

Stochastic Model to Find the Characteristic Function of Insulinotropic Action of Glucose-Dependent Insulinotropic Hormone Using Compound Poisson Process

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ABSTRACT:

The purpose of the Study was to evaluate the comparison of insulinotropic actions of exogenous incretin hormones GIP (Glucose-dependent Insulinotropic Hormone) in Nine type-2 diabetic patients and in Nine age- and weight-matched normal subjects. An oral glucose challenge (75g/300ml) was performed in the morning after an overnight fast between the two distinct groups. The GIP response after oral glucose tended to be lower in the type-2 diabetic patients than normal subjects. In this paper, the problem is investigated by valuation of the characteristic equation obtained by applying Laplace transform to the second order delay differential equation represented by a general version of compound Poisson process.

Key Words: GIP, Exogenous Incretin hormone, type-2 diabetic, Poisson process, Brownian motion, type-2diabetic patients. **2010 Mathematics Subject Classification:** 60G50; 60G51; 60G55

I. INTRODUCTION

In normal subjects, oral glucose enhances insulin secretion more than does intravenous glucose infusion [3], [18], [15], [16]. This augmentation of insulin secretion is due to the secretion and action of gut hormones with insulinotropic activity, namely glucose-dependent insulinotropic hormone; [6], [17] from the upper gut [2]. In type-2 diabetic patients, the incretin effect is reduced or lost [16], [20]. This does not seem to be a consequence of deficient release of GIP, in that most studies found a normal or even enhanced secretion of this incretin hormone in type-2 diabetic patients [11], [4]. By using GIP of the porcine amino acid sequence, several studies have uniformly described reduced insulinotropic effectiveness in type-2 diabetic patients as compared to normal subjects [9], [12]. Human GIP differs by two amino acids [9], [7] from porcine GIP [10], [14]. GIP responses after oral glucose tended to be lower in the type-2 diabetic patients.

In this paper the problem is investigated by valuation of the characteristic equation obtained by applying Laplace transform to the second order delay differential equation. The jump part in our model is represented by a general version of compound Poisson process. We incorporate a jump part in the stochastic model with delay [1]. We find some analytical closed forms for the expectation of the realized continuously sampled variance. The jump part in our model is represented by a general version of compound Poisson processes, and the expectation and the covariance of the jump sizes are assumed to be deterministic function.

Notations:

- β Scale parameter for model.
- λ Mean rate
- $K(t)$ Brownian Motion
- $I(t)$ Martingale
- $E^*(y)$ Expected value of realized variance
- $\Psi(q)$ Characteristic function

II. STOCHASTIC MODEL

2.1. Compound Poisson Process case

Let us consider the jumps represented by a compound Poisson Process, and it seems to allow the jump size to be a random number but not always one in Poisson Process, the model is more realistic.

The stochastic model can be defined as follows:

$$\frac{d\rho^2(t, Q_t)}{dt} = \beta U + \frac{\gamma}{s} \left[\int_{t-s}^t \rho(q, Q_q) dK^*(q) + \int_{t-s}^t x_q dM(q) - (\lambda - r)s \right]^2 - (\gamma + \beta)\rho^2(t, Q_t) \quad \text{----- (1)}$$

where $K^*(t)$ is a Brownian motion, $M(t)$ is a Poisson Process with intensity μ , and x_t is the jump size at time t which is identically independent normally distributed random variable. We assume that the mean of x_t is σ and the variance of x_t is δ . The Poisson intensity μ and the jump size x_t do not change since they are independent of the Brownian motion.

The Brownian motion and the compound Poisson process are independent. Letting

$$y(t) = E^*[\rho^2(t, Q_t)],$$

we obtain the following equation:

$$\frac{dy(t)}{dt} = \beta U + \frac{\gamma}{s} \left[t - \int_{t-s}^t y(q) dq + \text{Var}^* \left(\sum_{t-s \leq q \leq t} x_q \right) + \left(E^* \left(\sum_{t-s \leq q \leq t} x_q \right) \right)^2 + (\lambda - r)^2 s^2 - 2 E^* \left(\sum_{t-s \leq q \leq t} x_q \right) (\lambda - r)s \right] - (\gamma + \beta)y(t) \quad \text{---- (2)}$$

$$= \beta U + \gamma\mu(\sigma^2 + \delta) + \gamma\mu^2 s \sigma^2 - 2\gamma\mu s \sigma(\lambda - r) + \gamma s(\lambda - r)^2 + \frac{\gamma}{s} \int_{t-s}^t y(q) dq - (\gamma + \beta)y(t)$$

