Microscope-Study on the Relationship between Islet Cell Antibody and Cell Function in Children with Diabetes Mellitus

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Abstract: The purpose of this study was to investigate the relationship between islet cell antibodies and cell function in children with diabetes mellitus. Objective: To investigate the effects of insulin resistance and B-cell failure on blood glucose levels in children with diabetes, so as to provide theoretical basis for rational choice of hypoglycemic drugs and effective control of blood glucose. Methods: 81 children with diabetes mellitus were tested after eating 80g instant noodles for 0, 30, 60, 120 min of blood glucose and insulin. All cases were divided into group A (FPG < 8.92mmol /L) and group B (FPG≥ 8.89mmol /L) according to the fasting blood glucose (FFG) level. The contribution of cell function and insulin resistance to the blood glucose level was assessed in both groups. Results: The sensitivity of insulin and true insulin in group B was 65.5% and 64% of that in group A. After adjusting the effect of insulin resistance, the cell function in group B was only 1/5-1/7 of that in group A. Insulin swabs and cell function, measured by insulin, contributed half to glucose levels in group A, while cell function contributed eight times as much to glucose levels as insulin resistance in group B. Beta cell secretory function, measured with true insulin, explained 43% of the change in blood glucose in group A, 55% of the change in blood glucose in group B, and insulin sensitivity explained 13% of the change in group A, and 5.9% of the change in group B. Conclusion: Insulin resistance and cell failure were more serious in the group with higher fasting glucose level (≥ 8.89mmol /L), and the hyperglycemia was mainly caused by cell failure, suggesting that the combination of insulin sensitizer and insulin secretory agent was beneficial in the initial treatment.

Keywords: Pediatric Diabetes, Islet Cell Antibody, Beta Cell Function
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The prevalence of obesity is on the rise worldwide due to changes in diet and the improvement of living standards. In 2005, about 1.3 billion people were overweight, of whom nearly 400 million were obese. In 2015, the number of overweight and obese people increased to about 2.5 billion and 800 million, respectively. According to statistics, the prevalence of overweight and obesity among Chinese adults in 2010 was 27.6 percent and 5.2 percent. Previous studies have found that obesity is associated with insulin resistance, islet dysfunction, and diabetes in children. Obesity is often associated with hyperinsulinemia, and the risk of developing diabetes in children is 3 times that of people of normal weight. Insulin resistance and impaired secretion of pancreatic beta cells are the main risk factors for diabetes in children, so obesity may play an important role in insulin resistance and impaired secretion of pancreatic beta cells.

With the improvement of living standards, the incidence of diabetes is gradually increasing. It is estimated that the number of diabetes patients worldwide in 2030 will be three times that in 2000 [1]. The change of islet function plays an important role in the occurrence and development of childhood diabetes. Previous studies have shown that obese patients have significant dyslipidemia, which is the result of insulin resistance, aggravating the degree of IR in patients and causing insufficient

insulin secretion. Based on the characteristics of chronic delay, many complications, high disability and mortality of pediatric diabetes, it is of great significance to study its influencing factors and change rules [2].

Tushuizen et al. found no association between pancreatic fat and islet cells. The differences of these results may be related to the study population, glucose level in vivo, determination method of pancreatic fat and degree of pancreatic fat infiltration [3]. Wong et al. found that the correlation remained after adjusting for BMI, liver fat and other confounding factors [4]. In addition, some researchers isolated the islets of obese rats induced by high fat, and found that the expression of insulin receptor and receptor substrate proteins in the insulin transduction pathway in the pancreas decreased, and insulin signal transduction was blocked, resulting in insulin resistance.

Abnormal insulin secretion is an important factor in the development of diabetes mellitus. Studies have shown that early in the onset of childhood diabetes, there has been islet cell damage. Fasting insulin concentration increases, insulin resistance levels gradually increase, insulin sensitivity decreases, blood lipid levels increase, causing the compensated secretion of more insulin by the beta cells of the pancreas. The results of this study showed that the sensitivity of insulin and true insulin in group B was 65.5% and 64% of that in group A. After adjusting the effect of insulin resistance, the cell function in group B was only 1/5-1/7 of that in group A.

