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Mathematical Model for Hemodynamicand Hormonal Effects of Human Ghrelin in Healthy Volunteers

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Abstract
Hemodynamicand hormonal effects of human ghrelin in healthy volunteers.To investigate hemodynamic and hormonaleffects of ghrelin, a novel growth hormone (GH)-releasing peptide, we gave six healthy men an intravenousbolus of human ghrelin or placebo and vice versa1–2 wk apart in a randomized fashion. Ghrelin elicited amarked increase in circulating GH . The elevation ofGH lasted longer than 60 min after the bolus injection.Injection of ghrelin significantly decreased mean arterialpressure without a significant changein heart rate .In summary, human ghrelin elicited a potent, longlastingGH release and had beneficial hemodynamic effectsvia reducing cardiac afterload and increasing cardiac outputwithout an increase in heart rate. Thus, the purpose of thisstudy was to investigate hemodynamic and hormonaleffects of intravenous ghrelin in healthy volunteers. This paper discussed the constant stress level of healthy volunteers with times to damage of stress effect andrecoveries

keywords: hemodynamics; hormones; vasodilation,TTO,TTP

I. Introduction

Intravenous injectionof ghrelin elicited a potent, long-lasting GH release inhealthy volunteers and ghrelin decreased mean arterialpressure and increased cardiac output but didnot increase heart rate.We studied six healthy male hospital staffmembers, aged 30 -61 yr, who weighed 68- 65 kg. None ofthem had any history of cardiovascular, renal, respiratory,hepatic, or metabolic disease, and none were taking anydrugs. Physical examination and lectrocardiographic andechocardiographic findings were also normal. The study wasapproved by the ethics committee of the National CardiovascularCenter, and all subjects gave written informed consent.Human ghrelinwas obtained from the Peptide Institute, Osaka, Japan. Thehomogeneity of human ghrelin was confirmed by reversephase,high-performance liquid chromatography (RP-HPLC)and amino acid analysis. Ghrelin was dissolved in distilledwater with 4% D-mannitol and was sterilized by passagethrough a 0.22-mm filter (Millipore). Ghrelin was stored as 1ml volumes (each containing 600 mg ghrelin) at 280°C untilthe time of preparation for administration.

The subjects were studied on 2 separatedays (1 day, ghrelin; 1 day, placebo) 1–2 wk apart in arandomized, crossover fashion. This study was performedafter the subjects fasted overnight, because plasma ghrelinlevel has been shown to be altered by food intake was po-sitioned in the pulmonary artery through a jugular vein tomeasure pulmonary arterial pressure and pulmonary capillarywedge pressure. Cardiac output was determined bythermodilution method in triplicate [1,2]. A 22-gauge cannulawas inserted into a radial artery for measurement of heartrate and systemic arterial pressure. Another 22-gauge cannulawas inserted into a forearm vein for infusion of ghrelin.Ghrelin (10 mg/kg) was dissolved in 5 ml saline. After anequilibration period of 60 min, baseline measurements wereperformed. Then, 5 ml of ghrelin solution or placebo (0.9%saline) was administered as an intravenous bolus. Hemodynamicmeasurements were repeatedly performed until 120min after the injection