From this equation, if $\sigma = 1$ and $\delta = 0$, the compound Poisson process is just a Poisson process, and then (2) becomes

$$\frac{dy(t)}{dt} = \beta U + \gamma\mu + \gamma\mu^2 s - 2\gamma\mu s(\lambda - r) + \gamma s(\lambda - r)^2 + \frac{\gamma}{s} \int_{t-s}^t y(q) dq - (\gamma + \beta)y(t) \quad \text{----- (3)}$$

Equation (2) has a stationary solution

$$y(t) \equiv Z = U + \frac{[\gamma\mu(\sigma^2 + \delta) + \gamma\mu^2 s \sigma^2 - 2\gamma\mu s \sigma(\lambda - r) + \gamma s(\lambda - r)^2]}{\beta} \quad \text{----- (4)}$$

$$= U + D .$$

Where $D = \frac{\gamma}{\beta} [\mu(\sigma^2 + \delta) + s(\mu\sigma - \lambda + r)^2]$

The expectation of the realized variance for compound Poisson jump in stationary regime under risk neutral measure P^* is equal to

$$F_{\text{var}} = E^*[y] = \frac{1}{W} \int_0^W y(t) dt = U + D \quad \text{----- (5)}$$

In general case, we substitute $y(t) = Z + Ce^{-\tau t}$ in (2) where X is defined in (4).

Then the characteristic equation for τ is

$$\tau = \frac{\gamma}{\tau s} (1 - e^{-\tau s}) - (\gamma + \beta) \quad \text{----- (6)}$$

Therefore, the only solution to this equation is $\tau \approx -\beta$, and by the same method, we have,

$$y(t) = Z + Ce^{-\beta t} = U + D + Ce^{-\beta t}, \tag{7}$$

$$C = \rho_0^2 - U - D. \tag{8}$$

Hence, the expectation of the realized variance under risk-neutral measure P* is equal to

$$F_{\text{var}} = E^*[y] = \frac{1}{W} \int_0^W y(t) dt \approx U + D + C \frac{1 - e^{-\beta t}}{\beta t}, \tag{9}$$

Where C is given by (8)

Of course, (9) can also be written as

$$F_{\text{var}} \approx Z + (\rho_0^2 - Z) \frac{1 - e^{-\beta t}}{\beta t} \tag{10}$$

Where Z is given by (4)

Remark: It is interesting to see that when $s = 0$, which means there is no delay in the model, we have that

$$E^*[y] \approx \frac{1 - e^{-\beta t}}{\beta t} \left(\rho_0^2 - U - \frac{\gamma\mu(\sigma^2 + \delta)}{\beta} \right) + U + \frac{\gamma\mu(\sigma^2 + \delta)}{\beta}. \tag{11}$$

2.2. General Case

In the previous section, we assume that the mean value and variance of the jump size x_t , in the compound Poisson process are constants. Now we consider a more general case in which they are deterministic functions. The approach used in this section is different from the previous ones, which is a more general method and can be applied to derive the same formulae in the previous simple cases.

The stochastic model can be defined by

$$\frac{d\rho^2(t, Q_t)}{dt} = \beta U + \frac{\gamma}{s} \left[\int_{t-s}^t \rho(q, Q_q) dK^*(q) + \int_{t-s}^t x_q dM(q) - (\lambda - r)s \right]^2 - (\gamma + \beta)\rho^2(t, Q_t) \tag{12}$$

Where $K^*(t)$ is a Brownian motion, $M(t)$ is a Poisson process with intensity μ , and x_t is the jump size at time t . We assume that $E[x_t] = A(t)$, $E[x_q x_t] = C(q, t)$, $q < t$, and $E[x_t^2] = B(t) = C(t, t)$, where $A(t)$, $B(t)$ and $C(q, t)$ are all deterministic functions. Note that the change of measure does not change the Poisson intensity μ and the distribution of jump size x_t , since they are independent of the Brownian motion.

Let $y(t) = E^*[\rho^2(t, Q_t)]$ and take the expectation under risk-neutral probability P^* on both sides of (12).

