A Cumulative Exposure Model for the Release of Vasopressin

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Abstract: **The study was aimed to investigate the effect of the administration of Vasopressin . A cumulative exposure model with step-stress plans using fuzzy log-normal distribution was developed. Using this cumulative exposure model, the step-stress was calculated for several time intervals. The results shown that, the administration of Vasopressin induced a significant change in antidiuretic hormone release**.

Keywords: Cumulative exposure model, Vasopressin, fuzzy log-normal Distribution

I.INTRODUCTION

Nelson[1] is the first propose the step-stress scheme, with the cumulative exposure model and method of analysis. Mohammed et al.,[2] discussed the cumulative exposure model. Miller and Nelson[3], Balakrishnan et al.,[4] obtained the optimum simple step-stress accelerated life test plans for the case where the test units have exponentially distributed life times. Bai[5] and others extended the result of Miller and Nelson to the case of censoring. Bai put each experimental unit to only one of the stress levels. Some of the important early works in constant-stress test can be found in Kielpinski and Nelson[6], Meeker[7]. Khamis[8] compared the constant and step-stress scheme for small sample sizes using simulation.

Maximum people prefer to think in terms of the original rather than the log transformed data. This conception is indeed feasible and worthwhile for log-normal data, too, because the well-known properties of the normal distribution have their analogies in the log-normal distribution. To improve comprehension of log-normal distributions, to encourage their proper use, and to show their importance in life, we prefer a novel physical model for generating log-normal distributions

A variety of samples from medicine fit the log-normal distribution. Latent periods (time from infection to first symptoms) of infectious diseases have often been shown to be log-normally distributed. Kondo[9] and Sartwell[10] discussed lognormal distribution in biological models . The reasons governing frequency distributions in nature usually favor the log-normal, whereas people are in favor of the normal. For small coefficients of variation, normal and log-normal distributions both fit well.

Vasopressin is a hormone produced and released in the posterior pituitary gland which causes the kidneys to retain water, thus increasing the water content of the body. In high concentrations, it causes the constriction of blood vessels throughout the body and consequent rise of pressure. Vasopressin helps prevent the loss of water from the body by reducing urine output and helping the kidneys reabsorbs water in the body. Vasopressin is secreted by the cells of the hypothalamus nuclei and stored in the posterior pituitary for release as necessary. It stimulates contraction of the muscular tissues of the capillaries and arterioles, raising the blood pressure, and increase peristalsis, exert some influence on the uterus, and influences resorption of water by the kidney tubules, resulting in concentration of urine. Its rate of secretion is regulated chiefly by the osmolarityof the plasma. Also prepared synthetically or obtained from the posterior pituitary of domestic animals, used as an antidiuretic called antidiuretic hormone (ADH).

In contrast to the well-known peripheral antidiuretic effect of vasopressin, the administration of vasopressin into the lateral cerebral ventricles produced a diuretic response in normal animals [11] as well as in spinal transacted cats [12]. Since hemodynamic changes were observed concurrently and ADH blood level changes were not measured by these workers, it is difficult to attribute the diuretic response following intracerebral ventricular injection of vasopressin, to an inhibition of ADH release.

In this paper, we analyzed stress level by simple step-stress plans under a cumulative exposure model using the log normal distribution for the administration of Vasopressin in animals.

II. NOTATION

$\overline{G}(t)$ - Fuzzy log normal cumulative distribution function.

ϕ - Standard normal cumulative distribution function.

μ - Scale parameter

σ - Shape parameter

$\overline{G}(t)[\alpha]$ -Fuzzy alpha cut log normal cumulative distribution function

$\overline{\mu}[\alpha]$-Fuzzy alpha cut scale parameter

$\overline{\sigma}[\alpha]$- Fuzzy alpha cut shape parameter

III. FUZZY CUMULATIVE EXPOSURE MODEL

The relationship between lifetime and stress level under accelerated conditions is extrapolated to normal working condition. There are basically two types of accelerated life test schemes; the constant-stress test, and the step-stress test.

In the step-stress test, initial low stress is applied to all test units. If a unit does not fail in a specific time, the stress is increased .There can be more than one change of stress level. If there is a single change of stress, this is a simple step-stress test.The objectives are to choose time to change stress levels to minimize the variance of some estimate of a parameter under a normal stress level.

Under any constant stress, the life time of a test unit follows a lognormal distribution $G(t)=\phi\left[\frac{\log t-\mu}{\sigma}\right]$ where μ is the mean value of a log normal distribution and σ is the standard deviation of log normal distribution of the log life time of the unit under life testing.