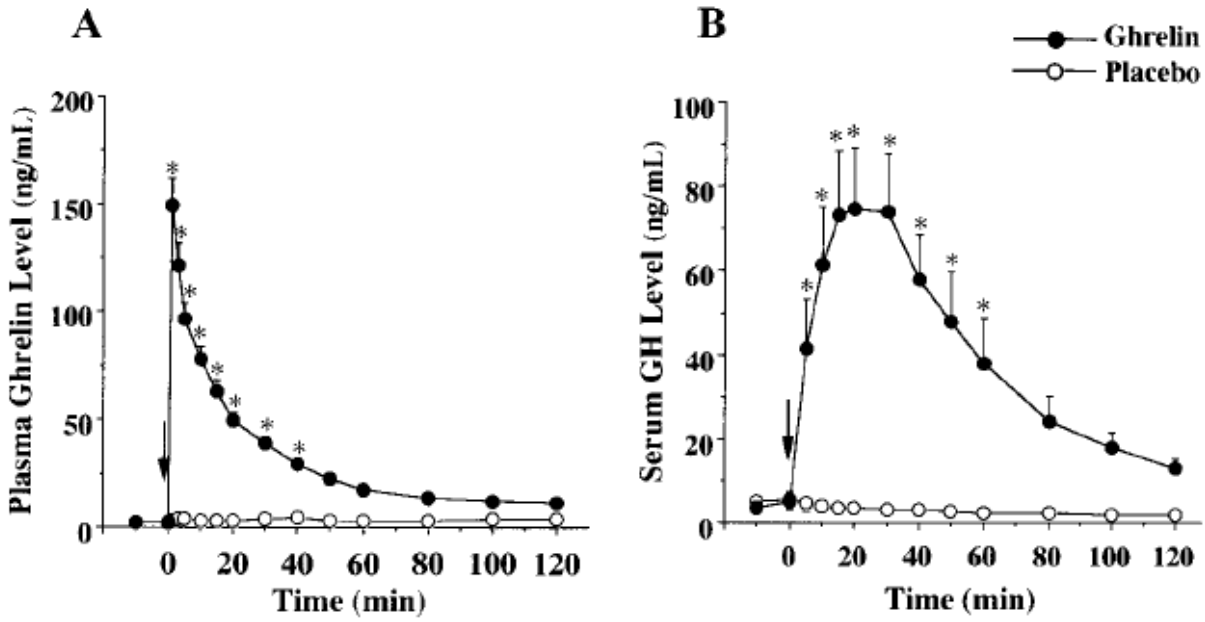


Fig. 1.Circulating ghrelin level after a singleinjection of ghrelin (*A*).Effects of ghrelin oncirculating growth hormone (GH) (*B*). Data aremeans 6 SE. **P* , 0.05 vs. placebo group. Thearrow indicates an intravenous injection of ghrelinor placebo.

Notations

A- Steady-state system availability
λ- Rate of failures (unplanned outages)
μ- Repair rate for unplanned outage
μ_2-Upgrade rate for planned outage
T-Time to damage of Ghrelin and GH level.
TTP-Time to planned outage

II. Mathematical Model

The steady-state availability of the system in this section canbe obtained from the general formula[4,]

A = [1++·]$^{-1}$

= [1++θ(λ) ·]$^{-1}$

α(λ) ≡

θ(λ) ≡

Now, the Availability [5]formula for the distribution of TTP is exponentially distributed.

Let TTP = T,

Also,let

F(x)≡1-exp(-x/T),T>0,x>0

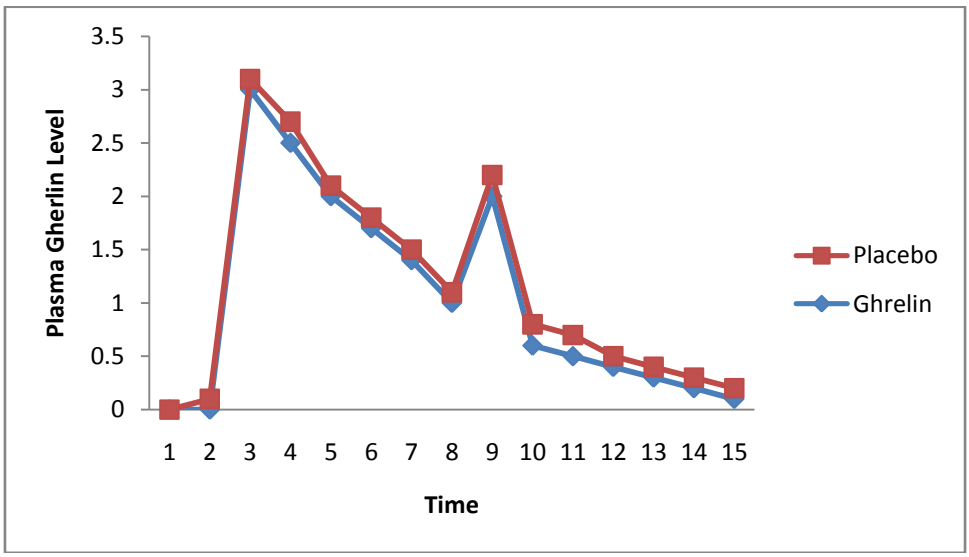
T=MTTP, λ_2=1/T;

