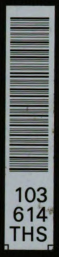
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TASTE ALTERATIONS IN PATIENTS

WITH RENAL DISEASE

presented by

JEAN CATHLEEN BURGE

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TASTE ALTERATIONS IN PATIENTS WITH RENAL DISEASE

by

Jean Cathleen Burge

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ABSTRACT

TASTE ALTERATIONS IN PATIENTS

WITH RENAL DISEASE

by

Jean Cathleen Burge

Low protein, high calorie, low electrolyte dietary programs have been used to delay the need for dialysis in patients with uremia. These programs depend upon a patient's ability to adhere to these restrictive diets. Anorexia is a common interfering factor with the success of these programs. Anorexia continues to be a problem among many patients undergoing hemodialysis. Taste abnormalities, a component of anorexia, may interfere with food acceptance among these patients. Since it is known that many disease states affect taste, this investagation was designed to assess the extent to which taste was affected in ESRD patients undergoing routine hemodialysis and to assess when in the progression of chronic renal failure (CRF) deterioration of taste occurs.

Recognition taste thresholds for four primary tastes, sour, sweet, salty and bitter were determined in 18 patients (age range 17 to 65 years) with end-stage renal disease undergoing maintenance hemodialysis and were

compared to 10 controls, matched for age and sex. In experimental subjects, mean taste thresholds before and after dialysis for tartaric acid were 0.004N and 0.002N, respectively, compared to 0.0002N for controls. For sucrose, before and after dialysis, mean thresholds were 0.039M and 0.023M, respectively, and 0.014M for controls. When we used the same modalities, that is, sweet or sour, all possible comparisons were significant except the one for sweet between patients after dialysis and controls. Mean recognition taste thresholds for salty and bitter were not significantly impaired in dialysis patients when compared to controls. Mean serum zinc concentrations were 77 µg/dl, both before and after dialysis. Since these are low-normal values, zinc could be a factor in loss of taste among these patients, but it can not explain the improvement seen in taste acuity associated with dialysis for 6 to 8 hours.

In the second phase of the study, 27 CRF patients were selected and divided according to their degree of renal insufficiency by creatinine clearance (CC) levels. Mild CRF (CC of 41-75 ml/min), moderate (CC of 15-40 ml/min) and severe (CC of <15 ml/min). Recognition taste thresholds were done for sucrose and tartaric acid using a staircase method and choice between distilled water and stimulus.

In severe CRF patients, mean recognition taste thresholds were significantly higher ($P<0.001$) than those with

mild CRF or those with moderate CRF ($P<0.05$). The mean threshold of tartaric acid was not significantly different with mild CRF and moderate CRF patients were compared even though the means almost doubled in value. Mean recognition thresholds for sucrose are not different among any of the patient groups tested; the trend, however, was tc increase threshold concentrations as renal function decreased (mean 0.016, 0.017, and 0.028M for mild, moderate and severe CRF patients, respectively). Serum zinc levels of CRF patients declined as renal function declined, 92.8, 82.8, and 75.0 µg/dl. The difference between mild and severe CRF patients was snigificant ($P<0.01$). Salivary zinc levels rose as renal function declined (mild, <30 ppb; moderate, 66.5 ppb; and severe 141 ppb) however, these differences were not significant. Urinary zinc excretion, when expressed in terms of creatinine in the urine, was not different in any of the three groups. Also, dietary zinc intakes did not differ in any of the groups studied.

Loss of taste may be associated with the accumulation of basic protein metabolites in the saliva which neutralize the ions which provide the sour stimulus. Loss of taste increases in severity as renal function declines and continues in patients on dialysis. Dialysis improves the patient's taste response and also decreases the concentration of these protein metabolites in the saliva.

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INTRODUCTION

In 1975, Congress classified chronic renal disease as a disabling condition and allowed social security payments for maintenance hemodialysis and kidney transplantation (Anonymous, 1975). It is estimated that approximately 8 million people in the United States are affected by kidney disease, and that 67-84 patients per million population will begin hemodialysis annually. Approximately 83 percent of all patients with end-stage renal disease chose chronic maintenance hemodialysis (Pearson, 1975). The success of chronic maintenance hemodialysis depends on a number of factors.

Nutritional care, including consumption of sufficient protein and calories and restriction of sodium, potassium and phosphorus, is important in providing and maintaining optimal health of the patient undergoing routine hemodialysis.

Anorexia coupled with increased caloric needs present problems in nutritional management. Altered taste perception is a distressing problem which may affect an individual's food and fluid intake (Carson, 1977). Meat, sweet desserts and supplements such as high calorie liquid glucose solutions, which are important sources of calories,

are frequently refused by patients with chronic renal disease. Bartoshuk (1978) states that meat is a food frequently avoided by dysguesics. Cachectic cancer patients have been shown to have an enhanced taste acuity for bitter (DeWys and Walters, 1975) which correlated with an aversion to meat. A number of amino acids, peptides, and purines in pure form have a bitter taste (Jones, 1969). Morrison (1978) also showed a correlation between increased taste acuity in respect to urea and aversion to meats and suggested that since meat was composed of high concentrations of amino acids and polypeptides, that this might be an explanation for the aversion reaction of these patients to meat.

Patients with renal disease are especially susceptible to malnutrition. Recently, Butterworth and Blackburn (1975) reported that malnutrition was a prevalent health problem among hospitalized patients. Appetite and those factors which affect food intake become important in the attempt to prevent malnutrition in the hospitalized patient population. Identification of ways in which taste is altered should lead to corrective measures or at least better understanding by professional personnel of the problems imposed upon the renal patient, especially in relationship to acceptance of special diets. Furthermore, it should help the food industry in the development of more acceptable food products for patients with renal

disease.

The present study was undertaken to evaluate taste alterations associated with renal disease, when in the progression of renal disease these changes occur and to determine whether or not there is a correlation between recognition taste thresholds and certain biochemical parameters such as, creatinine clearances, serum and salivary zinc levels and urinary zinc excretion over a 24 hour period.

REVIEW OF LITERATURE

Taste: A chemical sense

The human taste response requires the incorporation of minute amounts of a sapid substance into the neuro-epithelial cells of the taste buds (Alpern et al., 1967). Four distinct tastes; sweet, sour, salty and bitter are perceived by humans. The perception of sweet and salty occurs most acutely at the tip of the tongue, sour at the sides and bitter at the back of the tongue.

Taste buds are for the most part located on papillae, which are small elevations visible on the surface of the tongue. There are a number of receptor cells containing finger-like extensions known as microvilli located in each taste bud. Chemical materials in solution reach the microvilli by way of tiny pores in the papillae and produce a neural response in the sensitive taste receptors.

Pfaffman (1978) suggests that chemicals do not penetrate the taste cell membrane, but quickly absorb to the surface, to cause depolarization by some as yet unknown process. This is rapidly transmitted to the nerve fiber. Presumably, there are different molecular sites on the receptor cell membranes sensitive to different

chemical configurations for different basic tastes.

The sourness of a stimulus results from the presence of a weak acid in solution. H^+ ions in solution appear to be necessary for the normal taste experience of sour (Christman, 1971). The sourness of a solution may increase with falling pH; however, acid concentration alone does not correlate with sourness. A weak solution of acetic acid tastes just as sour as hydrochloric acid, even though HCl may have four or five times the acid concentration of acetic acid. The higher degree of dissociation of an acid, the more sour the taste will be, especially in weak acids (Gorman, 1964).

The cation chloride plays an important role in the experience of salty and an increase in the degree of dissociation may increase the sensation of saltiness elicited from a sodium chloride solution (Gorman, 1964). Sweet and bitter taste responses appear to be much more complex and may be mediated by enzymatic reactions (Christman, 1971). In general, compounds of sugars produce sweet, while most alkaloids produce bitter sensations.

