Investigative Study of Stress Effect on Control of Blood Glucose Level

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***Abstract* —Stress hormones such as cortisol, glucagon, epinephrine and epinephrine play an important role in affecting the blood glucose level in human body. Based on previous studies, increased stress hormones have caused the blood glucose level to elevate. A sudden increase of blood glucose level in patients body may lead to the occurrence of hyperglycemia when the blood glucose level is above the normal baseline. Thus, the objectives of this study are to determine the effect of stress on the control of blood glucose level by simulating an algorithm to control the blood glucose level by using a Rudimentary model. The simulation study was carried out by using MATLAB on virtual patient through the application of *in-silico* method. However, in this paper attention was focused solely on cortisol only and other stress hormones were neglected due to limited data. In conclusion, blood glucose level can be controlled through the simulation.**

***Keywords*—blood glucose level, mathematical model, stress hormones**

I. INTRODUCTION

Hyperglycemia and stress are usually related to each other as both involve with glucose levels. Hyperglycemia is a body condition when the blood sugar level in the body is above the normal range. Commonly, when human body experiences stress it will send a signal to the endocrine system to secrete hormones such as cortisol and glucagon. These secretions of hormones usually under the control of hypothalamic pituitary pituitary axis (Rai, Cohen, & Venkatesh, 2005). When these hormones enter the bloodstream, it can inhibit the function of insulin and lead to an increase of breathing rate, speed up heart rate and increase the blood pressure. Thus, the secretion of these hormones can cause more production of glucose. Thus, prolonged stress can cause the glucose to build up in the body which can lead to the hyperglycemia. Therefore, admitted patients with stress are more likely to suffer from hyperglycemia which results in an elevation on their blood glucose level. This condition is stress. Therefore, a significant increase in blood glucose level may lead to other serious illness such as diabetes mellitus (DM). However, not all patients with hyperglycemia are diagnosed with diabetes mellitus. It could be due to undiagnosed DM or comes from stress (Chang, Huang, Liu, Chen, & Hsieh, 2018). Hence, patients that are diagnosed with DM may not experience hyperglycemia but it could lead to other health problems.

Hyperglycemia is the term used when the blood glucose level is greater than 6.0 mmol/L in the patient body and it occurs if the body develops a resistance toward insulin or there is not enough insulin released by the pancreas in the bloodstream. This can bring a negative impact as it increases the risk of mortality of patients (Pérez-Calatayud et al., 2017). Stress can be considered as one of the significant factors that can affect the blood glucose level in human bodies (Mitra, 2008). In this paper, a mathematical model introduced by Rios-Guzman is used for the simulation study in which it was carried out by using MATLAB (Rios-guzman, 2017). Application of in-silico method was performed during the simulation work. For this simulation, only one stress hormone that is focused which is cortisol. Cortisol is a type of steroid hormone that regulates both processes of the metabolism and immune response. However, it has a very significant role when responded to stress.

II. METHODOLOGY

2.1 Data collection and extraction

All data required during the simulation work were obtained from the previous study by Scheur and Bondy (1957) (Bondy & Scheuer, 1957). The data obtained include gender, age and weight. All subjects were healthy male medical students with no history of diabetic and any serious illnesses. Throughout the experiment, the subjects were ambulatory and were on a normal diet. One subject was chosen for the simulation work and his data was extracted.

2.2 Model selection for the simulation study

The Rudimentary model introduced by Rios-Guzman in 2017 was chosen as the mathematical model for the simulation study. It has a multivariate function that can establish the alteration in blood glucose concentration prior to the elevation in the stress hormones above baseline. This model is developed to determine how four stress hormones (cortisol, glucagon, epinephrine, and norepinephrine) can affect plasma blood glucose concentration (Rios-guzman, 2017). The model equation is represented in equation (1) as follows:

$$G(c,\alpha,\alpha,e)=G_{baseline}\left[1+\frac{0.2\,c}{6\,mg\,(m^{-2}h^{-1})}+\frac{p_1\alpha}{4\,ng\,(kg^{-1}\min^{-1})}+\frac{p_2 e}{0.6\,\mu g\,(m^{-2}\min^{-1})}+\frac{p_3 n}{0.8\,\mu g\,(m^{-2}\min^{-1})}\right] \quad (1)$$

