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Survival function Of Realization process for Hemodynamic and hormonal effects of human GH in healthy volunteers

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Abstract
Hemodynamic and hormonal effects of human ghrelin in healthy volunteers. To investigate hemodynamic and hormonal effects of ghrelin, a novel growth hormone (GH)-releasing peptide, we gave six healthy men an intravenous bolus of human ghrelin or placebo and vice versa 1–2 wk apart in a randomized fashion. Ghrelin elicited a marked increase in circulating GH. The elevation of GH lasted longer than 60 min after the bolus injection. Injection of ghrelin significantly decreased mean arterial pressure without a significant change in heart rate .In summary, human ghrelin elicited a potent, long lasting GH release and had beneficial hemodynamic effects via reducing cardiac after load and increasing cardiac output without an increase in heart rate. Thus, the purpose of this study was to investigate hemodynamic and hormonal effects of intravenous ghrelin in healthy volunteers. This paper discussed the constant stress level of healthy volunteers with times to damage of stress effect and recoveries
keywords: hemodynamics; hormones; vasodilation

I. Introduction

Intravenous injection of ghrelin elicited a potent, long-lasting GH release in healthy volunteers and ghrelin decreased mean arterial pressure and increased cardiac output but did not increase heart rate. We studied six healthy male hospital staff members, aged 30 -61 yr, who weighed 68- 65 kg. None of them had any history of cardiovascular, renal, respiratory, hepatic, or metabolic disease, and none were taking any drugs. Physical examination and lector cardio graphic and echo cardio graphic findings were also normal. The study was approved by the ethics committee of the National Cardiovascular Center, and all subjects gave written informed consent. Human ghrelin was obtained from the Peptide Institute, Osaka, Japan. The homogeneity of human ghrelin was confirmed by reverse phase, high-performance liquid chromatography (RP-HPLC) and amino acid analysis. Ghrelin was dissolved in distilled water with 4% D-mannitol and was sterilized by passage through a 0.22-mm filter (Millipore). Ghrelin was stored as 1 ml volumes (each containing 600 mg ghrelin) at 280°C until the time of preparation for administration.

The subjects were studied on 2 separate days (1 day, ghrelin; 1 day, placebo) 1–2 wk apart in a randomized, crossover fashion. This study was performed after the subjects fasted overnight, because plasma ghrelin level has been shown to be altered by food intake was positioned in the pulmonary artery through a jugular vein to measure pulmonary arterial pressure and pulmonary capillary wedge pressure. Cardiac output was determined by thermo dilution method in triplicate [1,2]. A 22-gauge cannula was inserted into a radial artery for measurement of heart rate and systemic arterial pressure. Another 22-gauge cannula was inserted into a forearm vein for infusion of ghrelin. Ghrelin (10 mg/kg) was dissolved in 5 ml saline. After an equilibration period of 60 min, baseline measurements were performed[3]. Then, 5 ml of ghrelin solution or placebo (0.9% saline) was administered as an intravenous bolus. Hemodynamic measurements were repeatedly performed until 120 min after the injection

