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Opinion

Can sweat glands act as temporary or permanent replacement for the excretory function of kidney?

Kenneth A. Agu

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Authors:
K. A. Agu.
Department of Surgery, University of Nigeria Teaching Hospital Ituku/Ozalla,
P.M.B. 01129 Enugu 400001, Nigeria

drkena_agu@yahoo.co.uk

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Abstract

Uremic frost – the powdery whitish substance, comprising urea and uric acid salts, on the skin of some patients with end stage kidney disease could be an attempt by the sweat glands to take over the function of the failing kidneys. Currently end stage kidney disease is managed mainly by hemodialysis and eventually kidney transplantation. Kidneys are primarily the organs for excretion of metabolic wastes. A normal kidney contains 800,000 to 1.5 million nephrons. This excretory function, which is essential for life, consists of filtration and selective reabsorption / secretion to produce urine. The major nitrogenous waste in urine is urea. The sweat glands are basically organs of thermoregulation. However, they are also involved in excretion of metabolic wastes. The total number of sweat glands lies between 1.6 and 4.5 million. There are anatomical and physiological similarities between the nephron – the functional unit of the kidney and the sweat gland. This article proposes a functional similarity between the two. Anatomically, the sweat gland bears some resemblance to the nephron. A nephron has 2 basic components, the glomerulus and the tubules. Similarly, the sweat gland has a secretory unit consisting of a base rolled into a glomerulus, and a duct that carries the sweat away. Both the kidneys and the sweat glands excrete nitrogenous wastes, water and electrolytes. They are also involved in maintaining acid-base balance. The hypothesis is that the skin, via the sweat glands, constitutes an alternative excretory organ to the kidneys, though probably minor, and thus could act as temporary or permanent replacement for the kidneys.

Keywords excretion, nephron, sweat gland

Introduction

As a final year medical student I watched the horror of a patient in the terminal stages of end-stage renal disease. This was at a time when our center had no form of hemodialysis or peritoneal dialysis. Kidney transplantation was not available. I observed that the patient who later developed uremic encephalopathy had a whitish powdery substance that covered the skin. Later I learnt that this was called uremic frost. Then I wondered: was the skin via the sweat glands attempting to take over the function of the failing kidneys?

Highlights of the Study

- Sweat glands secrete metabolic waste products.
- The volume of sweat secreted daily can reach 8 liters.
- The amount of solutes in sweat gland increases on Kidney failure.
- The sweat glands can partly or wholly take over the excretory function of kidneys.

Functions of the kidney

Kidneys perform several roles but the most important is its excretory function – the removal of water-soluble waste products of metabolism. They are primarily involved in the excretion of urea, the major waste product of protein metabolism, other nitrogenous wastes, water, products of drug metabolism etc. They also serve homeostatic functions such as the regulation of water and electrolytes, maintenance of acid–base balance, and regulation of blood pressure (via maintaining the salt and water balance). Its functions are vital to life and are regulated by the endocrine system by hormones such as antidiuretic hormone, aldosterone, and parathyroid hormone [1]. The kidneys may also be regarded as endocrine organs producing hormones including calcitriol and erythropoietin. However, the excretory function of the kidney is emphasized in this article.

Nephron is the basic excretory functional unit of the kidney [2]. It consists of two parts – the renal corpuscle (glomerulus and Bowman's capsule); and the system of tubules. Filtration takes place in the renal corpuscle, while the tubules absorb, secrete and reabsorb water, electrolytes and other products. A normal kidney contains 800,000 to 1.5 million nephrons [3]. The kidney generates about 180 liters of filtrate a day, while reabsorbing a large percentage, allowing for the production of only approximately 1 liter of urine with a pH range of 4.5 - 8, a typical average being around 6.0 [4]. Urine is approximately 95% water and the other 5% consisting of solutes that are dissolved in the water as a component of urine.