Equation (1) above represents the stress hormones that are present above normal levels with variables of *c*, *a*, *e* and *n* which *c* represent cortisol hormones in mg ($m^{-2}h^{-1}$), *a* is glucagon hormone in ng ($kg^{-1}min^{-1}$), *e* is epinephrine hormone in µg ($m^{-2}min^{-1}$) and *n* is referring to norepinephrine hormone in µg ($m^{-2}min^{-1}$). Meanwhile, *G* indicates the glucose in either mg/dL or mmol/L. Also, $G_{baseline}$ acts as a constant parameter that represents a normal level of plasma glucose of a patient without any abnormal stress. According to Rios-Guzman study's, Equation (2) should be either zero or positive since all variables are referring to the amount of chemical.

$$G(c,\alpha,\alpha,e)=G_{baseline}\left[1+\frac{0.2\,c}{6\,mg\,(m^{-2}h^{-1})}+\frac{0.133\,\alpha}{4\,ng\,(kg^{-1}\min^{-1})}+\frac{0.133\,e}{0.6\,\mu g\,(m^{-2}\min^{-1})}+\frac{0.133\,n}{0.8\,\mu g\,(m^{-2}\min^{-1})}\right] \quad (2)$$

However, this model is said only applicable for a nondiabetic individual since it assumes a constant baseline glucose. The equation is focuses solely more on cortisol compared to other stress hormones. This is prior to only cortisol contributes in increased glucose concentration and its function is more accurate to the data. Due to excess input of artificial amount of cortisol, the estimation of blood glucose level is achieved by using the model. Thus, restrictions such as limited data, the simplicity of the model and limited to nondiabetic have become issues in this study (Rios-guzman, 2017).

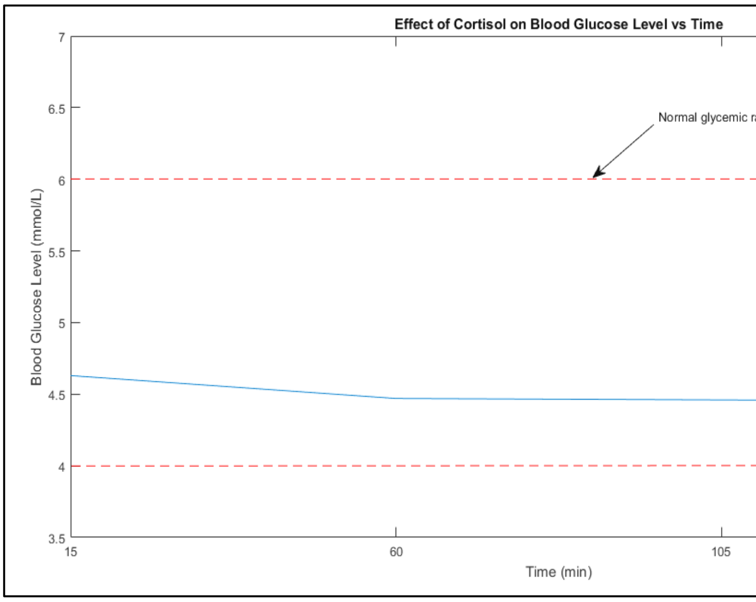


Fig. 1: Blood glucose level of a subject at 15 minutes until 1

III. RESULTS AND DISCUSSION

Figure 1 demonstrates the effect of cortisol on blood glucose level (BGL) of a subject at time 15 minutes until 150 minutes by using the Rudimentary model. The subject is a healthy young adult man and his weight is 72.8 kg. The subject had no history of major illness and was stated ambulatory (Bondy & Scheuer, 1957). From Figure 1, the blood glucose level decreased slightly from 4.63 mmol/L at the first 15 minutes to 4.45 mmol/L at 150 minutes. At 15 minutes, the cortisol level of the subject is 1.256 mg/h and keeps decreasing until 0.0156 mg/h at 150 minutes. During the first infusion of cortisol, it was assumed that cortisol was no longer secreted by the adrenal gland, thus, it was present relatively very small in the body. According to Gelfand et al studies (Gelfand, Matthews, Bier, & Sherwin, 1984), a smaller rise in blood glucose can be caused by the infusion cortisol alone.

