

# NMWD Model for Effect of Isotonic Saline, Hypertonic Saline on Plasma Renin

Geetha .T<sup>1</sup>, Balamurugan .K<sup>2</sup>

<sup>1</sup>Assistant Professor of Mathematics .K. N. Government Arts College for Women. Thanjavur. Tamilnadu. South India

<sup>2</sup>Assistant Professor of Mathematics. Dhanalakshmi Srinivasan Engineering College, Perambalur Tamilnadu. South India

**Abstract:** *In this paper we found survival function and cumulative hazard rate function for renin, the renal distal nephron plays an important role in the maintenance of sodium balance, extra cellular volume and blood pressure. The degree of water transport, via aquaporin2 water channels (AQP2), and sodium transport, via epithelial sodium channels (ENaC) in renal collecting duct principal cells are reflected by the level of urinary excretion of AQP2 (u-AQP2) and the  $\gamma$ -fraction of ENaC (u-ENaC $\gamma$ ). The effects of an acute intravenous volume load with isotonic saline, hypertonic saline and glucose on u-AQP2, u-ENaC $\gamma$  and underlying mechanisms have never been studied in a randomized, placebo-controlled trial in healthy humans. The effects of 0.9% saline (23 ml/kg), 3% saline (7 ml/kg) and 5% glucose (23 ml/kg) on u-AQP2 and u-ENaC $\gamma$ , fractional sodium excretion (FENa), free water clearance (CH<sub>2</sub>O), and plasma concentrations of vasopressin (AVP), renin (PRC), angiotensin II (ANG II) and aldosterone (Aldo) in a randomized and also we found the analysis of survival function and cumulative hazard rate function for renin.*

**Keywords:** Cumulative hrf, NMWD, isotonic saline, hypertonic saline, PRC

## 1. Introduction

The distal nephron plays an important role in the maintenance of sodium balance, extra cellular fluid volume and blood pressure [1]. It is well known that inappropriate water and sodium retention is thought to be a key factor in several forms of hypertension, and that aquaporin2 water channels (AQP2) play a key role in several water balance disorders [2]. The effect of an acute intravenous volume load, with isotonic and hypertonic saline and glucose, on urinary excretion of AQP2 (u-AQP2), urinary excretion of ENaC gamma subunit fractions (u-ENaC $\gamma$ ) and its relationship to vasopressin (AVP) and kidney function in healthy humans has not been studied by simultaneous measurement of other important regulatory hormones of water and sodium homeostasis such as the renin-angiotensin-aldosterone system (RAAS). In order to analyse these physiological mechanisms, we performed a randomized, crossover study in healthy subjects. We investigated the effects of infusion with isotonic- and hypertonic saline and isotonic glucose on urinary excretion of AQP2 and ENaC $\gamma$  corrected for creatinine (u-AQP2<sub>CR</sub> and u-ENaC $\gamma$ <sub>CR</sub>), renal function and sodium handling, vasoactive hormones and systemic blood pressure.

## 2. Methods

### 2.1 Inclusion Criteria

Healthy non-smoking men and women with age between 18 – 45 years were included in this study.

### 2.2 Exclusion Criteria

Subjects with clinical signs or history of heart, lung, kidney, endocrine or malignant disease; abnormal findings in ECG, urine dipstick or biochemistry (blood cell count, plasma concentrations of haemoglobin, sodium, potassium,

creatinine, albumin, glucose, bilirubin, alanine aminotransferase, alkaline phosphatase and cholesterol); arterial hypertension (ambulatory BP >130/80 mmHg); medical treatment; alcohol and substance abuse; present smoking; pregnancy; breast feeding; donation of blood within one month prior to the study and obesity (BMI > 32 kg/m<sup>2</sup>) were excluded from this study.

Here PRC, Ang II and Aldo were suppressed to the same extent in all three parameters in response to 0.9% NaCl and 3% NaCl with no significant difference between interventions. There was a primary decrease during glucose infusion (90–150 min), but when infusion ceased values returned to baseline levels with no overall significant change (figure A)

AVP did not change in response to 0.9% NaCl and glucose, but increased significantly after 3% NaCl with a maximum at 150 minutes and a steady fall during the post infusion period). In addition to AVP, the renin-angiotensin-aldosterone system (RAAS) is a key regulator of renal sodium excretion and thereby of body fluid volume. It is well known that sodium depletion activates and that chronic sodium load reduces the RAAS [3]. After glucose infusion, we measured no significant change in PRC, p-AngII or p-Aldo. This was expected, as glucose infusion does not cause any marked change in extracellular volume. Our study was not designed to allow any regulatory effects of aldosterone as the action of aldosterone occurs over hours or days. Therefore other factors must be implicated in the regulation of ENaC.

