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EXTENDED RELIABILITY GROWTH MODEL TO CALCULATE THE INFLUENCE OF INSULIN ON CIRCULATING GHRELIN USING GAMMA DISTRIBUTION

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Abstract:
Ghrelin is a novel peptide that acts on the growth hormone (GH) secretagogue receptor in the pituitary and hypothalamus. It may functions as a third physiological regulator of GH secretion, along with GH-releasing hormone and somatostatin. In addition to the action of ghrelin on the GH axis, it appears to have a role in the determination of energy homeostasis. Although feeding suppresses ghrelin production and fasting stimulates ghrelin release, the underlying mechanisms controlling this process remain unclear. Our data suggest that insulin may suppress circulating ghrelin independently of glucose, although glucose may have an additional effect. This paper presents an extended model that addresses this practical situation and allows for preemptive corrective actions. The purpose of this study was to estimate the influence of insulin on circulating ghrelin using gamma distribution with the help of growth model.

Key Words: Insulin, Ghrelin, Euhypohyperglycemic Glucose Clamp, Stress Management & Extended Reliability Growth Model

Introduction:

Ghrelin is a novel peptide that acts on the growth hormone (GH) secretagogue receptor in the pituitary and hypothalamus, possibly functioning as a third physiological regulator of GH secretion along with GH releasing hormone (GHRH) and somatostatin. In addition to the action of ghrelin on the GH axis, it appears to have a role in the determination of energy homeostasis [1-2] & [3]. Ghrelin acts as an orexigenic hormone, stimulating both neuropeptide Y (NPY) and agoutirelated peptide, and thus feeding [4 & 6].

Although feeding suppresses ghrelin production and fasting stimulates ghrelin release, the underlying mechanisms controlling these processes remain unclear [12 & 13]. This relationship is the opposite of that seen with leptin [14], which has been shown to be increased by insulin [14]. Specifically, the roles that alterations in plasma glucose and insulin have in regulating ghrelin secretion have not been established. The purpose of this study was to estimate the influence of insulin on circulating ghrelin using gamma distribution with the help of growth model.

In today's environment of compressed schedules and limited testing, every opportunity to identify and correct reliability deficiencies in a new design is a prime objective. A metric for tracking system reliability before development testing based on preemptive corrective actions for potential problem modes is discussed [9].

In the test fix test strategy problem modes are found during testing and corrective actions for these problems are incorporated during the test. For the test-find-test strategy problem modes are found during testing but all corrective actions for these problems are delayed and incorporated after the completion of the test.

Background on the Widely Used Test Fix Test and Test Find Test Models:

To lay the groundwork for the Extended Model we first give some background on the two widely used basic models. For reliability growth during test-fix-test development testing states that the instantaneous system MTBF at cumulative test time t is

$$M(t) = \left[\lambda\beta t^{\beta-1}\right]^{-1} \quad (1)$$

Where $0 < \lambda$ and $0 < \beta$ are parameters. The Non-homogeneous Poisson process (NHPP) with intensity in [10] is defined by

$$r(t) = \lambda\beta t^{\beta-1} \quad (2)$$

Thus allowing for statistical procedures based on this process for reliability growth analyses. This model is applicable to text-fix-test data not test-fix-find-test. Estimation procedures, confidence intervals, etc, in [11].

The parameter λ is referred to as the scale parameter and β is the shape parameter. For β = 1, there is no reliability growth. For β < 1, there is positive reliability growth.

That is, the system reliability is improving due to corrective actions. For β >1, there is negative reliability growth.

The basic model the achieved or demonstrated failure intensity at time T, the end of the test is given by r (T). We denote the achieved failure intensity by

$$\lambda_{CA} = r(T) \quad (3)$$

Suppose a development testing program begins at time 0 and is conducted until time T and stopped. Let N be the total number of failures recorded and let $0 < X_1 < X_2 < \ldots\ldots X_N < T$ denote the N successive failure times on a cumulative time scale. We assume that the NHPP assumption applies to this set of data in [7].