These solutes are traditionally divided into two: organic molecules and inorganic ions. Chief among the organic molecules is urea, the major end-product of protein metabolism. Others include creatinine, uric acid and ammonia. Other substances found in small amounts are simple sugars like glucose, enzymes, fatty acids, hormones, pigments like bile and urobilinogen and mucins. Electrolytes like sodium, potassium, chloride, calcium and magnesium are found in varying amounts depending on the diet and action of hormones like aldosterone and parathyroid hormone. Other ions include ammonium, sulphates and phosphates.

Functions of the sweat glands

Sweat glands are type of exocrine gland that produce and secrete substances onto an epithelial surface by way of a duct. They are small tubular structures of the skin that produce sweat. Two types of sweat glands are found in the body: eccrine glands and apocrine glands. The eccrine sweat glands are distributed over much of the body while apocrine glands are mostly limited to the axilla and perianal areas in humans [5]. There is a third group of sweat glands that share characteristics of both eccrine and apocrine sweat glands. These are called apoeccrine glands. The total number of sweat glands lies between 1.6 and 4.5 million, and is greatest on the plantar skin of the feet [6].

Sweating, also known as perspiration or diaphoresis is the production and release of fluids secreted by the sweat glands onto the skin surface [7]. There are two situations in which the nerves will stimulate the sweat glands, causing perspiration: during physical heat and during emotional stress. Both eccrine and apocrine sweat glands participate in thermal (thermoregulatory) sweating [8]. Emotionally induced sweating, on the other hand, is restricted to palms, soles, armpits, and sometimes the forehead, while physical heat-induced sweating occurs throughout the body [9].

Sweat glands are used to regulate temperature and remove waste by secreting water, sodium salts, and nitrogenous waste (such as urea) onto the skin surface. Sweating is primarily a means of reducing the temperature of the body. This is achieved by evaporation of sweat, which takes the latent heat of vaporization from the body, thereby producing a cooling effect. When the body temperature is elevated either by external sources like hot weather or from heat production during vigorous muscle activity, more sweat is produced. When first secreted, the fluid is similar to interstitial fluid in composition. It is modified by the action mainly of the basal cells as it passes along the duct, which reabsorbs sodium, chloride and some water. The hormone aldosterone enhances this activity. Sweat contains mainly water with a salty taste due to the substantial content of sodium chloride. The volume of water lost in sweat every day is highly variable, ranging from 100ml to 8,000 ml/day. The solute loss can be as much as 350 mmol/day (or 90 mmol/day for the acclimatized subject) of sodium under the most extreme conditions. During average intensity exercise, sweat losses can average up to1 to 2 liters of water per hour. However, amount of sweat released by each gland is determined by several factors, including gender, genetics, environmental conditions, age or fitness level. Two of the major contributors to sweat rate are an individual's fitness level and weight. If an individual weighs more, sweat rate is likely to increase because the body must exert more energy to function and there is more body mass to cool down. On the other hand, a fit person will start sweating earlier and easier. As someone becomes fit, the body becomes more efficient at regulating the body's temperature and sweat glands adapt along with the other body systems.

Predicted whole body sodium concentration has been determined as 18.2-70.8 mmol/l. Absolute and relative whole-body sweating rates were 0.26-5.73 L/h and 3.3-69.7 ml/kg/h respectively [10-11]. The second role of sweating is the excretion of waste products from the body. Apart from water, sweat also contains other minerals, lactate, urea and other nitrogenous wastes. The volume of sweat and its mineral composition vary with the individual, their acclimatization to heat, exercise and sweating, the particular stress source, the duration of sweating, and the composition of minerals in the body. An indication of the minerals content is sodium (0.9 g/l), potassium (0.2 g/l), calcium (0.015 g/l), and magnesium (0.0013 g/l) [12]. Additionally, many other trace elements are excreted in sweat, again an indication of the concentrating ability of the sweat glands. Reported values of these substances, although measurements can vary fifteen-fold, are as follows: zinc (0.4 milligrams/liter), copper (0.3–0.8 mg/l), iron (1 mg/l), chromium (0.1 mg/l), nickel (0.05 mg/l), and lead (0.05 mg/l) [13-14]. Sweat typically is found at moderately acidic to neutral pH levels, typically between 4.5 and 7.0. [15].