Noting that the Brownian motion and the Poisson process are independent, we obtain the following equation:

$$\frac{dy(t)}{dt} = \beta U + \frac{\gamma}{s} \left[\int_{t-s}^t y(q) dq + E^* \left(\int_{t-s}^t x_q dM(q) \right)^2 + (\lambda - r)^2 s^2 - 2 E^* \left(\int_{t-s}^t x_q dM(q) \right) (\lambda - r)s \right] - (\gamma + \beta)y(t). \tag{13}$$

In order to compute the two expectations in this equation, we first introduce two lemmas as follows [5].

Lemma2.3. Define $I(t) = \int_0^t x_q d(M(q) - \mu q)$; ; then $I(t)$ is a martingale and $EI(t) = 0$.

Lemma2.4. Define $I(t) = \int_0^t x_q d(M(q) - \mu q)$; then $EI^2(t) = \mu E \int_0^t x_q^2 dq$.

Therefore,

$$E^* \left(\int_{t-s}^t x_q dM(q) \right) = E^* \left(\int_{t-s}^t x_q d(M(q) - \mu q) \right) + E^* \left(\int_{t-s}^t x_q d\mu q \right)$$

$$= \mu E^* \left(\int_{t-s}^t x_q dq \right) \tag{14}$$

$$= \mu \int_{t-s}^t A(q) dq ,$$

$$\begin{aligned} E^* \left(\int_{t-s}^t x_q dM(q) \right)^2 &= E^* \left(\int_{t-s}^t x_q d(M(q) - \mu q) \right)^2 + E^* \left(\int_{t-s}^t x_q d\mu q \right)^2 \\ &= \mu \int_{t-s}^t E^* x_q^2 dq + \mu^2 E^* \left(\int_{t-s}^t x_q dq \right)^2 \\ &= \mu \int_{t-s}^t B(q) dq + \mu^2 E^* \left(\int_{t-s}^t x_q dq \right)^2 . \end{aligned} \tag{15}$$

To compute $E^* \left(\int_{t-s}^t x_q dq \right)^2$, we take the derivative of $\left(\int_{t-s}^t x_q dq \right)^2$ and then integrate it:

$$\begin{aligned} d \left(\int_{t-s}^t x_q dq \right)^2 &= 2 \int_{t-s}^t x_q dq (x_t - x_{t-s}) dt \\ &= 2 \int_{t-s}^t (x_q x_t - x_q x_{t-s}) dq dt , \end{aligned} \tag{16}$$

$$\begin{aligned} \left(\int_{t-s}^t x_q dq \right)^2 &= 2 \int_0^t \int_{v-s}^v (x_q x_v - x_q x_{v-s}) dq dv + \left(\int_{-s}^0 x_q dq \right)^2 \\ &= 2 \int_0^t \int_{v-s}^v (x_q x_v - x_q x_{v-s}) dq dv + \int_{-s-s}^0 \int_0^0 x_q x_v dq dv . \end{aligned}$$

Now take the expectation under risk-neutral probability, we have that

$$\begin{aligned} E^* \left(\int_{t-s}^t x_q dq \right)^2 &= 2 \int_0^t \int_{v-s}^v (C(q, v) - C(q, v-s)) dq dv + \int_{-s-s}^0 \int_0^0 C(q, v) dq dv \\ &= F(t, s) + H , \end{aligned} \tag{17}$$

Where $F(t, s) = 2 \int_0^t \int_{v-s}^v (C(q, v) - C(q, v-s)) dq dv$

and $H = \int_{-s-s}^0 \int_0^0 C(q, v) dq dv .$

Taking into account (14), (15), and (17), equation (13) becomes

$$\frac{dy(t)}{dt} = \beta U + \frac{\gamma}{s} \left[\int_{t-s}^t y(q) dq + \mu \int_{t-s}^t B(q) dq + \mu^2 (F(t, s) + H) + (\lambda - r)^2 s^2 - 2\mu s(\lambda - r) \int_{t-s}^t A(q) dq \right] - (\gamma + \beta) y(t). \tag{18}$$

We can check that (2) is a special case of (18) with

$A(t) = E[x_t] = \sigma, B(t) = E[x_t^2] = Var[x_t] + (E[x_t])^2 = \delta + \sigma^2$, and

$C(q, t) = E[x_q x_t] = E[x_q]E[x_t] = \sigma^2$.

To get the expectation of the realized variance in the risk-neutral world $E^*[y]$, we have to find a solution to (18) a nonhomogeneous integrodifferential equation with delay.