Under the basic model the maximum likelihood estimates for λ and β (Numerator of MLE for β adjusted from N to N-1 to obtain unbiased estimate) are

$$\hat{\lambda} = \frac{N}{\hat{T}\beta}, \hat{\beta} = \frac{N-1}{\sum_{i=1}^{N} \log \frac{T}{X_i}} \quad (4)$$

And

$$\lambda^* = \frac{N}{\hat{T}\beta^*} \quad (5)$$

$$\beta^* = \frac{N-1}{\sum_{j=1}^{n} \log \frac{T}{X_j}} \quad (6)$$

If it is assumed that no corrective actions are incorporated into the system during $\beta < 1$ the test and then this is equivalent to assuming that for λ_{CA} and λ^*_{CA} is estimated in [7 & 8]. The estimated projected failure intensity

$$\lambda_p = \lambda_{AT} + \sum_{i}^{N} (1 - E_i) + \hat{E}h(T/AT) \quad (7)$$

$$\lambda^*_p = \lambda^*_{AG} + \sum_{i}^{N} (1 - E^*_i) + \hat{E}h(T/AG) \quad (8)$$

The extended model projected failure intensity is

$$\lambda_{EM} = \lambda_{CA} - \lambda_{AT} + \sum_{i}^{N}(1-E_i)\frac{N_i}{T} + \hat{E}h(T/AT) \quad (9)$$

$$\lambda^*_{EM} = \lambda^*_{CA} - \lambda^*_{AT} + \sum_{j}^{N}(1-E^*_j)\frac{N_j}{T} + \hat{E}h(T/AG) \quad (10)$$

The extended model projected MTBT is

$$M_{EM} = \frac{1}{\lambda_{EM}} \text{ and } M^*_{EM} = \frac{1}{\lambda^*_{EM}} \quad (11)$$

Example:

Eleven young adult volunteers (9 women, 2 men) participated in the study. The age of the subjects was 24 ± 4 yr (range 18–31 yr), and the body mass index was 22.1 ± 2.8 kg/m2 (18.4–26.6 kg/m2). All subjects were healthy and taking no medication. They were instructed to maintain their normal physical activity and to consume a normal diet containing ≥200 g of carbohydrate for 3 days before the study. Before the study, a small Teflon catheter was inserted into an antecubital vein for infusion of insulin and glucose. A second catheter was inserted in a retrograde direction into a wrist vein in the opposite arm for blood sampling. This was kept patent with a slow infusion of isotonic saline. The hand was then placed in a heated box to achieve a temperature of 65°C to obtain arterialized blood through the wrist catheter.

After a baseline period of 1 h, a three step euhypohyperglycemic glucose clamp was then performed [4]. A primed continuous infusion of insulin was administered at a rate of 1 $mU^{-1}kg^{-1}$ min^{-1}. Each step of the study was maintained for 60 min, with a 15-min period of adjustment between steps. Throughout the study, plasma glucose concentrations were monitored every 5 min and used to regulate plasma glucose by the adjustment of a variable infusion of 20% dextrose. Plasma glucose was maintained at 90 mg/dl during the euglycemic phase of the study, at 50 mg/dl during hypoglycemia, and at 160 mg/dl during hyperglycemia. Two samples for measurement of insulin, GH, and ghrelin were taken in the hour preceding the study and repeated during the three steps of the clamp procedure. The glucose and insulin data from these studies are included in another study that examined the accuracy of glucose sensor measurements [6].

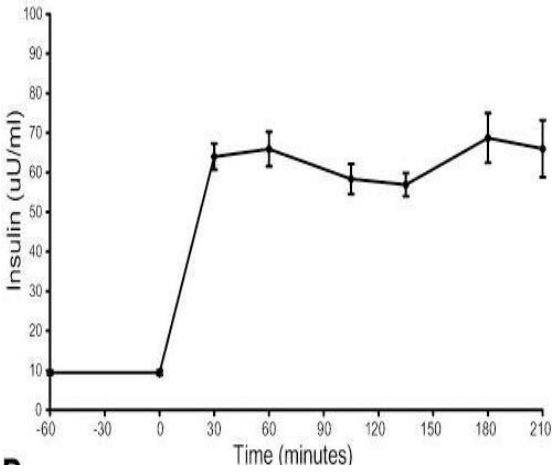

Figure (1): Insulin concentrations during a stepped euhypohyperglycemic glucose clamp.