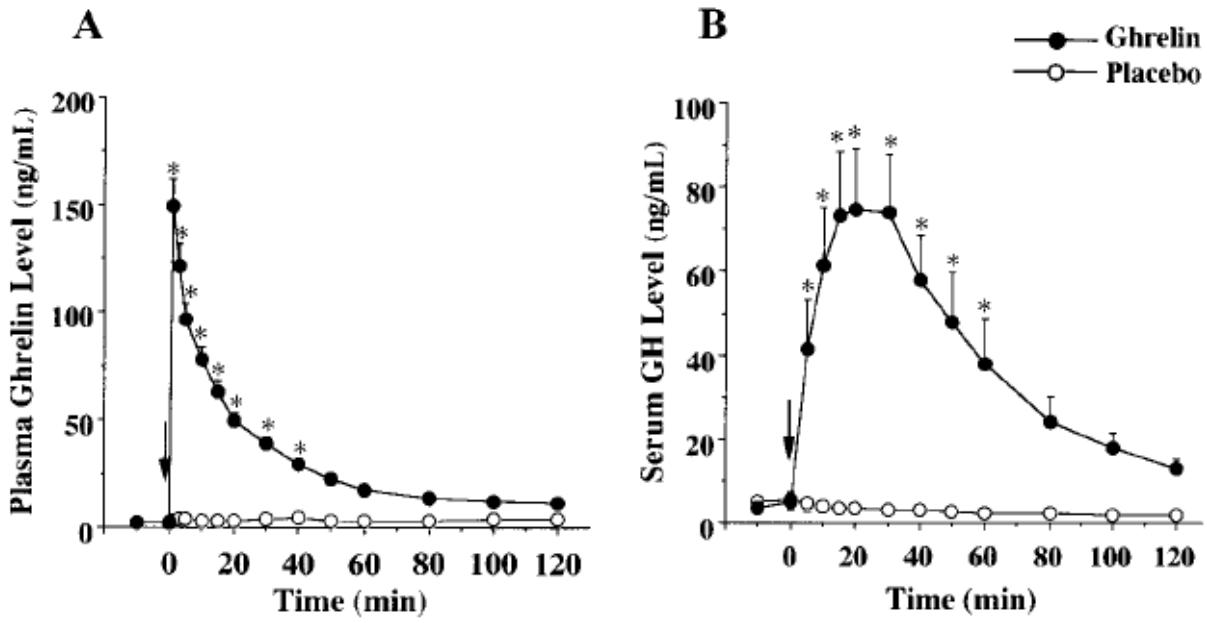


Fig. Circulating ghrelin level after a single injection of ghrelin (*A*). Effects of ghrelin on circulating growth hormone (GH) (*B*). Data are means 6 SE. **P* , 0.05 vs. placebo group. The arrow indicates an intravenous injection of ghrelin or placebo.

Mathematical Model

Notations

T_n - The time interval between two consecutive stress effects.

C_n - The magnitude of GH secretion due to n^{th} stress.

$N(t) = \max\{n \geq 0, \sum_{i=1}^{n} T_i \leq t\}$ be the number of stimuli.

Z - A known threshold or pre specified value of GH secretion

Realization of the process

Here the damage is allowed to decrease between successive stimuli.

That is, 'recovery' takes place in some deterministic fashion

$Z = \{Z(t), t \geq 0\}$, Such that $Z(0) = 0$ and $Z(t) \geq 0$ for all $t > 0$ with probability 1.

$T_x = \inf \{t \geq 0; Z(t) > x\}$ is first passage time[4,5]. $\overline{F}(t)$ Bounds of survival function.

The survival function of T_x is

$$\overline{F}(t) = e^{-\lambda t} \sum_{k=0}^{1+[t/\alpha]} \frac{(\lambda t)^k}{k!} \left[1 - \frac{(k-1)\alpha}{t}\right]^k, \; t \geq 0 \qquad \ldots(1)$$

When t is large the numerical computation of (1) can be radius, because for large t, the number of terms in the sum is large. Derived the following bounds of $\overline{F}(t)$,

$(1-\alpha/\lambda)e^{(a-\lambda)\alpha}e^{-at} \leq \overline{F}(t) \leq e^{(a-\lambda)\alpha}e^{-at} \equiv \overline{H}(t) t \leq 0,$ where $a = -s$ and s is the largest real root of $s + \lambda = \lambda\, e^{-(s+\lambda)\alpha}$ here $\lambda = 1$ and $\alpha = 1.$ For fixed t_0 , $\overline{F}(t) \leq [\overline{F}(t_0)]^k, t \geq 0$ and $kt_0 \leq t \leq (k+1)t_0, k = 0,1,2,3,\ldots$

Therefore, upper bound of $\overline{F}(t)$ is:

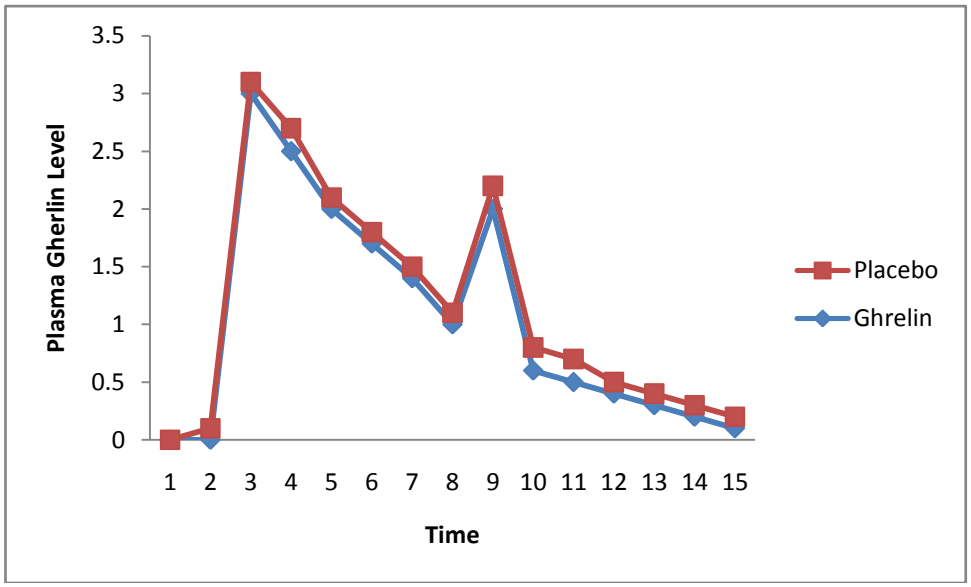
$$\overline{F}(t) \leq \min\,[\ \overline{H}\ (t), [\ \overline{F}(t_0)]^k\ ]$$

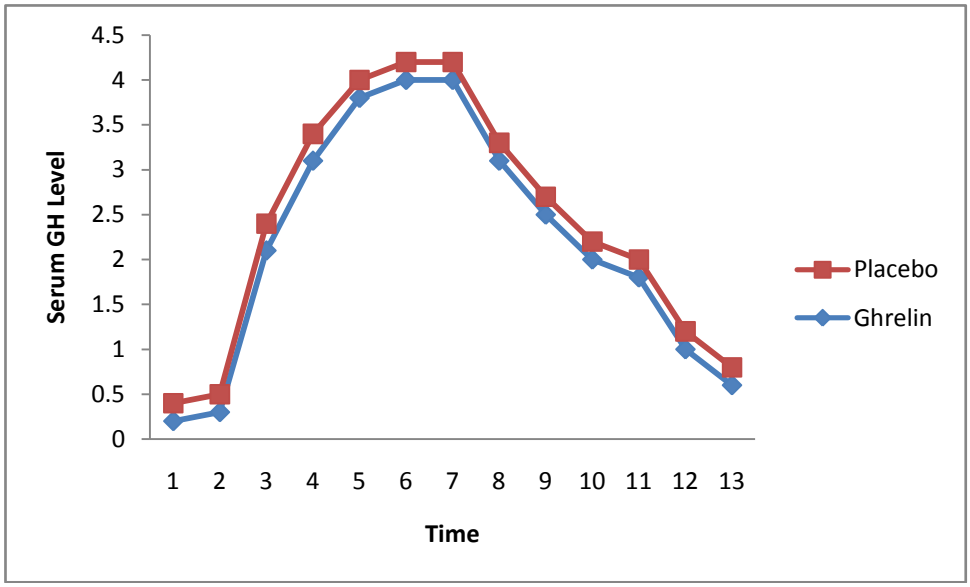
When t is large enough, then

$$e^{(a-\lambda)\alpha} e^{-at} < [\overline{F}(t_0)]^k$$

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

Case	**α**	**Π**	**t**	$\overline{F}(t)$
Gherlin	0.0344	0.01 3	1 2 3 4	0.999993 0.999985 0.999972 0.999954
GH	0.0464	0.0114	1 2 3 4	0.999992 0.999984 0.999975 0.999961





II. Conclusion:

In the paper we found the constant stress level of healthy volunteers with times to damage of stress effect and recoveries for hemodynamic and hormonal effects of ghrelin, a novel growth hormone (GH)-releasing peptide.

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