Measurements of taste acuity

Hollingsworth and Paffenberger (1917) state that sensations of taste perceived from weak solutions depends upon many other factors besides concentration of the solution. These factors include:

1. The amount of solution applied
2. The extent of surface excited
3. The duration of the application
4. The temperature of the solution
5. The state of rest or movement of the sense organ
6. The nature of the preceeding stimuli.

The effect of area, exposure duration and temperature

Mueller (1965) reports that there is an inverse relation between the size of the stimulated area and the threshold concentration. Lower concentrations of stimulus are required to elicit a taste response when large numbers of taste buds are exposed to the solution. The area of the tongue stimulated must be held relatively constant. Bartoshuk (1978) states that variation in the condition of the tongue as in some disease or deficiency states might effect the spread of small amounts of stimulus and produce differences in patient and control populations that are actually artifacts of the method, and not true taste differences.

Temperature influences on taste sensitivity differ with each of the four basic tastes. Shimizie et al. (1959) reports that the greatest taste sensitivity for sucrose and sodium chloride occurred at 30-35^{o} C.; however, this temperature did not elicit the greatest taste sensitivity for acid and quinine. Pfaffman (1951) reports that the

sensitivity for some sweet substances, for example dulcin, may rise with an increase in temperature up to 37° C. and then decrease above 37° C. Others like glycol produce no change in sweet taste thresholds with alterations in temperature, and still others may show intermediate effects. He further suggests that stimulation of the taste receptors can not be a simple chemical reaction between stimulus and taste cell. If this were so, one would expect the reaction to be enhanced as temperature increases.

Recognition taste thresholds

O'Mahony et al. (1976) defines recognition threshold as that concentration of a solution which elicits the characteristic taste of the stimulus, while at lower concentrations the detection threshold is that concentration at which the stimulus can be distinguished from distilled water. Determination of thresholds have been done using several different methods, which for reasons cited in the previous section may result in different threshold values.

The three drop method first described by Henkin et al. (1971) requires the subject to distinguish a difference between two drops of distilled water and a single drop of stimulus. These drops are placed on the protruding tongue in a random sequence. Due to the limited area

exposed to the stimulus, this method may result in a higher taste threshold than the sipping method. The data derived may be difficult to reproduce both within the subjects or between subjects (Bartoshuk, 1978) due to changes in the geography of the tongue which may result from disease or deficiency states.

A second method; the sipping or swishing method requires a subject to swish a specified amount of stimulus in the mouth, usually 10 cc or more, and swallow or expectorate the sample. The subject may be asked to distinguish the test stimulus from distilled water, and/or identify the stimulus. Cornsweet (1962) describes a method where the concentration of the stimulus changes depending upon the subjects response to the previous stimulus. If the subject indicates the presence of the correct stimulus, then the concentration of the test stimulus is decreased; if the subject can no longer identify the stimulus, the concentration is increased. This up and down or staircase method continues until 6 to 8 runs or reversals are completed. The first two runs are discarded and the next 4 to 6 runs are averaged in order to determine threshold. Either detection or recognition thresholds can be determined using this method. The problem of insufficient numbers of taste buds being stimulated is eliminated by this method.

Taste thresholds in disease states

As early as 1917, investigators noticed changes in taste thresholds associated with disease states. Hollingsworth and Paffenburger (1917) reported that elevated blood glucose decreases sensitivity to sweetness. Fabbi in 1954, reported an impairment of taste for a variety of substances including sugar in aged diabetic subjects. Schaupp in 1969, also reported that diabetic subjects had decreased sensitivity to sweet, which appeared to be related to the blood sugar level. Plausible explanations for this include: 1) Diabetic neuropathy, which may be related to a generalized taste deficit in this population, or; 2) adaptation of the tongue to high sugar levels which may interfere with sweet perception alone. Schellings et al. in 1965, reported that in 63 diabetic patients tested, there was no change in salt thresholds while there was an increase in the threshold for dextrose. In addition, these investigators could not find a correlation between these taste differences and the blood sugar levels of their subjects. Both treated and untreated subjects revealed abnormal sweet taste thresholds. Schellings and co-workers postulated that this change could be due to; 1) genetic differences in the diabetic population, or 2) due to a chronic elevation of blood sugar.

Obesity does not appear to result from or cause changes in sweet thresholds. Grinker in 1978, reported no difference in taste thresholds for sweet between subjects 55 to 211% overweight and normal weight control subjects. The degree of obesity, however, was positively correlated with the degree of sucrose aversion. Underwood in 1977, also reported a lower sweet preference function for obese subjects than for normal weight subjects.

Enhanced sensitivity to taste in cystic fibrotic patients and patients with adrenal cortical insufficiency was reported by Henkin in 1962. Henkin and co-workers, (1962) reported that patients with cystic fibrosis had taste sensitivity of 100 times greater than controls. Patients with adrenal insufficiency showed similar hypersensitivity which was corrected by carbohydrate-active steroids (Henkin, 1963). Wotman et al. in 1964, Desor and Maller in 1975, and Hertz et al. in 1974, could not reproduce these findings in patients with cystic fibrosis. Wotman, Desor and Hertz used a sipping method coupled with a forced choice descrimination method. In addition, each group asked their subjects to rinse with distilled water between each sample. They found no differences in salt taste thresholds between control and cystic fibrotic children.

The controversy as to whether a generalized abnormal sensitivity of the chemoreceptive system exists in

cystic fibrotic children may be due to differences in the methods used to assess sensitivity or to differences in the clinical populations tested. Henkin used a three drop forced choice method which requires the subject to identify which stimulus is different from water. Whether the stimulus is stronger or weaker in taste than the other two distilled water samples is not asked. Adaptation of the tongue to a stimulus may occur in cystic fibrotic patients, resulting from higher levels of sodium via their own saliva, than normal subjects (Frawley et al., 1951). This adaptation phenomenon may have interfered with the detection of salt in the study. A low concentration of sodium chloride or sucrose could give rise to a just-detectable decrement in bitterness or sourness of water and thus allow for discrimination from the test stimulus. Henkin's subjects were not asked to rinse with distilled water between each sample as was the case in the other three reports.

Changes in salt taste thresholds associated with hypertension is a second area which is controversial. Fallis et al. in 1962, reported that hypertensive subjects showed a decreased ability to recognize sodium chloride as compared with non-hypertensive controls. Detection thresholds for sodium chloride and sucrose between hypertensive and control subjects were not different . Wotman et al. confirmed these findings among

a similar group of subjects in 1967. Bisht et al. (1971) further reported that offspring of hypertensive adults had higher salt taste thresholds (decreased ability to recognize salt) than did children of normotensive adults. Henkin (1974) could not confirm these reports, however, and suggested that there was no difference in taste thresholds. Henkin did report that uncontrolled hypertensive subjects showed a preference for saline solutions over distilled water. Schrechter et al. in 1974, found that hypertensive individuals consumed more than four times as much salt as did normotensive controls, when given the choice between water and saline. These investigators further suggested that controlling blood pressure with antihypertensive medications decreased the desire for salt. Lauer et al. in 1976, did not find any differences in salt thresholds or preference in children with a wide range of blood pressures.

Stinbaugh et al. in 1975, reported that salt taste thresholds were not associated with changes in extracellular volume or external sodium balance alterations. Conteras in 1978, also reported that salt thresholds were not altered by sodium deficiency in rats.