We first specify the α-cuts of $\overline{\mu}$ as $\overline{\mu}[\alpha]$. If $\overline{\mu}[\alpha]=[\overline{\mu}_1[\alpha],\overline{\mu}_2[\alpha]]$, then similarly the α-cuts of $\overline{\sigma}$ is $\overline{\sigma}[\alpha]$ and $\overline{\sigma}[\alpha]=[\overline{\sigma}_1[\alpha],\overline{\sigma}_2[\alpha]]$

Under any constant stress,the life time of a test unit follows a fuzzy lognormal distribution $\overline{G}(t)=\phi\left[\frac{\log t-\overline{\mu}}{\overline{\sigma}}\right]$. Then α-cuts of $\overline{G}(t)[\alpha]=[\overline{G}_1(t)[\alpha],\overline{G}_2(t)[\alpha]]$. The minimum (maximum) of the expression on the right side of the above equation is

$$\overline{G}_1(t)[\alpha]=Mini\left[\phi\left[\frac{\log t-\mu_1[\alpha]}{\sigma_1[\alpha]}\right]\right]$$

$$\overline{G}_2(t)[\alpha]=Max\left[\phi\left[\frac{\log t-\mu_2[\alpha]}{\sigma_2[\alpha]}\right]\right]$$

IV. APPLICATION

The diuretic response of urine flow level was observed with 1.0 unit of vasopressin started within 10-20 min after injection, the peak effect was observed within 40-60 min and gradual recovery occurred in 90-120 min .With smaller doses (<1.0 unit) of vasopressin (i.c.v.) the diuretic response was of shorter duration depending upon the dose. The observed values are given in Fig.4.1.

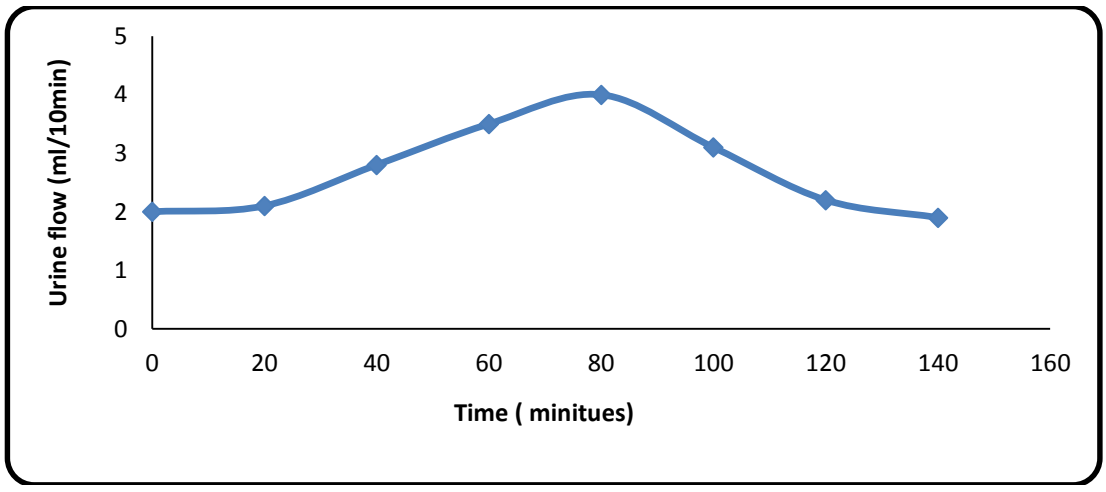

Figure4.1 Urine flow level effort of lower doses vasopressin

Higher doses of vasopressin (1.5-2.0 u, i.c.v.), on the other hand, induced an antidiuretic response of urine flow level, with a concomitant increase in blood ADH titre. With all the doses of vasopressin (i.c.v.) there was a rise in blood pressure with 1.0 unit of vasopressin, ranging from 5 to 20 mmHg. In all instances, the pressure response never lasted more than 10-20 minutes. The observed values are given in Fig.4.2.