Over a period of time, the level of cortisol in a subject started to decrease, thus maintaining the blood glucose level within the safe range. At the time between 15 minutes to 60 minutes, there is a drop in blood glucose level prior to a sudden decrease in cortisol level and after 60 minutes the blood glucose level starts to become constant.

Meanwhile, Figure 2 shows the effect of cortisol on blood glucose level in a subject at 150 minutes until 420 minutes. From Figure 2, it can be concluded that the blood glucose level has been constant over time. This is due to a very small difference in cortisol level in the subject body. Compared to the first infusion at time 15 minutes, the cortisol levels in the body gradually decrease with time prior to the disappearance of cortisol. The elevation of blood glucose levels depends on the level of cortisol that is present in the body. Therefore, increased cortisol over the long term may cause a sudden rise in glucose production which eventually could lead to an increase in blood glucose levels.

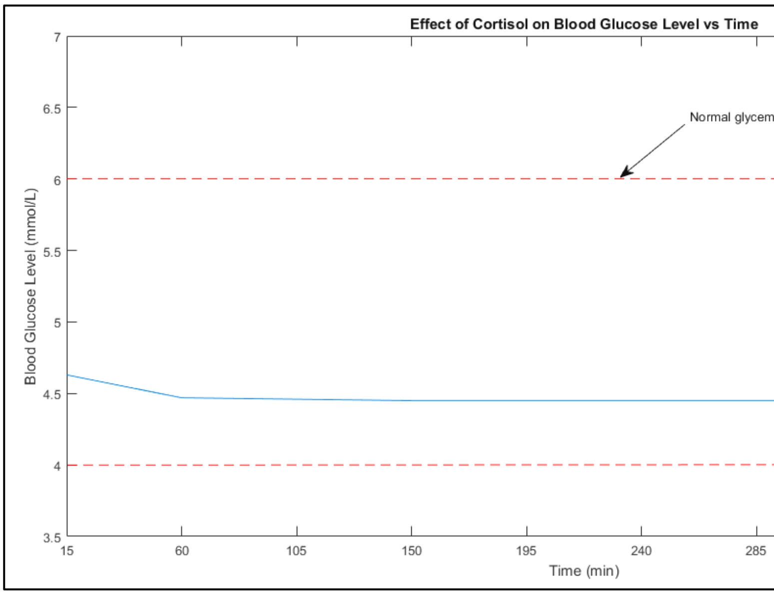
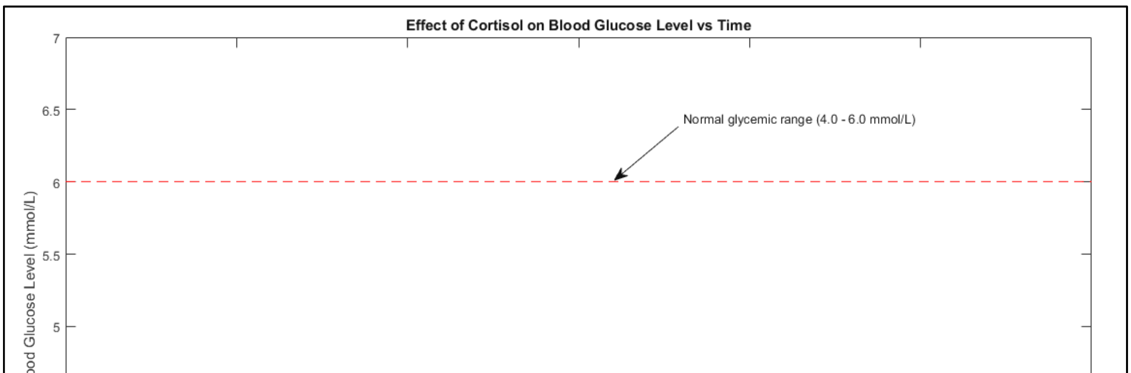


