphia, Pa: Saunders Elsevier; **2007**, chap 246.
[24] Zadik Z, De Lacerda L, De Carmargo LA, Hamilton BB, Migeon CJ, Kowarski AA. *J Clin Endocrinol Metab*, **1980**, 51, 1099-1101.