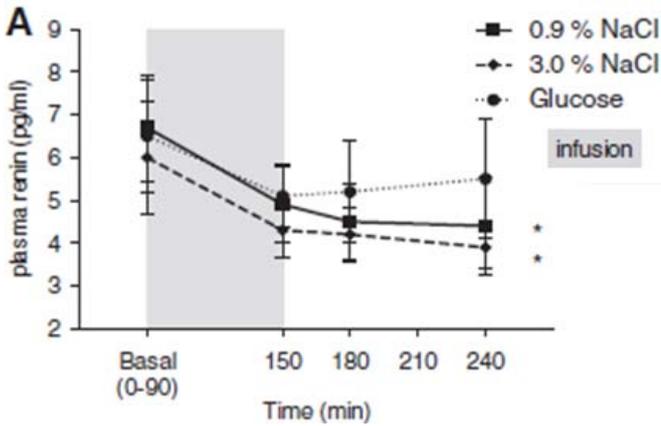


Figure A Effects of isotonic 0.9% saline (■), hypertonic 3% saline (◆) and isotonic glucose (●) on plasma renin. (Values are expressed as mean ± SEM)

### 3. Mathematical Model

#### Acronyms

hrf – Hazard Rate Function  
 NMWD – New modified Weibull distribution  
 Sf – Survival Function

#### Notations

a, b - NMWD parameters  $a > 0, b > 0$  for renin  
 $h(t)$  – hrf of renin  
 $H(t)$  – cumulative hrf of renin  
 $t$  – time of renin  
 $\bar{F}(t)$  – Sf of renin

### 4. NMWD Model

Here, The usual 2-parameter Weibull distribution can be specified through its Sf:

$$\bar{F}(t; \beta, \lambda) = \exp[-(\lambda \cdot t)^\beta] \quad (1)$$

The lifetime distribution for NMWD arises from taking appropriate limits on the Beta integrated distribution from [4,5,6] The Sf is

$$\bar{F}(t; \beta, \lambda) = \exp[-a \cdot t^\beta \cdot (\lambda \cdot t)] \quad (2)$$

With parameters  $a > 0, b \geq 0$  and  $\lambda > 0$ .

The pdf and hrf are:

$$f(t) = a \cdot (b + \lambda \cdot t) \cdot t^{b-1} \cdot \exp(\lambda \cdot t) \cdot \exp[-a \cdot t^b \cdot \exp(\lambda \cdot t)] \quad (3)$$

$$h(t) = a \cdot (b + \lambda \cdot t) \cdot t^{b-1} \cdot \exp(\lambda \cdot t) \quad (4)$$

The derivative of  $h(t)$  intersects the  $t$  axis only once, at  $t^*$  for  $t > 0$ .  $h(t)$  is decreasing for

$t < t^*$ , and is increasing for  $t > t^*$  which is given by

$$t^* = \frac{\sqrt{b-b}}{\lambda} \quad (5)$$

The interesting feature is that  $t^*$  decreases as  $\lambda$  increases.

For  $\lambda = 0$  in (2) NMWD reduces to  $\bar{F}(t) = \exp[-a \cdot t^b]$  (6) Which is a common 2-parameter Weibull distribution.

The beta-integrated model was first introduced in [5]. The model's cumulative hrf and sf are:

$$H(t) = a \cdot t^b \cdot (1 - d \cdot t)^c, \quad 0 < t < 1/d; \quad (7)$$

$$\bar{F}(t) = \exp[-H(t)]; \quad a, b, d > 0; \quad c < 0; \quad (8)$$

Set  $d=1/n, c = \lambda \cdot n$ , For  $n \rightarrow \infty$ ,

$$\left(1 - \frac{t}{n}\right)^{-\lambda \cdot n} \rightarrow \exp(\lambda \cdot t).$$

and this yields

$$H(t) = a \cdot t^b \cdot \exp(\lambda \cdot t). \quad (9)$$

Which is the cumulative hrf for NMWD.

The data is fitted with the distribution and the corresponding values for case:1, case:2, case:3 are obtained as follows

Case 1: 0.9% NaCl

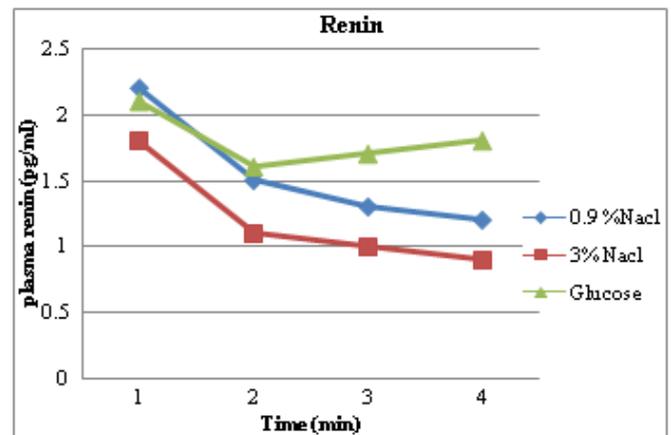
If  $a=1.728, b=3.560, t=4.3$  then  $H(t) = 0.6656, \bar{F}(t) = 0$

Case 2: 3% NaCl

If  $a=1.358, b=3.030, t=4.3$  then  $H(t) = 0.6131, \bar{F}(t) = 0$

Case 3: Glucose

If  $a=1.896, b=8.541, t=4.3$  then  $H(t) = 0.1048, \bar{F}(t) = 0$



### 5. Conclusions

There is no significance difference of the NMWD model for the survival function of 0.9% NaCl, 3% NaCl, glucose and also found hrf decrease in glucose.

### References

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