Anorexia has been associated with cancer for some time (DeWys, 1974). MacCarty-Leventhal (1959) described a personal account of her battle with post radiation

mouth blindness following treatment for cancer of the pharynx. She described fruit as cinders, and juice as an acid liquid flavored with bicarbonate of soda or copper, and found food palatable only if it was hot and steaming so as to stimulate the sense of smell. DeWys and Walters in 1975, reported altered taste thresholds among 50 cancer patients with reduced appetite. Detection thresholds for sodium chloride and HCl were essentially similar in the control group and cancer patients. The detection threshold for sucrose was increased in the tumor group as compared to the controls and there was a trend of lower urea thresholds in the tumor group. The specific tumors were not identified in this study. Similar patterns were observed for the recognition thresholds, sodium chloride and HCl were not significantly different whereas sucrose recognition thresholds were elevated and urea recognition thresholds were decreased. DeWys (1974) further reported that decreased taste activity for sucrose in cancer patients could be positively correlated with the presence of decreased taste sensation in response to food and depressed appetite. Enhanced urea taste activity positively correlated with the presence of a meat aversion in this same group of cancer patients.

Carson and Gormican in 1977, studied 48 cancer patients with breast and colonic cancer before and after

treatment with 5-fluorouracil, a cancer chemotherapeutic agent. The ability to recognize salty solutions was impaired among both cancer groups prior to treatment when compared to controls. The salt recognition was significantly impaired among patients with active cancer when compared to resected tumor patients, in addition, colonic cancer patients tended to have greater salt taste impairment than did the breast cancer patients. Sweet recognition was also slightly impaired in the cancer patients when compared to controls, however, unlike DeWys, urea recognition was not different. Treatment with 5-fluorouracil resulted in slight but non-significant changes in all taste recognition thresholds.

Williams and Cohen in 1978, observed that in patients with lung cancer, recognition of sour was significantly impaired, sweet recognition was also impaired, although not significantly. Ten percent of the patients were also hypersensitive to bitter, however, the lung tumor group as a whole were not significantly different from the controls with respect to urea thresholds. Salt taste recognition thresholds were not different in the cancer patients when compared to the controls.

Differences in taste threshold results reported by various investigators studying cancer may be due to differences in patient populations and/or the type of cancers studied.

Differences in treatment modes may also affect the taste threshold results. Bonanni and Perazzi (1965) reported that bitter and sour acuity were most often affected in patients who received oropharyngeal radiation treatments. The other factor which may have affected the results is the degree of involvement of the tumor. Carson and Gormican (1977) were the only investigators who identified the degree of involvement of tumor in their population.

Several other disease states also affect taste. Cohen et al. in 1973, reported hypogeusia with elevated detection and recognition thresholds for each taste quality among thermal burn patients. Decreased ability to detect sucrose was reported by Wrobel (1978) in caries active naval recruits when compared to caries-free controls. Hypothyroidism has also been reported to decrease taste sensitivity (McConnel et al., 1975).

Although very little work has been done on taste acuity among patients with end-stage renal disease, anorexia and meat aversion is a common problem in these patients. In our dialysis unit we have frequently observed aversions for sweet products as well. Atkin-Thor et al. (1978) recently reported hypogeusia among renal patients which improved when zinc supplementation was begun. These investigators did not identify which tastes were altered, nor did they look at the effect of hemodi-

alysis treatment upon the altered taste.

Zinc and taste

Zinc Absorption

Approximately 20 to 30 percent of dietary zinc is absorbed from the duodenum, illeum and jejunum with very little being absorbed from the colon or stomach (Underwood, 1977). Control of body zinc levels is regulated by variations in zinc absorption. Zinc uptake by the intestinal wall of the zinc-deficient rat was four times that of the pair-fed and twice that of the ad-libitum fed control (Schwarz et al., 1974). Evans and co-workers (1975) have described a low molecular weight zinc-binding factor in the intestinal lumen of the rat. The uptake of zinc-65 by epithelial cells from everted intestinal rat segments was enhanced by the presence of this zinc-binding ligand from pancreatic secretions. Evans et al. (1975) has postulated a series of events associated with zinc absorption. These include: 1) The pancreas secretes a zinc-binding ligand into the intestinal lumen; 2) in the intestinal lumen, zinc binds to ligand; 3) the complexed zinc plus zinc ligand, is transported through the intestinal microvillus and into the epithelial cell; 4) in the epithelial cell, zinc is transported to binding sites on the basolateral plasma membrane, or; 5) metal-free albumin interacts with the plasma membrane

and removes zinc from the receptor site. The quantity of zinc entering the body is determined by the quantity of metal-free albumin available. Prasad (1977) suggests that although most zinc is bound to albumin in plasma, other proteins such as alpha-2-macroglobulin, transferrin and ceruloplasmin also bind zinc.

Zinc absorption depends upon a number of factors. Zinc is more available for absorption from animal protein than from cereal grains and fruits. Other factors that appear to have some effect upon absorption are body size, level of zinc in the diet and the presence of potentially interfering substances in the diet, such as; phytate, fiber, chelating agents, calcium and vitamin D.

Calcium interfers with zinc absorption and may potentiate a zinc deficiency (Underwood, 1977). On the other hand, low calcium intakes may result in elevating plasma zinc. Bone resorption that may occur in calcium depleted states results in the release of zinc from bone (Tao, 1975). Vitamin D has been reported to increase zinc absorption, but this appears to be an indirect effect of the vitamin resulting from a homeostatic response to increased zinc requirements which accompanies stimulated skeletal calcification and growth.

The average American diet contains from 10 to 15 mg zinc per day (Osis, 1972). Vegetarian diets, when com-

pared to animal protein diets, contain less zinc (approximately 12 mg zinc per day). The increased intake of cereal grains and therefore phytates by vegetarians, may further decrease the availability of zinc in these diets. In diets containing 40 grams of protein or less per day, the zinc content may be as low as 4 to 7 mg zinc per day. Osis et al. (1972) reported a value of 4.75 mg zinc in a 37 gram protein diet. Diets which derive most of their protein from fish and poultry, such as a low cholesterol diet may also be low in zinc, as these particular protein sources are not high in zinc, approximately .7 mg/100 grams (Brown, 1976).

Excretion

Zinc is excreted primarily via the feces, which accounts for approximately 1 to 2 mg per day. Urinary zinc losses account for approximately 0.5 mg per day and losses in perspiration account for an additional 0.5 mg or more per day. With a 20 to 30 percent absorption rate and an average loss of 2 to 4 mg zinc per day, the recommended zinc intake is 15 mg per day. The ingestion of 15 mg. zinc would result in the absorption of approximately 3 to 4.5 mg per day and zinc homeostasis in an adult. In a child, when bone growth is rapid, zinc requirements are increased.

Zinc in disease and stress

Profound changes occur in tissue and plasma levels of zinc in response to various diseases. Halsted and Smith (1970) reviewed several diseases which affect zinc levels in humans. They reported significant depression in serum zinc in patients with leg ulcers, liver disease, active pulmonary tuberculosis, acute and chronic pulmonary infection, uremia, pregnancy, oral contraceptive users, and children with cystic fibrosis. These investigators also reported that plasma zinc levels fell to 75 percent of control levels within 24 to 48 hours post myocardial infarction. These levels gradually rose to normal levels by two weeks after recovery. Lindeman et al. (1972) described the influence of acute tissue injury on plasma and urinary zinc concentrations in post surgical, post myocardial infarction and acute suppurative infection patients. The plasma zinc levels in surgical patients fell from 77±4.7 µg/dl to a low of 53±2.0 µg/dl, 24 hours post-operatively. Mean plasma zinc concentrations fell to 58±3.8 µg/dl on the second post infarction day; while mean levels of zinc in plasma fell to 68±8.1 µg/dl in infection patients. Although urinary zinc losses significantly increased after surgery, patients with suppurative infection and myocardial infarction did not experience any significant increase in urinary loss of zinc.