The effect of pilocarpine

Pilocarpine hydrochloride is a parasympathomimetic alkaloid obtained from the leaves of tropical South American shrubs from the genus *Pilocarpus*. It is a non-selective muscarinic receptor agonist in the parasympathetic nervous system, which acts therapeutically at the muscarinic acetylcholine receptor M_3 [16]. Pilocarpine stimulates the secretion of large amounts of saliva. Its effect on the sweat gland where it causes excessive production of sweat is regarded as a side effect or adverse reaction. Few queries regarding this are that whether in a paradigm shift, is it possible to regard this apparent side effect as the main desired effect and will it be possible to design similar drugs that will selectively stimulate the muscarinic receptor of the sweat gland. If the answers to these questions are affirmative, then the possibility of converting the sweat gland to an alternative nephron exists. Probably drugs could be developed which will not only increase the amount of sweat secreted, but also the concentrating capacity of the sweat glands.

The sweat gland functioning as nephron

Just like the kidney performs other functions in addition to its major function as an excretory organ, so also the sweat gland. Apart from its major function in thermoregulation, it also performs other functions. Anatomically, the sweat gland bears some resemblance to the nephron. A nephron has two basic components, glomerulus and tubules. In a similar way, the sweat gland has a secretory unit consisting of a base rolled into a glomerulum, and a duct that carries the sweat away [17].

In certain pathological disorders such as cholera and uremia, the sweat glands may assume some of the functions of the kidneys and excrete urea of such quality that the entire skin surface is covered with very fine crystals. This is called as uremic frost which has been defined as powdery deposits on the skin, especially the face, including urea and uric acid salts, due to excretion of nitrogenous compounds in the sweat; seen in severe uremia.

In hot weather, there is an increase in sweat production and a decrease in urine production. Similarly in cold weather, the rate of sweating decreases while urine production increases. It appears there is an inverse relationship between the excretory functions of the two organs. It could be argued that the kidneys are trying to conserve water due to the additional loss in sweat during hot weather, but a study is needed to establish whether the kidneys excrete the same amount of solutes in such conditions.

The analogy with the nephron is strengthened by the demonstration by Fasciolo et al that antidiuretic hormone (ADH) can inhibit sweating when introduced sub-dermally [18].

Hypothesis

The skin via sweat glands, constitute an alternative, though probably minor, excretory organ to the kidneys. Apart from urea there are many other substances including trace elements excreted in sweat. If sweating is purely for thermoregulation, why would the body expend such energy in excreting and concentrating these substances in sweat especially as these processes mainly involve active transport?
The corollary to this hypothesis is that the excretory function of the sweat glands can be enhanced using physical or pharmacologic means to act as a temporary/permanent kidney replacement or as an effective alternative to hemodialysis.

Evaluation of the hypothesis

Healthy subjects can be recruited adhering to principles of medical ethics. They can be divided into two groups matched according to age, gender, and race and body surface area. They can be placed on the same diet and each day during the selected period of study, the first group can be stimulated either physically or pharmacologically to secrete large amounts of sweat which can be collected and analyzed for volume, pH and concentrations of various solutes especially nitrogenous wastes. The urine can also be collected and similarly analyzed. The second group can be kept under a cold room temperature to discourage sweating and urine can also be analyzed in this situation. For both groups, the plasma pH, osmolality and concentrations of substances analyzed in the urine and sweat can also be obtained before and after the experiment. Statistical tests can be applied to determine whether there is any significant difference between the rate of excretion by the kidneys and sweat glands in the two groups. Alternatively, same subjects can be used as two arms on different days and same comparisons can be made.

At a second level, drugs could be developed which will maximally stimulate the sweat gland receptors to selectively secrete unwanted substances.

Conclusion

Nephron and the sweat gland share similarities in anatomical structure and function. With an advancement in science and technology, it is possible to explore the possibility of physically or pharmacologically converting the sweat gland to a nephron. If effectively done, the process may become an alternative to hemodialysis to handle the excretory function of kidney.

Conflict of interest statement

The author declares no conflict of interest.

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