After taking the first derivative of this equation, we obtain

$$y''(t) = \frac{\gamma}{s}[y(t) - y(t-s)] - (\gamma + \beta)y'(t) + h(t,s), \tag{19}$$

Where $h(t,s) = \left(\frac{\gamma}{s}\right) \left[\mu(B(t) - B(t-s)) + \mu^2 F'(t,s) - 2\mu s(\lambda - r)(A(t) - A(t-s)) \right]$.

This is a second – order delay differential equation with constant coefficients, and so Laplace transform can be applied to find its solution with initial condition $y(t) = \rho(t, Q_t), t \in [-s, 0]$, which is already known [8], [19].

Let us denote the Laplace transform of a function $f(t)$ as

$$L\{f(t)\} = \int_0^\infty f(t)e^{-qt} dt \tag{20}$$

and do the Laplace transform for (19)

$$L\{y''(t)\} = \frac{\gamma}{s}[L\{y(t)\} - L\{y(t-s)\}] - (\gamma + \beta)L\{y'(t)\} + L\{h(t,s)\} \tag{21}$$

By change of variable and the property of Laplace transform, 19 yields

$$\left[q^2 + (\gamma + \beta)q - \frac{\gamma}{s}(1 - e^{-qs}) \right] L\{y(t)\} = y'(0) + (q + \gamma + \beta)y(0) - \frac{\gamma}{s}e^{-qs} \int_{-s}^0 y(t)e^{-qt} dt + L\{h(t,s)\}. \tag{22}$$

The characteristic function of 17 is

$$C(q) = q^2 + (\gamma + \beta)q - \frac{\gamma}{s}(1 - e^{-qs}) \approx q^2 + \beta q. \tag{23}$$

Therefore,

$$L\{y(t)\} = C^{-1}(q) \left[y'(0) + (q + \gamma + \beta)y(0) - \frac{\gamma}{s}e^{-qs} \int_{-s}^0 y(t)e^{-qt} dt + L\{h(t,s)\} \right]. \tag{24}$$

Applying the inverse transform 19, we have that

$$y(t) \approx \frac{1 - e^{-\beta t}}{\beta} y'(0) + \left[\frac{\gamma}{\beta}(1 - e^{-\beta t}) + 1 \right] y(0) - \frac{\gamma}{\beta s} \int_{-s}^0 y(q)[1 - e^{-\beta(t-q-s)}]dq + \frac{1}{\beta} \int_0^t h(q,s)[1 - e^{-\beta(t-q)}]dq + C. \tag{25}$$

By the initial condition,

$$C = \frac{\gamma}{\beta s} \int_{-s}^0 y(q)[1 - e^{-\beta(q+s)}]dq. \tag{26}$$

Hence, the expectation of the realized variance for compound Poisson jump under risk-neutral measure P^* can be obtained by

$$F_{var} = E^*[y] = \frac{1}{W} \int_0^W y(t)dt, \tag{27}$$

III. EXAMPLE

The Fig. (1) shows the GIP responses after oral glucose tended to be lower in the type-2 diabetic patients as defined in [13]. With high rate of GIP infusion, a greater insulin secretary response was elicited in normal subjects, but in type-2 diabetic even the pharmacological concentrations of GIP reached only marginally stimulated insulin secretion. Whereas in normal subjects the glucose infusion had to be increased owing to GIP-stimulated insulin release, the glucose infusion rate hardly had to be increased in type-2 diabetic patients.

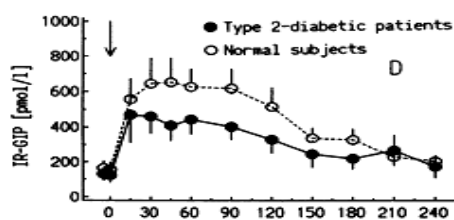


Fig. (1)

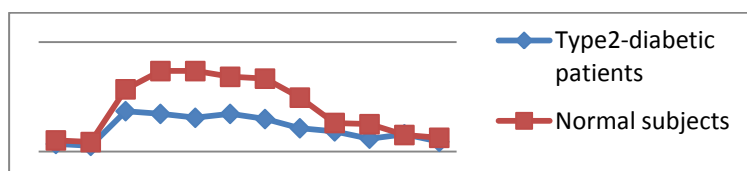


Fig. (2)

IV. CONCLUSION

Evaluation of the GIP response after oral glucose tended to be lower in the type-2 diabetic patients than normal subjects fitted with the characteristic equation obtained by applying Laplace transform to the second order delay differential equation with jump represented by compound Poisson process is graphically shown in Fig(2). The result coincides with the mathematical and medical report.

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