Lindeman concluded that an acute fall in plasma zinc occurs post tissue injury regardless of origin and that an effective homeostatic mechanism operates to return plasma zinc levels to normal. Wacker et al. (1956) also noted a significant fall in plasma zinc in patients after acute myocardial infarction. Concomitant with this decreased plasma zinc was an increase in malic and lactic dehydrogenase activity. Lactic dehydrogenase and malic dehydrogenase are both zinc metalloenzymes (Riordan, 1976) and Wacker suggested that a redistribution of zinc occurs post myocardial infarction to account for falls in plasma zinc levels.

Tissue injury, infections and bacterial endotoxins result in the release of leukocyte endogenous mediator (L.E.M.). L.E.M. is a heat liable trace protein possibly identical with endogenous pyrogen. Liberation of L.E.M. following tissue injury results in a series of events which include; 1) a net flow of amino acids into the liver, 2) uptake of iron by the reticuloendothelial system, and 3) a net flux of plasma zinc to the liver. This uptake of zinc by the liver is followed by a hepatic synthesis of acute phase reactants over the next few hours. These acute phase reactants include fibrinogen, α_1-acid glycoprotein, α_2-acute phase globulins and haptoglobin (Burch and Sullivan, 1976). Beisel (1976) postulated that leukocytic endogenous mediator was responsible for the

redistribution of zinc and iron from serum into the liver following acute tissue injury.

Tucker (1976) reported a case of severe zinc deficiency which occurred in a patient receiving total parenteral nutrition support. This deficiency was manifested by suppressed serum and hair zinc levels, along with cutaneous lesions typical of acrodermatitis enteropathica and alopecia. Both of these symptoms were corrected after zinc supplementation. Prasad (1976) reported decreased levels of zinc in hair, red blood cells and plasma of adult patients with sickle cell disease. The zinc excretion in the urine of the patients with sickle cell disease was increased. Retarded growth and hypogonadism was an apparent side effect of sickle cell disease seen in many of these patients.

The information concerning zinc metabolism among hemodialysis patients is controversial. Mahler et al. (1971) and Mansouri et al. (1970) reported decreased concentrations of serum zinc among end-stage renal disease patients on hemodialysis, whereas Bloomfield et al. (1969) and Rose et al. (1972) reported normal or slightly elevated concentrations of serum zinc in their patients. Mahajan et al. (1978) reported that although patients with chronic renal failure had mean plasma zinc levels significantly lower than controls; the mean erythrocyte

zinc level was significantly higher in all patients with chronic renal failure than in the controls. These investigators postulated that the low plasma and high erythrocyte zinc concentrations in chronic renal failure could be secondary to an abnormal shift of plasma zinc into erythrocytes or the result of an ineffective erythropoiesis associated with decreased rate of cell division and maturation.

Zinc and taste

A physiological role of zinc in taste acuity was first reported by Henkin in 1971. Cohen et al. (1973) and Henkin (1971) reported improvement of taste acuity associated with thermal burns and patients with idiopathic hypogeusia by zinc supplementation. Hambridge et al. (1976) reported that poor growth and appetite together with hypogeusia in young children in Denver was associated with subnormal zinc in hair. Supplementation with zinc improved growth, normalized taste acuity and increased hair zinc concentrations.

Henkin et al. (1971) has suggested that zinc acts as a cofactor involved in the gustatory protein called gustin. This protein has been postulated to be a carrier for the chemical responsible for a particular taste to the taste receptor. Henkin et al. (1975) measured parotid saliva zinc concentrations in normal and control

subjects who complained of hypogeusia. Henkin reported depressed parotid saliva zinc levels in the hypogeusia subjects. These investigators consequently believed that even though serum and other tissue levels of zinc are normal, salivary zinc levels may play an important role in taste acuity.

METHODS

HEMODIALYSIS STUDY

Subjects

Eighteen ambulatory end-stage renal disease (ESRD) patients, who were routinely hemodialyzed for 6 hours three times per week at the Michigan Nephrology Center, were selected as experimental subjects. There were 9 males and 9 females between the ages of 17 and 65 years (mean age 46.5 years). All 10 control subjects, 3 males and 7 females between the ages of 21 and 65 years (mean age 45.8 years), were hospital personnel or patient's spouses.

Measurement of recognition thresholds for primary tastes

The solutions used for evaluation of each recognition threshold were USP purity quinine sulfate (bitter), tartaric acid (sour), sodium chloride (salty), and sucrose (sweet). All solutions were made fresh daily with sterile distilled water used as solvent. Table 1. lists the concentrations of the solutions for each taste modality.

All subjects were asked to fast and not smoke for at least 2 hours prior to tasting. Recognition thresholds for representative solutions of the four primary tastes

Table 1. Concentration of solutions used for recognition taste testing for subjects on hemodialysis and control subjects.

Sucrose[a] M	Tartaric Acid[a] N	Sodium Chloride M	Quinine Sulfate M
0	0	0	$1X10^{-6}$
0.01	0.0001	0.005	$2X10^{-6}$
0.02	0.0002	0.010	$4X10^{-6}$
0.03	0.0004	0.020	$8X10^{-6}$
0.04	0.0008	0.030	$10X10^{-6}$
0.05	0.001	0.040	$15X10^{-6}$
0.06	0.002	0.050	$20X10^{-6}$
0.07	0.003	0.060	$25X10^{-6}$
0.08	0.004	0.070	$30X10^{-6}$
0.09	0.005	0.080	$35X10^{-6}$
0.10	0.006	0.090	$40X10^{-6}$
	0.007	0.100	
	0.008		
	0.009		
	0.010		

were determined in each subject. This was done between 0 and 30 minutes before dialysis and repeated between 0 and 30 minutes after dialysis. For tasting, each subject swished 10 cc of solution around in the mouth and then expectorated. The subject described the taste of each solution in the series as being either sweet, sour, salty, bitter or having no taste, and indicated the intensity of taste on a scale of one to ten (from slight to extreme). Each subject then waited one minute before continuing to the next sample. After the subject correctly identified two consecutive samples, the sample with the lower concentration of solute was defined as the recognition threshold. All subjects were tested for the same taste modality on at least two occasions.

During the second testing period, solutions with concentrations between the first recognizable concentration and the last negative response stimulus were prepared and used for testing. As an example, if subject A recognized a .05M solution of sucrose as sweet, .04, .041, .042, etc. solutions were used for the second testing. Again, after the subject correctly identified two consecutive samples, the sample with the lower concentration of solute was defined as the recognition threshold. The patient was offered different taste stimulus before and after dialysis treatments the same

day, in order to eliminate guessing or criteria changes due to knowledge of taste stimulus.

Blood analyses

A 10 ml sample of blood was taken from the venous shunt of each experimental subject 0 to 30 minutes prior to dialysis and 0 to 30 minutes after dialysis, and by venipuncture from each control and was placed into heparinized tubes. Hematocrits were done, and the remainder of the blood was prepared for use as serum samples. The latter were frozen and subsequently analyzed for creatinine by the Folin and Wu technique (1919) and serum urea nitrogen (SUN) by the technique of Marsch, Fingerhut and Miller (1965). Serum zinc concentration was determined with an atomic absorption method (Burch et al., 1975) on 15 ESRD patients both before and after dialysis.

CHRONIC RENAL FAILURE STUDY

Subjects

Twenty-seven ambulatory chronic renal failure patients were selected as experimental subjects. The subjects were separated into three groups of subjects according to their creatinine clearances: Group I, n=9, creatinine clearance of 41-75 ml/min; Group II, n=8, creatinine clearance of 15-40 ml/min; Group III, n=10, creatinine clearance of less than 15 ml/min. There

were twenty males and seven females between the ages of 17 and 74 years (mean age 49.7 years). There were 3 females in Group I and two females in the remaining two groups.