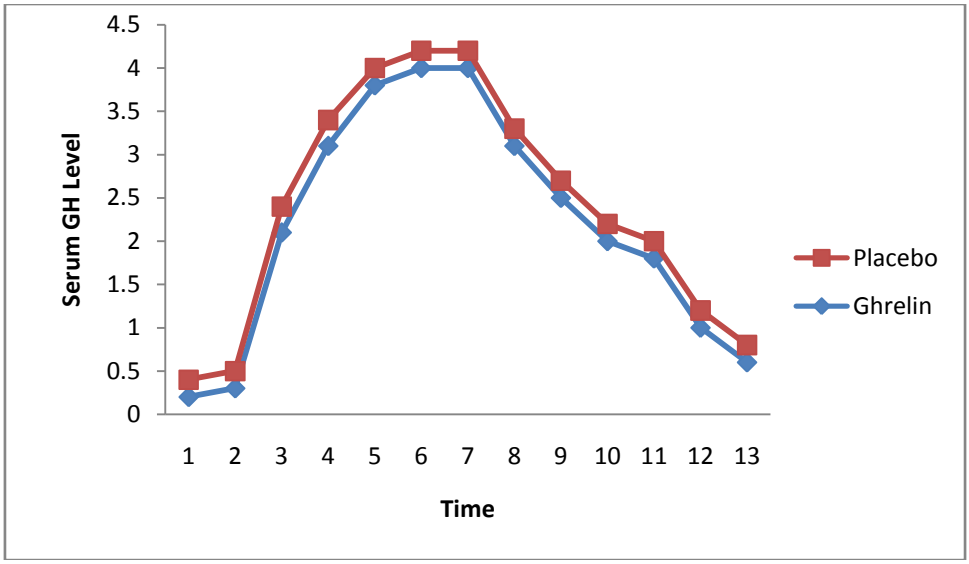
Now, $A_D(T)$=[1++]$^{-1}$

RESULTS:

TABLE:1

	GHRELIN					PLACEBO				
PLASMA	λ	μ	μ_2	T	$A_D(T)$	λ	μ	μ_2	T	$A_D(T)$
GHRELIN LEVEL	0.241	4.421	6.525	0.8	0.8025	0.340	3.139	7.049	0.8	0.7778
				2.5	0.8962				2.5	0.8583
				4.1	0.9158				4.1	0.8750
				5.7	0.9247				5.7	0.8825
				7.4	0.9300				7.4	0.8869
				9	0.9332				9	0.8896
				10.7	0.9356				10.7	0.8916
SERUM GH LEVEL	0.350	3.208	2.944	0.9	0.6727	0.357	2.997	6.542	0.9	0.7744
				2.6	0.8066				2.6	0.8490
				4.4	0.8429				4.4	0.8667
				6	0.8578				6	0.8737
				7.8	0.8676				7.8	0.8782
				9.5	0.8735				9.5	0.8809
				11.3	0.8778				11.3	0.8829





III. Conclusion

Humanghrelin elicited a potent, longlasting GH release and had beneficial hemodynamic effects via reducing cardiac afterload and increasing cardiac output without an increase in heart rate and found the steady state availability of exponentially distributed model of Gherlin, GH levels due to stress.

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Consider the system with a weibul distribution. The pdf of the weibul distribution with parameters β and θ is given by

$f(y) = \beta/\theta\ (y/\theta)^{\beta-1} \exp(-y/\theta)^{\beta}$, $y > 0$, $\beta, \theta > 0$ where $\beta = 1.430$; $\theta = 4.949$

The pdf of the random leadtime of an order is,

$g(x) = \exp(-x/\mu)$, $x > 0$, $\mu > 0$. Where $\mu = 4.2750$

Suppose the random repair cost [1,2,3] is ω, If $\omega \leq \delta(y).c_{\infty}$ (c_{∞} ≡ the constant cost) then there is a minimal repair.

If δ(y).can be explained as a fraction of the constant cost , c_{∞} , at age y and $0 \leq \delta(y) \leq 1$.

Let $\delta(y) \equiv \delta(\exp(-\lambda,y))$ with $0 \leq \delta(y) \leq 1$ & $\lambda \geq 0$.

The optimal time T* [7,8] which minimizes $C_1(T^*) = \lambda C_1 (1-g(x))\ e^{-\lambda(1-g(x))T^*}$

When $C_1=1.6$

$\lambda=0.234$

$g(x)=0.2181$

$T^*=0.3$ then $C_1(T^*) =0.0673$

Conclusion