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Effect of Glycerol-Induced Hypertonicity on Plasma Renin Concentration in Humans (40900)

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Abstract. Glycerol in hypertonic solution (80 g in 160 ml) was ingested by 36 patients during evaluation for Meniere's disease. One hour after glycerol, serum osmolality rose an average of 5.7% (17 mOsm/liter), and plasma renin concentration fell an average of 41%. Possible mechanisms for suppression of renin release by hypertonic glycerol are discussed.

Glycerol is frequently administered to patients to aid in the diagnosis of hearing disorders. Improvement of auditory function following oral glycerol is taken as evidence for the osmotic removal of the excess intralabarynthine fluid that is characteristic of Meniere's disease (1). Glycerol also functions as an osmotic diuretic. Because of glycerol's effects on serum osmolality, and the fluid shifts that ensue, we postulated that oral glycerol would affect plasma renin levels. This report shows that oral glycerol acutely suppresses renin release in humans. The results confirm in humans receiving glycerol what would be predicted from other studies on animals receiving other osmotic diuretics.

Materials and methods. Subjects were selected from patients attending the otolaryngology clinics at the University of Wisconsin Hospital and the Veterans Administration Hospital, Madison, Wisconsin. Their diets were *ad libitum*. The glycerol test was performed as part of a diagnostic sequence in the course of the work-up for Meniere's disease. Glycerol was administered orally in a single dose of 90 g (1 mole) dissolved in water to make 180 ml of solution. Criteria for the clinical diagnosis of Meniere's disease encompassed several features, including the audiometric response to oral glycerol (2). A total of 36 patients were studied, 25 males and 11 females. The mean age of patients with Meniere's disease was 45, and of patients with other conditions, 43.

Informed consent was obtained to withdraw blood for renin determinations. Venous blood was drawn before and at hourly intervals after the administration of glycerol, except when patients were undergoing audiometry, or were discharged from the clinic. The patients remained seated from 30 min before glycerol administration to the end of the test, except to void.

Serum osmolality was measured with an Osmette A osmometer, manufactured by Precision Systems, Waltham, Massachusetts. Blood for renin determinations was collected in evacuated tubes that contained aqueous solutions of Na_2 EDTA so that the final concentration in blood was 1 mg/ml. Cells were removed by centrifugation in the cold, and the plasma was frozen within 1 hr of venipuncture. Renin concentration was measured by the method of Freedlender and Goodfriend, using plasma from anephric sheep as the source of renin substrate (3). To control for day-to-day variations in renin measurements, each determination was compared to a freshly thawed aliquot of pooled normal human plasma, and the data were expressed as a percentage of renin in the pool. All specimens from a single test were measured together. The mean absolute level of renin in the pool was 6.1 ng AI/ml/hr.

Results. Oral glycerol raised serum osmolality within 60 min in 33 of 36 patients. In all but 4 patients, the rise in serum osmolality was accompanied by a fall in plasma renin concentration. Figure 1 shows the time course of events in 9 cases who were studied for at least 3 hr and who showed the most pronounced changes. The data for the 60-min samples from all 36 cases are shown in Fig. 2. The mean renin for all patients fell an average of 41 ± 5%

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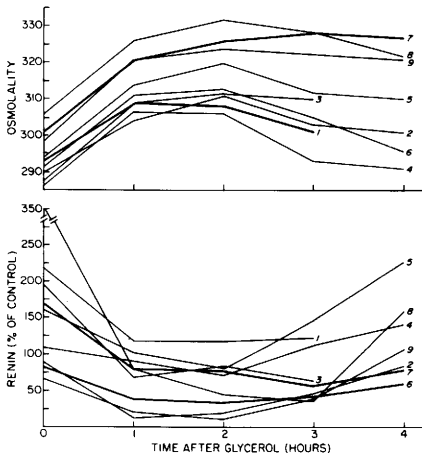

FIG. 1. Serum osmolality and plasma renin concentrations in 9 subjects following ingestion of 90 g of glycerol in 180 ml of aqueous solution. Renin concentrations are expressed as percentages of a pool of plasma from 15 normal, ambulatory adults. That pool had a mean absolute renin level of 6.1 ng AI/ml/hr.

from its starting level, while the osmolality increased an average of 5.7 ± 0.6%, from 294 to 310 mOsm/liter. No direct correlation was found between the magnitude of the rise in osmolality and the fall in renin,

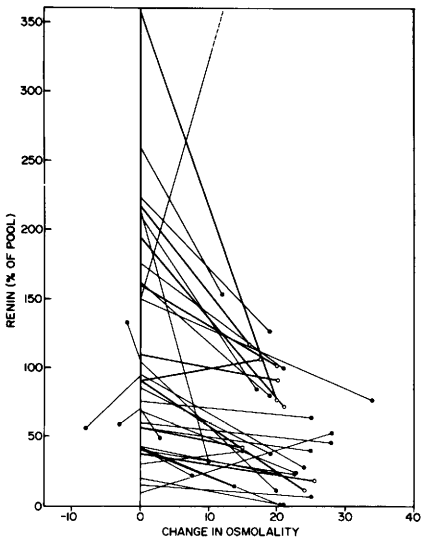

FIG. 2. Changes in plasma renin concentration as a function of changes in serum osmolality 1 hr after ingestion of 90 g of glycerol. Points indicated by solid circles represent patients with Meniere's disease. Those indicated by open circles represent patients with other otolaryngological disorders or no disease.

but the change of each parameter from baseline was significant at the 0.01 level.

The fall in renin with a rise in osmolality was seen in patients with Meniere's disease and those with other otolaryngological disorders. No statistical difference between these groups was found.

Discussion. Renin concentration in plasma is the resultant of renin release from the juxtaglomerular cells of the kidneys and renin inactivation by the liver. All factors known to affect plasma renin concentration, except those causing gross hepatic damage, act on renin release (4). Glycerol is not known to increase hepatic metabolism, so its depressant effect on renin is most likely mediated by the kidney.

Glycerol in hypertonic solution, such as that used in our study, causes a temporary rise in extracellular fluid osmolality, followed by movement of intracellular fluid to the extracellular space, and finally an osmotic diuresis. Reduced renin release after glycerol administration could be caused by increased plasma volume, by withdrawal of water from the renal parenchyma, by antidiuretic hormone released in response to hypertonicity, by a direct effect of glycerol on juxtaglomerular cells, and/or by changes in tubular sodium flux (4).

Inhibition of renin release by osmotic diuretics has been noted by others studying intact animals (5–7). Churchill *et al.* interpreted their results as mediated by a reciprocal relationship between tubular sodium load and renin release. However, Frederiksen *et al.* (8) studied renin release from isolated rat juxtaglomerular cells, and found an inverse relationship between renin release and osmolality, whether the osmolality was varied by changes in sodium, potassium or sucrose concentration. Their figure depicting a fall in renin as a function of increasing osmolality is similar to Fig. 2 in this report. Therefore, we postulate that the changes in renin we observed were caused by a direct effect of glycerol-induced hyperosmolality acting on juxtaglomerular cells, and not by indirect effects on fluid volumes or dynamics.

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