Measurements of recognition thresholds for sour and sweet

The solutions used for evaluation of each recognition threshold were USP purity tartaric acid (sour) and sucrose (sweet). All solutions were made fresh daily with sterile distilled water as solvent. Table 2. lists the concentrations of the solutions for each taste modality.

All subjects were asked to fast and not smoke for at least four hours prior to tasting. Recognition thresholds for tartaric acid and sucrose were determined in each subject. For tasting, each subject swished 10 cc of solution around in the mouth and then swallowed the solution. The subject was asked to discriminate between the test solution and distilled water. Each subject rinsed with distilled water between each set of samples and waited approximately one minute before proceeding to the next sample set. The staircase method of Cornsweet (1962) was used to determine threshold. Figure 1. shows a representative test. The first two trials of each test were discarded and the average of the next four trials was used as the value of the recognition taste threshold.

Table 2. Concentrations of solutions used for recognition taste testing for chronic renal failure subjects.

Sucrose M	Tartaric Acid N
0	0
0.0025	0.0004
0.005	0.0008
0.010	0.0016
0.015	0.0024
0.020	0.0032
0.030	0.0048
0.040	0.0064
0.050	0.0080

Figure 1. Recognition taste threshold data sheet (sweet).

	Trials					
Solution Concentration	1	2	3	4	5	6
0	N[a]					
0.0025	N					
0.005	N					
0.010	N					
0.015	-	N	N	N	N	N
0.020	Salty	Sweet	N	Sweet	Sweet	
0.030	-	Sweet	Sweet			
0.040	Sweet					
Direction of sampling	↓	↑	↓	↑	↓	↑

a. N = not different from distilled water.

Biological fluid analysis

A 15 ml sample of blood was taken by venipuncture from each experimental subject and transferred into plastic vials. Blood was prepared for use as serum and red blood cell samples immediately following collection. Both samples were frozen and subsequently analyzed for zinc using an atomic absorption method (Burch et al. 1975). The serum samples were also analyzed for creatinine by the Folin and Wu technique (1919).

A 24 hour urine sample was collected on the day prior to testing and analyzed for zinc using an atomic absorption method (Burch et al., 1975), and creatinine by the Folin and Wu technique (1919).

For saliva collection each subject, after a 12 hour fast and prior to tasting the test solutions, tilted their head forward and allowed saliva to collect in the front of the mouth. The subject then expectorated this accumulated saliva into a plastic cup until 10 cc of total saliva was collected. This was unstimulated saliva. All collections were completed between 8:00 A.M. and 10:00 A.M., the collection was completed within 15 to 30 minutes. The saliva was immediately frozen and subsequently analyzed by a testing laboratory.[a]

[a]Trace Elements Inc., 460 S. Northwest Hwy., Park Ridge, Illinois, 60068.

Each subject kept a food diary which included the amounts of all food consumed for two days prior to testing. Zinc content was calculated using provisional zinc tables (Murphy et al., 1975, and Freeland et al., 1976). Protein was calculated using Agricultural Department Handbook No. 456. Analysis of Variance, Duncans multiple range test (1957) and least significant difference tests (Sokal and Rohlf, 1969) were used to determine if significant differences existed between each group.

RESULTS

Hemodialysis Study

Mean recognition thresholds

Mean recognition taste thresholds of tartaric acid (sour) for ESRD subjects before dialysis were significantly higher ($P < 0.001$) than those of control subjects (0.004N vs. 0.002N) as shown in Figure 2. and Table 3. Following hemodialysis, mean recognition taste thresholds improved ($P < 0.01$) twofold to a value of 0.002N, but this was still significantly higher than that of controls ($P < 0.01$). Mean recognition taste thresholds for sucrose (sweet) of ESRD subjects before dialysis were also significantly higher than that of controls ($P < 0.01$) (0.03M vs 0.014M). Hemodialysis brought about significant improvement ($P < 0.05$) in the mean recognition taste thresholds for sweet, but at no time did it reach the levels of the control subjects even though differences between post- dialytic patients and controls were never significant ($P > 0.05$).

Although the mean recognition taste thresholds of 0.043M sodium chloride before dialysis and 0.034M sodium chloride after dialysis were not significantly higher than the control value of 0.026M sodium chloride, the

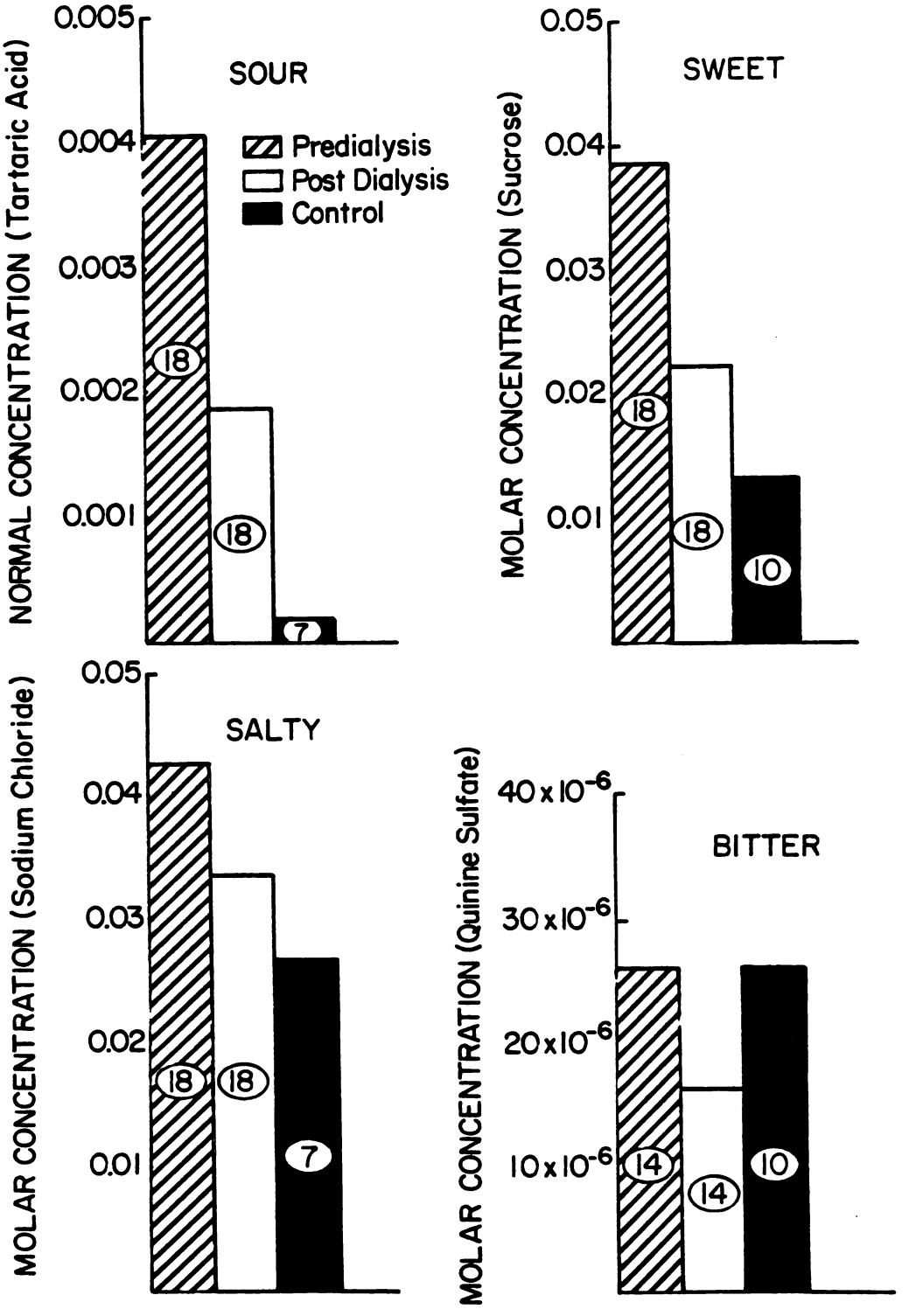

Figure 2. Mean taste recognition thresholds for sour, sweet, salty, and bitter for end-stage renal disease patients before and after hemodialysis and control subjects.