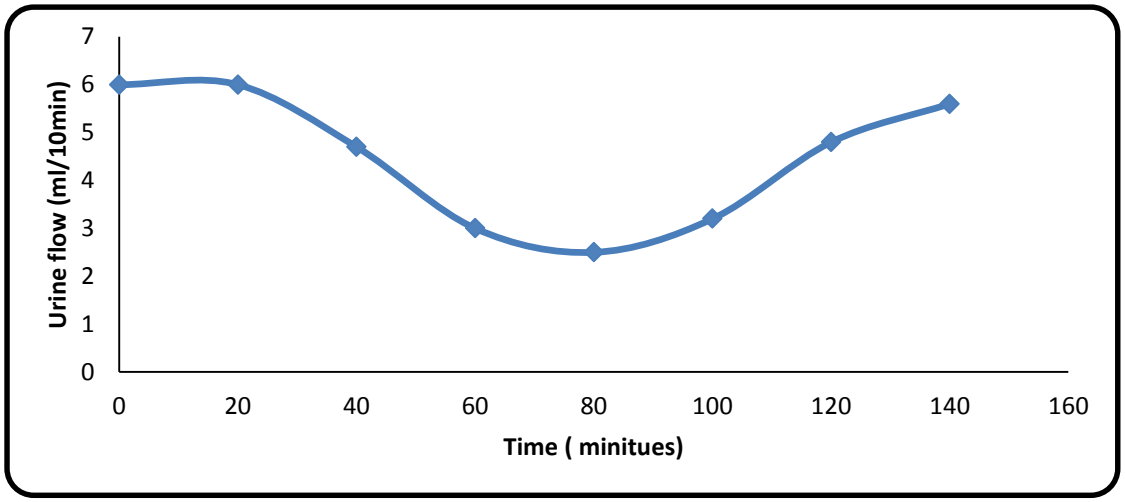

Figure4.2 Urine flow level effort of higher doses vasopressin

The mean and standard deviation are calculated as

μ = 4.3 and σ= 0.3

Fuzzy triangle number is $\overline{\mu}$ = [4, 4.3,4.6],

$\overline{\sigma}$ =[0.1, 0.3,0.5] and

Fuzzy alpla cut valuesare $\overline{\mu}[\alpha]$=[4+0.3α , 4.6-0.3α] ,

$\overline{\sigma}[\alpha]$=[0.1+0.2α , 0.5-0.2α]

Using the cumulative exposure model, the step-stress $\overline{G}(t)$ was calculated for various time intervals(t=45, 50, 55 & 60) during the lower and higher doses of vasopressin. The calculated values of lower step stress and higher step stress for various time intervals are given in Table 4.1.

Table 4.1 The step-stress value for various time intervals

t=45		
A	Lower step-stress values	Upper step-stress values
0	0.003126552	0.012419504
0.1	0.004243471	0.010813497
0.2	0.005247248	0.00921073
0.3	0.006133424	0.007632651
0.4	0.006911856	0.006106961
0.5	0.007596138	0.004668309
0.6	0.008199677	0.003358136
0.7	0.008734403	0.002222644
0.8	0.009210499	0.001307274
0.9	0.009636506	0.000645723
1	0.010019541	0.000242939

t=50		
A	Lowerstep-stressvalues	Upper step-stress values
0	0.106716185	0.025833809
0.1	0.08220794	0.02386133
0.2	0.067484188	0.021775096
0.3	0.057846762	0.019575188
0.4	0.051127159	0.01726654
0.5	0.046211607	0.014861758
0.6	0.042478509	0.012385275
0.7	0.03955733	0.009879267
0.8	0.037215109	0.007411526
0.9	0.035298826	0.005084368
1	0.033704217	0.003040221

t=55		
α	Lower step-stress values	Upper step-stress values
0	0.541299025	0.046838264
0.1	0.39468416	0.045223473
0.2	0.297357745	0.043443176
0.3	0.232487832	0.04147241
0.4	0.188025978	0.039281643
0.5	0.156533668	0.03683608
0.6	0.13351151	0.034095173
0.7	0.116194854	0.03101282
0.8	0.102838796	0.027539369
0.9	0.092309306	0.023627972
1	0.08384805	0.019251147

t=60		
α	Lower step-stress values	Upper step-stress values
0	0.908936344	0.076328442
0.1	0.775866672	0.076182071
0.2	0.635678974	0.076016001
0.3	0.515315965	0.075825967
0.4	0.420127171	0.075606379
0.5	0.346959097	0.075349765
0.6	0.290949152	0.075045899
0.7	0.247775622	0.074680409
0.8	0.214104214	0.074232442
0.9	0.187487248	0.073670542
1	0.08384805	0.072944941

V. CONCLUSION

A cumulative exposure model with simple step-stress plans using fuzzy log-normal distribution was used to compute the fuzzy step stress for lower and higher doses of vasopressin. In the first case,the lower doses of Intracerebralventricular (i.c.v.) administered vasopressin (0.001-1.0 u) in dogs anaesthetized with chloralose produced a dose-dependent increase in urine flow with a concomitant decrease in the levels of antidiuretic hormone (ADH) in jugular vein blood.In the second case,the higher doses of vasopressin (1.5-2.0 u, i.c.v.) had an antidiuretic effect and produced an increase in blood ADH level. The results exposed that, the administration of Vasopressin induced a significant variation in antidiuretic hormone release.

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