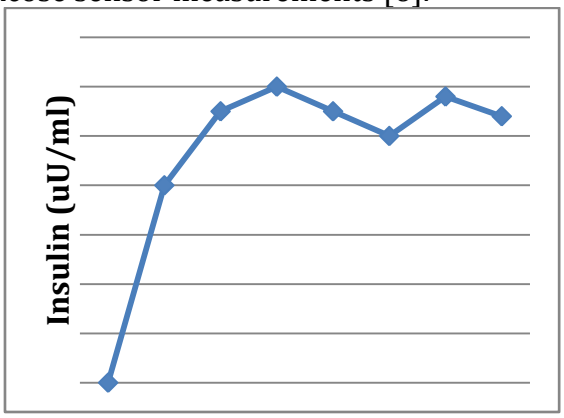

Figure (2): Insulin concentrations during a stepped euhypohyperglycemic glucose clamp
(Using Gamma Distribution)

Conclusion:

It has been repeatedly demonstrated that circulating GH levels are reduced in obese subjects who are insulin resistant and hyperinsulinemic. We have reported that

such compensatory hyperinsulinemia suppresses IGF-binding protein-1 levels, which in turn may lead to increased bioavailability of free IGF-I and feedback suppression of GH secretion. It is intriguing to speculate that insulin-induced suppression of ghrelin may also play a role in the reduction in GH secretion observed in obesity. Growth model with gamma distribution gives the same as the medical report. There is no significance difference between medical and mathematical reports. The medical reports are beautifully fitted with the mathematical model. Hence the mathematical report {Figure (2)} is coincide with the medical report {Figure (1)}. At the completion of the reliability growth test, it concludes that from {Figure (2)}, the results coincide with the medical findings.

References:

1. Attia N, Tamborlane W V, Heptulla R, Maggs D, Grozman A, Sherwin R S & Caprio S, "The metabolic syndrome and insulin-like growth factor I regulation in adolescent obesity", Journal of Clinical Endocrinology Metabolism, Volume 83, Page Number 1467–1471, 1998.
2. Barbetti F, Crescenti C, Negri M, Leonetti F, Grossi A & Tamburrano G, "Growth hormone does not inhibit its own secretion during prolonged hypoglycemia in man", Journal of Clinical Endocrinology Metabolism, Volume 70, Page Number 1371–1374, 1990.
3. DeFronzo R A, Tobin J D & Andres R, "Glucose clamp technique: a method for quantifying insulin secretion and resistance", American Journal of Physiology Endocrinology Metabolism, Number 237, Page Number 214–223, 1979.
4. Jaffe C A, DeMott Friberg R & Barkan A L, "Endogenous growth hormone (GH) releasing hormone is required for GH responses to Pharmacological Stimuli", Journal of Clinical Investigation, Volume 97, Page Number 934–940, 1996.
5. John S & Usher, "Reliability Models and Misconceptions", Quality Engineering, Volume 6 Issue 2, Page Number 261-271, 1993.
6. Kojima M, Hosoda H, Date Y, Nakazato M, Matsuo H & Kangawa K, "Ghrelin is a growth hormone releasing acylated peptide from stomach", Nature, Number 402, Page Number 656–660, 1999.
7. Lakshmi S, "Stochastic Model for Stress Effects of Homeostatic Systems", The Journal of the Indian Academy of Mathematics, Volume 26(2), 2004.
8. Lakshmi S & Karthik R, "Mathematical Model for the Secretion of GnRH in Beef Cows by Using Extended Reliability Growth Model", Bio Science Research Bulletin, Volume 27, Page Number 1-5, 2011.
9. Larry H. Crow, "An Extended Reliability Growth Model for Managing and Assessing Corrective Actions", Reliability and Maintainability Symposium, Los Angeles, CA.
10. L.H. Crow, "Reliability analysis for Complex, Repairable systems, in Reliability and Biometry, ed. By F. Proschan and R.J. Serfing, Page Number 379-410, 1974, Philadelphia, SIAM.
11. Reliability Growth – Statistical test and estimation methods, IEC International Standard, IEC 61164, International Electrotechnical Commission, 1995.
12. Tannenbaum G S, Martin J B & Colle E, "Ultradian growth hormone rhythm in the rat: effects of feeding, hyperglycemia, and insulin-induced hypoglycemia", Endocrinology, Number 99, Page Number 720–727, 1976.
13. Thorner M O, Chapman I M, Gaylinn B D, Pezzoli S S & Hartman M L, "Growth hormone releasing hormone and growth hormone releasing peptide as

therapeutic agents to enhance growth hormone secretion in disease and aging", Recent Prognosis Homology, Number 52, Page Number 215–244, 1997.
14. Trayhurn P, Hoggard N, Mercer J G & Rayner D V, "Leptin: fundamental aspects", International Journal of Obese Related Metabolism Disorders, Volume 23, Supplementary, Number 1, Page Number 22–28, 1999.