Table 3. Individual blood and serum values and recognition taste thresholds

Subject	Serum urea nitrogen mg/dl		Serum creatinine mg/dl		Hematocrit % whole blood	
	Pre[a]	Post	Pre	Post	Pre	Post
1	112.0	36.0	13.4	5.7	23.5	27.0
2	106.0	42.0	10.2	5.2	24.0	26.5
3	104.0	46.0	17.0	8.9	23.0	25.0
4	104.0	34.5	12.8	5.5	15.0	15.0
5	102.0	44.5	11.6	6.6	25.0	27.0
6	98.0	48.0	12.8	9.6	28.5	27.5
7	96.0	47.0	16.8	9.4	24.5	25.0

a. Prehemodialysis or posthemodialysis

Table 3. Individual blood and serum values and recognition taste thresholds (cont.).

Subject	Serum urea nitrogen mg/dl		Serum creatinine mg/dl		Hematocrit % whole blood	
	Pre[a]	Post	Pre	Post	Pre	Post
8	96.0	47.0	11.8	6.6	32.0	34.0
9	84.0	29.5	11.8	4.6	17.5	20.0
10	82.0	38.0	13.8	6.6	23.5	24.0
11	74.0	29.0	14.0	6.7	27.0	27.0
12	68.0	--	12.6	--	37.0	37.0
13	51.0	20.0	9.0	4.0	32.0	34.0
14	48.0	--	7.9	--	34.0	34.0

a. Prehemodialysis or posthemodialysis.

Table 3. Individual blood and serum values and recognition taste thresholds (cont.).

	Recognition taste threshold					
	Sour, N[b]		Sweet, M		Salty, M	
Subject	Pre	Post	Pre	Post	Pre	Post
1	0.0035	0.0002	0.07	0.07	0.026	0.020
2	0.0034	0.0011	0.07	0.07	0.030	0.018
3	0.0007	0.0009	0.041	0.003	0.014	0.006
4	0.0075	0.0049	0.002	0.002	0.022	0.007
5	0.0100	0.0090	0.070	0.060	>0.100	0.10
6	0.0033	0.0004	0.026	0.026	0.010	0.004
7	0.0033	0.0003	0.026	0.002	0.022	0.020

b. Normal (N) or molar (M) solutions.

Table 3. Individual blood and serum values and recognition taste thresholds (cont.).

	Recognition taste threshold					
	Sour, N[b]		Sweet, M		Salty, M	
Subject	Pre	Post	Pre	Post	Pre	Post
8	0.0056	0.0032	0.035	0.040	>0.10	0.054
9	0.005	0.001	0.016	0.011	0.028	0.028
10	0.0002	0.0003	0.060	0.016	0.028	0.020
11	0.0011	0.0015	0.070	0.009	>0.10	0.092
12	0.008	0.001	0.026	0.016	0.007	0.009
13	0.0042	0.0003	0.026	0.003	0.049	0.020
14	0.0033	0.0007	0.036	0.016	0.030	0.015

b. Normal (N) or molar (M) solutions.

Table 4. Zinc in serum of end-stage renal disease (ESRD) subjects.

Status of subjects	N	Serum zinc, µg/dl		
		Mean	SD	Range
Predialysis	15	77	18	50-114
Postdialysis	15	77	18	39-111

mean value for pre and post dialysis subjects was calculated using a recognition taste threshold of 0.100M for four subjects who were unable to detect sodium (salty) below this range. Although ideally these subjects should have been further tested to identify their true recognition taste threshold, that was not possible, since for various reasons they were no longer available to the unit. If, indeed, their true recognition taste thresholds could have been determined, this group would surely have approached significance. As serum urea nitrogen increased in value, there was a tendency for patients to be less able to detect saltiness.

Serum zinc concentrations for 15 experimental subjects ranged from 50 to 114 µg/dl before dialysis and 39 to 111 µg/dl after dialysis (Table 4.). The remaining three subjects were not available for zinc analysis. Zinc serum values were in the low range for normal (75 to 160 µg/dl) for the method (Burch et al., 1973) used.

Chronic Renal Failure Study

Mean recognition thresholds

Mean recognition thresholds of tartaric acid (sour) for patients with severe renal failure, creatinine clearance less than 15 ml/min, were significantly higher ($P < 0.05$) than those of patients with moderate

renal failure, creatinine clearance 15 to 40 ml/min. These mean recognition thresholds for tartaric acid (sour) for patients with severe renal failure were also significantly higher ($P < 0.001$) than those patients with mild renal failure, creatinine clearance 75 to 41 ml/min. That is, patients with severe renal failure had significantly decreased ability to recognize sour when compared to moderate and mild renal failure patients. The mean recognition thresholds of tartaric acid were not significantly different when mild chronic renal failure patients were compared to moderate chronic renal failure patients, even though the means doubled in value (.0007N, .0014N, and .0026N) Figure 3. Individual data are shown in Tables 5, 6, and 7.

Mean recognition thresholds for sucrose were not different in any of the groups tested, although, the trend was to increase threshold concentrations as renal function decreased (mean 0.016, 0.017, and 0.028) for mild, moderate and severe renal failure patients respectively, Figure 4. That is as renal function decreased, taste acuity in respect to sucrose also decreased.

Zinc levels

Serum zinc levels of patients with chronic renal disease declined as renal function declined (92.8 µg/dl, 82.8 µg/dl and 75 µg/dl) (Table 8.) for patients with

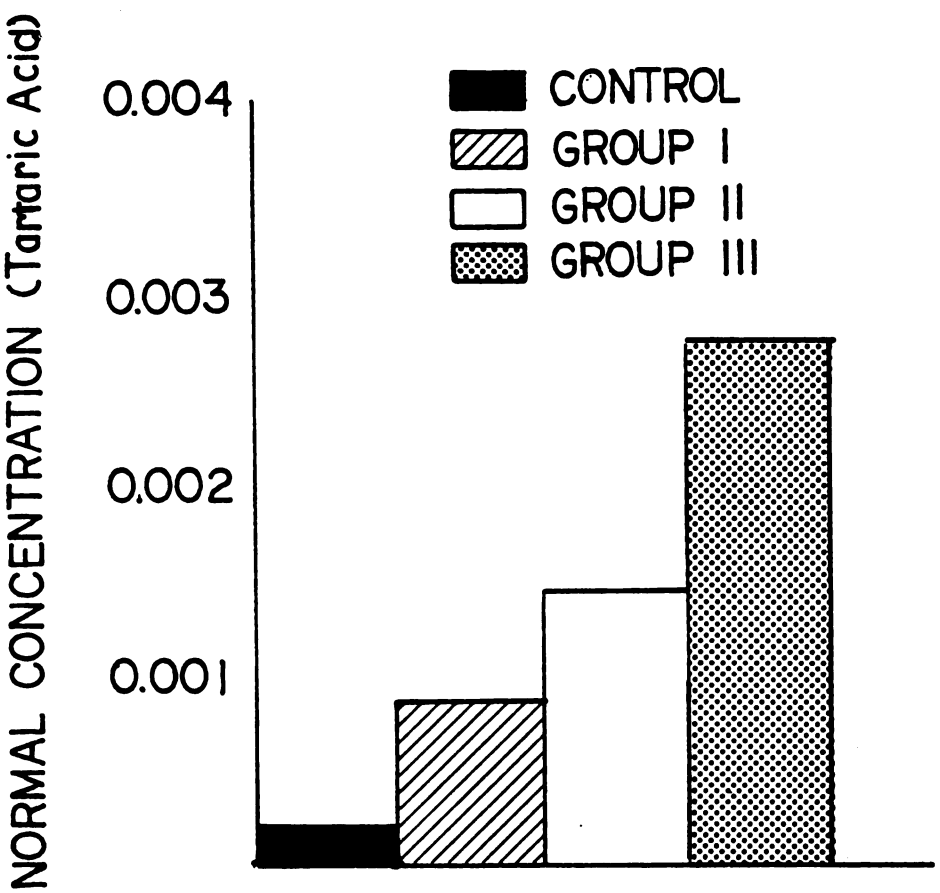

Figure 3. Mean taste recognition thresholds for sour for patients with mild, moderate, and severe renal failure and control subjects.

