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Longer Fasting After Rybelsus Administration Contributes Higher Efficacy

Miki K[1], Bando H[1,2,3,*], Hayashi K[1], Dohi A[3] and Kamoto A[1]

[1]*Hayashi Hospital, Tokushima, Japan*
[2]*Tokushima University / Medical Research, Japan*
[3]*Japan Low Carbohydrate Diet Promotion Association (JLCDPA), Kyoto, Japan*

[*]**Corresponding author:** Bando H, Tokushima University, Medical Research, Japan; E-mail: pianomed@bronze.ocn.ne.jp

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Abstract

Recent pharmacological topic for diabetes includes clinical application of Glucagon-like peptide 1 receptor agonists (GLP-1 RAs). Among them, oral semaglutide (Rybelsus) has been developed as the first oral form of GLP-1RA by useful application of sodium N-(8-[2-hydroxybenzoyl] amino) caprylate (SNAC). Semaglutide concentration in the blood was compared when fasting time period after Rybelsus administration would be 15, 30, 60 and 120 minutes. As a result, the concentration ratio after 4 hours was 1.00, 1.67, 2.60 and 3.06, respectively. Authors have experienced a diabetic case of remarkable efficacy as HbA1c -1.4% and weight -5kg, who kept 3-4 hours fasting after Rybelsus intake.

Keywords: Glucagon-like peptide 1 receptor agonists (GLP-1 RAs); Oral semaglutide (Rybelsus); Sodium N-(8-[2-hydroxybenzoyl] amino) caprylate (SNAC); Fasting time period

Introduction

Non-communicable diseases (NCDs) have been increasing across the world [1]. Among them, type 2 diabetes mellitus (T2DM) has become crucial medical and social problems. Adequate treatment for T2DM includes oral hypoglycemic agents (OHAs), insulin and other injectable agents such as effective Glucagon-like peptide 1 receptor agonists (GLP-1 RAs) [2]. GLP-1Ras have recently evolved rapidly for beneficial efficacy including promoting insulin secretion, decreasing glucagon secretion, reducing hunger and enhancing satiety. As latest novel development, oral semaglutide (Rybelsus) has been introduced to actual practice [3]. This article introduces the points about the basic clinical features of Rybelsus [4].

GLP-1RA has been evaluated as second line treatment for T2DM and also for possible agent for obesity [5]. From cardiovascular (CV) outcome results, it was proved to show reduction of various CV risk for case with established CV problems. This is firstly approved as oral GLP-1RA, and this peptidic agent would be considered as quintessential for actual treatment for T2DM. Thus, in modern clinical practice, drugs that are beneficial for diabetes, obesity, and cardiovascular disease are significant, and oral drugs are considered to be more useful than injectable drugs. Several types of GLP-1RA have been observed. Among them, only semaglutide has injectable and oral types [6]. Oral semaglutide is the first oral agent of GLP-1RA as brand name Rybelsus [7]. Regarding the molecular structure, semaglutide is 94% homologous to human GLP-1, which has some significant changes to achieve a longer half-life of about 1 week [8,9].

Oral semaglutide was developed as oral agent by the combination of absorption enhancer, that is known as sodium N-(8-[2-hydroxybenzoyl]amino) caprylate (SNAC) [10,11]. SNAC will form a non-covalent bondage with GLP-1 for a concentration dependent manner. It can elevate lipophilicity degree and increase transcellular absorption of the agent through epithelium of the stomach mucosa [11,12]. Furthermore, it can act as locally pH buffer, increase soluble degree, and protect the degradation of the agent. The activity of SNAC is reversible and short, and then it easily separates from semaglutide on reaching the bloodstream. As semaglutide shows well-defined pharmacokinetics, it will be actually absorbed completely in the stomach. The blood concentration reaches maximum approximately 15-35 min after

ingestion [10]. Rybelsus is novel agent of oral semaglutide, which is one of human GLP-1RA. Two kinds of investigation were conducted including food influence before taking agent and fasting time period after taking the agent [13]. Regarding food-influence exam, 78 case were divided to 3 groups, which are i) fed 30-min pre-dose, ii) fasting overnight and 4-hour post-dose, iii) reference fasting overnight and 30-min-post-dose. As to dosing exam, 161 case were randomized for 8 groups including fasting time duration post-dose 15-30-60-120 minutes with water 50 or 120 cc (Table 1,2).

Table 1 Semaglutide concentration for fasting and reference

protocol	Seamaglutide conc. 2 hours (nmol/L)	Seamaglutide conc. 4 hours (nmol/L)	Seamaglutide conc. 24 hours (nmol/L)		Ratio of conc. 2 hours	Ratio of conc. 4 hours	Ratio of conc. 24 hours
Fasting	18.4	18.6	14.5		1.44	1.50	1.41
Reference	12.8	12.4	10.3		1.00	1.00	1.00

Time (2,4 and 24 hours) shows the period from oral adminstration.

Table 2 Semaglutide concentration for fasting time

Fasting time (min)	Seamaglutide conc. 2 hours (nmol/L)	Seamaglutide conc. 4 hours (nmol/L)	Seamaglutide conc. 24 hours (nmol/L)		Ratio of conc. 2 hours	Ratio of conc. 4 hours	Ratio of conc. 24 hours
15	8.7	8.6	7.4		1.00	1.00	1.00
30	14.6	14.4	12.3		1.68	1.67	1.66
60	22.5	22.4	18.2		2.59	2.60	2.46
120	28	26.3	22.5		3.22	3.06	3.04

Fasting time means the continuation of fasting after oral adminstration of semaglutide.

Among various results of the study, meaningful data was summarized and measured from related figures [13]. Semaglutide concentration in the blood was compared between fasting situations and non-fasting with fed before taking medicine (reference). As a result, the blood concentration showed 1.41-1.50 times higher in fasting condition. Semaglutide concentration in the blood was compared when fasting time period after taking medicine as 15-120 min. When the standard level is set 1.00 at 15 min, concentration ratio for 4 hours would be elevated 1.67, 2.60 and 3.06 times in 30, 60 and 120 min, respectively. Furthermore, water amount of 50ml and 120ml revealed no significant changes. These data would indicate stable beneficial effect of combined semaglutide and SNAC in the actual clinical practice. Consequently, the standard method of intake for Rybelsus was decided as i) taking medicine just after waking up in the morning for fasting condition, ii) at least 30 min fasting time period is necessary after taking the agent, iii) water intake is between 50 to 120 mL [14]. These data for recommended amount were from previous study of phase 3 clinical trials [15,16].

Author's diabetic research group has experienced a case with T2DM, which had remarkable improvement by Rybelsus for 3mg, 7mg and 14mg in every month. The changes in HbA1c and weight were 8.5% to 7.1% and 96kg to 91kg for 3 months [17]. The case has continued regular lifestyle habit with no breakfast and then fasting time was 3-4 hours after taking Rybelsus. This situation may be involved in the satisfactory result. When fasting period is longer, clinical effect becomes higher. Rybelsus will provide broad benefit for patients, physicians and medical staffs because of clinically useful and convenient treatment method [18,19]. Consequently, primary care physician can provide adequate management for maintaining diabetic better control of lots of patients with T2DM [2]. This article will hopefully give a impressive key to health and happiness to people.

Conflict of Interest

The authors declare no conflict of interest.

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