Fig. 3: Combine blood glucose level of a subject at 15 minutes



Based on the previous study, infusion of cortisol is likely to cause a drop in blood glucose level in a normal individual. However, infusion of cortisol in diabetic patients may have different outcomes as it promotes an elevation in plasma glucose (Shamoon, Hendler, & Sherwin, 1980). The effect of cortisol on blood glucose levels of a chosen subject in one experiment can be shown in Figure 3. This figure shows the overall blood glucose level of a subject upon receiving the infusion of cortisol. The blood glucose levels dropped slightly at 15 minutes after the infusion of cortisol. However, the blood glucose level for this subject remained within the normal range of blood sugar level which is between 4.0 to 6.0 mmol/L, thereafter.

Thus, the subject does not experience any hypoglycemia or hyperglycemia. Therefore, to study the effect of stress on blood glucose level, cortisol which is the steroid hormone is injected into the subject body to imitate the releasing of cortisol hormone by the adrenal gland when the human body experiences stress. Releasing of cortisol causes the hormone to increase the breathing rate and speed up the heart rate of an individual. Therefore, the infusion rate of the cortisol is important to be controlled to regulate the blood glucose level. However, these consequences might increase the production of glucose in the body which can lead to high blood glucose level (Mitra, 2008).

In this experiment, MATLAB was used in the simulation of the mathematical modeling by using the Rudimentary model. The model proposed involved four types of stress hormones namely; cortisol, glucagon, epinephrine and norepinephrine in which all the information were obtained from Gelfand et al. (Gelfand et al., 1984). Eventually, cortisol was the only stress hormone believed to have an effect on glucose production since its function in the model was the only one which demonstrated an accurate data. Cortisol concentration was more related as it affects the plasma glucose compared to other stress hormones such as glucagon and epinephrine concentrations (O'Neill, Davies, Fullerton, & Bennett, 2011). As for other hormones, they are considered as negligible due to lack of knowledge and study. Prior to the limitation of patients data related to the stress hormone, it is quite difficult to prove the significant effect of stress hormone in blood glucose level.

IV. CONCLUSION

Simulation work of the chosen mathematical modeling was performed to determine the effect of stress hormones on the control of blood glucose level. From the simulation, it was found that the elevation of blood glucose level was dependent on the infusion rate of the stress hormone. Therefore, the objectives of the study of stress effect on the control of blood glucose level and to simulate an algorithm to control the blood glucose level by using Rudimentary model were achieved. The focused was only on cortisol hormones during the simulation work because of the availability of data. After the infusion of cortisol hormones, the blood glucose level of the subject gradually decreasing from 4.63 mmol/L to 4.44 mmol/L after the first 15 minutes of infusion time. This is because the cortisol level in the body started to decrease with time due to the disappearance of cortisol. However, the blood glucose level of the subject remained within the normal range for glucose level, thus, the subject does not have hyperglycemia or hypoglycemia. Therefore, the rise in blood glucose level can be affected by the cortisol level that presents in the body.

From the simulation conducted, the stress disturbance on the blood glucose level can be monitored in the subject by the infusion of stress hormones. This is to imitate the secretion of hormones by the adrenal gland when the subject is in stress. Hence, the infusion rate of stress hormones can determine the alterations in patient blood glucose level. However, due to some limitations such as limited experimental data and study make it hard to verify the relationship between the stress hormone and blood glucose level. It is recommended that in future, this existing model can be improved or be fused with other models to determine the importance of stress hormones in blood glucose level.

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