Table 5. Recognition thresholds for sour and sweet of patient with mild chronic renal failure (CC 41-75 ml/min).

Subject	Creatinine Clearance ml/min	Recognition Thresholds	
		Sour N	Sweet M
1.	72.8	0.0003	0.010
2.	64.2	0.0016	0.028
3.	61.0	0.0020	0.015
4.	59.2	0.0016	0.013
5.	49.9	0.0003	0.011
6.	48.1	0.0008	0.025
7.	48.0	0.0005	0.013
8.	44.8	0.0011	0.020
9.	41.3	0.0012	0.010

Table 6. Recognition thresholds for sour and sweet of patients with moderate chronic renal failure (CC 15-40 ml/min).

Subjects	Creatinine Clearance ml/min	Recognition Thresholds	
		Sour N	Sweet M
1.	33.1	0.0003	0.006
2.	29.9	0.0008	0.040
3.	27.4	0.0008	0.018
4.	23.4	0.0012	0.013
5.	22.3	0.0032	0.015
6.	21.0	0.0011	0.014
7.	18.3	0.0020	0.020
8.	16.1	0.0015	0.013

Table 7. Recognition thresholds for sour and sweet of patients with severe chronic renal failure (CC less than 15 ml/min).

Subject	Creatinine Clearance ml/min	Recognition Thresholds	
		Sour N	Sweet M
1.	13.0	0.0024	0.080
2.	12.8	0.0016	0.030
3.	12.1	0.0016	0.030
4.	11.4	0.0064	0.018
5.	11.3	0.0016	0.020
6.	10.9	0.0026	0.005
7.	10.0	0.0036	0.035
8.	10.0	0.0024	0.020
9.	9.6	0.0016	0.015
10.	5.3	0.0025	0.028

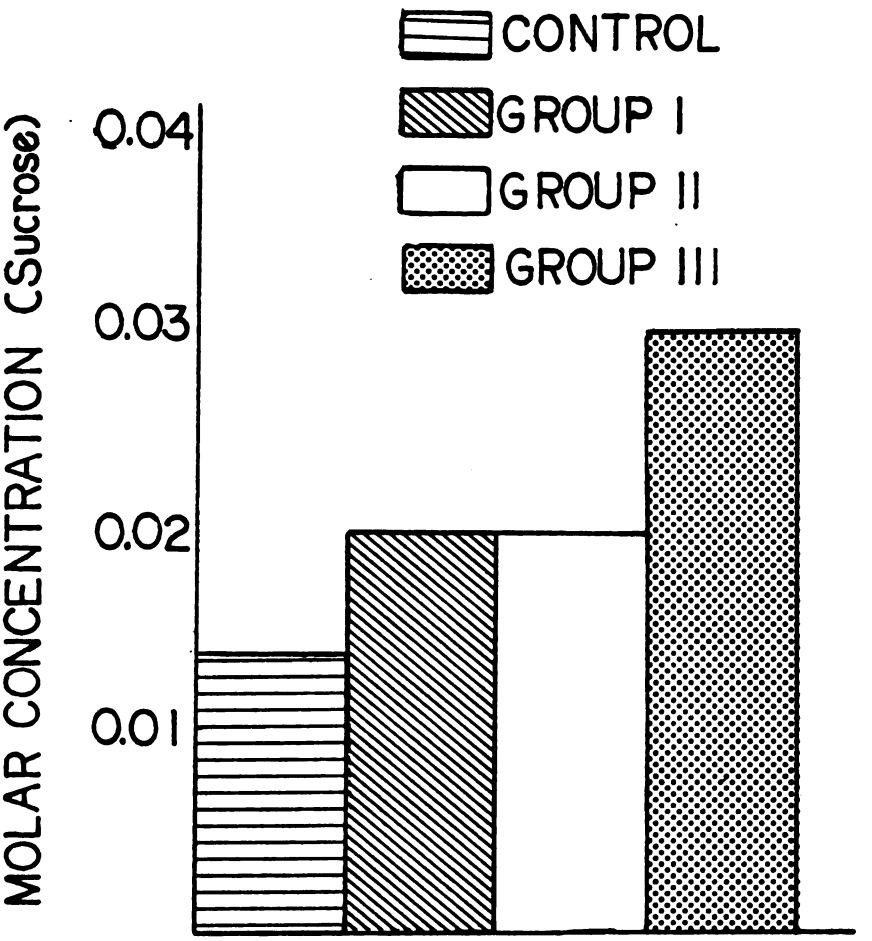

Figure 4. Mean taste recognition thresholds for sweet for patients with mild, moderate, and severe renal failure and control subjects.

Table 8. Zinc in serum, saliva, urine of patients with chronic renal disease.

Status of subjects	N	Serum µg/dl SD	Saliva[d.] ppb SD	Urine µg/24° SD	Creat. gm/24°	Urine µg zinc/gm. creat.
Group I[a.]	9	92.8±10.0	<30±0.0	1064.8±422.0	1.6	0.62±0.24
Group II[b.]	8	82.8±9.4	76±55.4	502.1±234.9	1.6	0.36±0.18
Group III[c.]	10	75.1±14.1	141±206.5	477.5±344.4	1.1	0.45±0.28

a. (CC 41-75 ml/min) b. (CC 15-40 ml/min) c. (CC <15 ml/min)

d. Mean of 8 control subjects = <30 ppb ± 0.00.

mild, moderate and severe renal failure. The patients with mild renal impairment had significantly higher ($P < 0.01$) serum zinc levels than did the patients with severe renal impairment. Urinary zinc, when expressed as $\mu g/24^{o}$ also decreased significantly with severe renal impairment when compared to mild renal impairment ($P \leq 0.05$), however, if expressed as µg/gm creatinine, there was no significant difference among the three groups. However, the difference between Group I, mild renal failure, and Group III, severe renal failure, did approach significance ($P < .057$). Salivary zinc levels rose as renal function declined: Mild ≤30 ppb; moderate 66.5 ppb; and severe 141 ppb zinc. (Table 8.) However, these differences were not significant.

Mean dietary zinc intake did not differ between the three groups of patients (10.0 mg, 13.5 mg and 14 mg /24 hours) with mild, moderate and severe chronic renal failure respectively. Dietary zinc intake generally fell as protein intake decreased (Table 9.), however, depending upon the sources of protein, this was not always true. Patient PN consumed wine and nuts which are high in zinc, whereas patient AV consumed primarily eggs, milk products and hotdogs which are not high in zinc. Many of the patients in Group III, severe renal impairment, had not yet decreased their intake of protein and

Table 9. Protein and zinc content of food diaries.

Patient and Group[a]		Zinc[b]	Protein[b]	Major Source of Zinc
PN	III	18	72	Wine, chicken, nuts
BS	III	17	80	Beef, whole wheat
CF	II	16	80	Beef, cheese
ML	II	14	80	Pork, Inst. Breakfast
FC	I	13	65	Cheese
KH	II	12	50	Beef
AV	I	11	120	Meat, milk
TT	I	11	95	Meat, milk
CK	I	8	60	Beef
EK	I	8	50	Cheese, dried beans
RM	III	8	48	Port
OW	III	8	42	Pork, beef
VH	II	5	40	Bread

a. Group I creatinine clearance 41-75 ml/min; Group II creatinine clearance 15-40 ml/min; Group III creatinine clearance less than 15 ml/min.

b. grams per 24 hours, average of 2 day food diary, protein

milligrams per 24 hours, average of 2 day food diary, zinc

averaged an intake of 64.4 gms protein per day (range 42-80 gm protein per day). Patients in Groups I and II were not on any dietary restrictions at the time of the study and averaged 78.0 gm protein per day (range 50-120 gm protein per day) for Group I and 60.0 gm protein per day (range 40-80 gm protein per day) for Group II.

DISCUSSION

End-stage renal disease patients (ESRD) undergoing hemodialysis had impaired ability to recognize primary tastes. Recognition of sour and sweet taste was more seriously impaired than salty and bitter. Improvement of all four primary taste recognition thresholds occurred following hemodialysis. The impairment in the ability to recognize sour appears to precede end-stage renal disease. Patients with moderate renal impairment also begin to require greater concentrations of solutions of tartaric acid in order to recognize sour. The sweet taste, however, begins to deteriorate later in the progression of renal disease and does not become significantly impaired until end-stage renal disease occurs. Salty and bitter recognition thresholds do not appear to change in response to renal disease, although for some patients, salt recognition thresholds may be impaired.

Zinc has been implicated in many conditions associated with hypogeusia including end-stage renal disease (Atkin-Thor et al., 1978). Henkin et al. (1972) have postulated that zinc acts as a cofactor in a gustatory protein called gustin. This protein has been proposed

as the carrier of the chemical responsible for a particular taste to the taste receptor. Gershoff (1977) postulated that the zinc molecule may interact with the membrane of the taste pore in order that chemicals may more easily penetrate the taste pore and reach the taste bud. The information concerning zinc metabolism among hemodialyzed patients is controversial. Mahler et al. (1970), and Mansouri et al. (1970) reported decreased concentrations of serum zinc among end-stage renal disease patients, whereas Bloomfield et al in 1969, and Rose et al. in 1972, reported normal or slightly elevated concentrations of serum zinc in their patients. Atkin-Thor and co-workers (1978) reported that 95% of their dialysis patients tested had some degree of hypogeusia, although specific taste abnormalities were not identified. Six weeks after supplementation with 440 mg zinc sulfate, three times per week, taste acuity and appetite improved in 90% of the experimental subjects. Improvement in taste acuity was seen, even though in 5 patients there was a decrease in hair zinc concentration following supplementation. Two patients with increased hair zinc concentrations experienced no improvement in taste acuity. Fifteen percent of patients on zinc supplementation experienced side effects which resembled hypoglycemia. Petrie and Row (1977) reported 11 cases of zinc toxicity in patients who

were dialyzed using a galvanized piping system for water delivery to the dialyzer. Severe anemias developed in all patients, with hemoglobin as low as 3.2 g/dl. There was no evidence of blood loss, however, red cell life spans averaged three days. The amount of zinc present in the dialysate solution was 6.54 µg/dl. Nausea and vomiting was also noted among these patients.

Serum zinc values for ESRD patients in the present study did not change after dialysis, and were low-normal both before and after dialysis. Although several patients in this study had low-normal serum zinc concentrations, there was improvement in taste acuity after dialysis. Since no changes in serum zinc concentrations occurred, this would tend to disqualify zinc deficiency as an explanation for the observed hypogeusia. Other measurements for zinc deficiency also failed to provide evidence for a causal relationship between zinc deficiency and hypogeusia in the chronic renal disease patient population. Salivary levels of zinc rose as kidney function decreased, rather than fell as others have reported for patients with hypcgeusia (Henkin, 1975).

If zinc deficiency were the explanation for hypogeusia among these patients, one would expect to see impairment of all four tastes. Instead, we observed impairment of sour and sweet in the hemodialysis patients, and

sour alone in patients with moderate to severe renal impairment.

Considering the clinical complications which have been identified with zinc supplementation programs, further research identifying a close relationship with zinc deficiency in the ESRD patient and taste impairment should be completed before widespread zinc supplementation programs are advanced.

The presence of H^+ ions in solution appear to be necessary for the normal experience of sour, and the sourness of a solution can be decreased by neutralization with an anion. Simenhoff and co-workers (1977) have shown that the level of dimethyl and trimethyl amines are increased in patients with end-stage renal disease. A significant decrease in these amines also occurs after a hemodialysis treatment. Dimethyl and trimethyl amines are strong basic compounds which may result in neutralizing an acid solution placed in the mouth. Consequently, higher concentrations of the acid would be required to elicit a sour response. This phenomenon may be a reasonable explanation for sour taste recognition impairment among ESRD and chronic renal disease patients, and further identify a plausible reason why these thresholds improve with a single dialysis treatment.

The taste threshold test is a relatively inexpensive

and simple test which may be useful in assessing the adequacy of hemodialysis programs. Sour and sweet taste threshold measurements appear to be the most sensitive in delineating potential gustatory differences in these patients. These modalities are significantly impaired before dialysis and improve significantly with a single dialysis treatment.

End-stage renal disease patients who are maintained on routine hemodialysis have an increased need for calories. Many of these calories must come from low-electrolyte, low-protein sources. Many patients find it difficult to ingest sufficient amounts of these products, and consequently, they lose body weight. One factor which affects palatability of food is the ability to taste food. Identification of mechanisms for taste alterations should lead to correction, or at least a better understanding by professional personnel of the problems imposed upon these patients in acceptance of special diets. In addition, it could help the food industry to prepare palatable and acceptable foods for renal failure patients. Some food companies are already employing taste panels composed of patients with end-stage renal disease to identify acceptable products for this patient population.

CONCLUSIONS AND SUGGESTIONS FOR FURTHER STUDIES

1. Recognition taste thresholds for tartaric acid (sour) and sucrose (sweet) are significantly impaired in end-stage renal disease patients, as compared to controls, prior to a hemodialysis treatment. Quinine sulfate (bitter) and sodium chloride (salty) recognition thresholds are not significantly altered in patients with end-stage renal disease.

2. Recognition taste thresholds for the first two taste modalities (sour, sweet) improve significantly after a single hemodialysis treatment.

3. Taste acuity in respect to tartaric acid (sour) declines as renal function declines in patients with chronic renal disease, and becomes significantly impaired when creatinine clearance falls below 15 ml/min.

4. Serum zinc levels fall as creatinine clearance declines, however, serum zinc levels do not significantly change with a single hemodialysis treatment.

5. Salivary zinc levels rise as creatinine clearances decline, however, these trends are not significant.

6. Dietary zinc levels tend to fall as protein intake falls. There was no correlation with average zinc intake and taste acuity. Specific food differences greatly affect zinc intake and are independent of protein intake.

Taste acuity impairment was most apparent in respect to sour. Changes in salivary concentrations of trimethyl and dimethyl amines may be a plausible explanation for this alteration. Determining levels of these amines in the ESRD patient, and correlating these findings with the degree of taste threshold impairment would be a stronger defense of this theory. In addition, a study of the pH changes which occur in saliva in response to additions of graded amounts of these chemicals would identify whether these pH changes would be sufficient to neutralize the H^+ ions present in the sour solutions.

We noted increases in salivary zinc as renal function decreased. The possibility of salivary concentration, due to decreased salivary flow was not ruled out as an explanation of this zinc accumulation. Identifying whether there are changes in salivary flow rate with progressive decline in renal function may not only identify a mechanism for the increased zinc levels in saliva, but may also identify a mechanism for meat aversion or decreased appetite in this patient population.

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