RELATIONSHIP BETWEEN ISLET CELL ANTIBODY AND CELL FUNCTION IN CHILDREN WITH DIABETES MELLITUS

Normal Insulin Secretion Rhythm

In normal bodies, insulin cells are produced in two phases when stimulated by glucose. According to the glucose clamp test, insulin stored in cell granulocyte was rapidly released into the blood under the stimulation of continuous high glucose. The increase of plasma insulin level reached its peak in 3-5 minutes, and then gradually decreased until it returned to the baseline level. It was secreted as a sharp peak for about 10 minutes [5]. The amount of insulin released at this time accounts for 2 to 3 percent of the secretion of beta cells in the pancreas. Known as the first phase of insulin secretion, also known as the rapid secretion phase. It mainly reflects the reserve function of islet cells and the ability to respond to acute glucose stimulation. The main effect is to inhibit endogenous glucose production, inhibit glucagon production, reduce fatty decomposition and free fatty acid release, and accelerate the response of insulin-sensitive tissues. After 10-20 minutes of glucose stimulation, insulin secretion gradually increases again, and peaks again 2-3 hours later. Insulin decreases gradually until blood glucose returns to normal [6]. At this time, part of the insulin comes from the secretory particles stored in the original beta cells, and the rest comes from the newly synthesized insulin, which accounts for about 20% of the secretion of the beta cells. This is called the second secretory phase of insulin, also known as the delayed secretory phase. It mainly reflects the synthesis and secretion function of cells after glucose stimulation, and has certain effect on inhibiting glucagon secretion. Under normal conditions, phase II secretion remains high as long as blood glucose does not return to baseline. When the body is chronically stimulated by hyperglycemia, the beta cell load of the pancreas increases, releasing large amounts of unprocessed insulin precursors. If the first phase of insulin secretion is secreted earlier, the postprandial blood glucose is more likely to be maintained at a stable level. If the first phase secretion is slightly abnormal, postprandial blood glucose can be significantly affected [7]. Abnormal secretion of the first phase of insulin is an important risk factor for abnormal glucose tolerance. The lower the first phase secretion, the greater the likelihood of abnormal glucose tolerance, and is not affected by obesity and insulin resistance. With the prolongation of the course of diabetes, the function of islet decreased, and the secretion of insulin decreased gradually.

Measurement of Pancreatic Fat

Pathological biopsy is the gold standard for the quantification of pancreatic fat, which is quantified by observing whether there are fat droplets in pancreatic acinar cells or islet cells, and the content of adipose tissue in pancreatic parenchyma, but there is still no uniform standard. According to the proportion of interlobular fat cells and interlobular fat cells under microscope, pancreatic fat cells were classified into 6 grades: 0 (0-7%), 1 (8%-14%), 2 (15%-25%), 3 (26%-50%), 4 (51-75%), and 5 (>75%). In addition, some researchers also assessed the degree of pancreatic fat infiltration based on the

ratio of interlobular and interlobular adipocytes to total tissue, with 15% as the critical value [8]. However, histological examination is not the main method for the quantification of pancreatic fat due to its difficult operation and invasive examination [9]. At present, pancreatic fat deposition is measured by modern imaging techniques such as ultrasound, computed tomography and magnetic resonance imaging.

Ultrasound examination includes trans abdominal ultrasound and endoscopic ultrasound. Compared with liver, pancreas in trans abdominal ultrasound indicates fat deposition if there is relatively high echo, which is simple, convenient, non-invasive and economical. However, this method is less accurate, subject to subjective factors of the measurement, and pancreas is not always visible, especially in obese patients. Compared with trans abdominal ultrasound, endoscopic ultrasonography can not only observe the overall echo of the pancreas at close range, but also observe adjacent organs such as liver and spleen at the same time, which has been used to diagnose and evaluate pancreatic fat deposition [10]. However, it also depends on subjective factors of the operator. More importantly, pancreatic hyper echo is not a specific manifestation of pancreatic fat deposition. When the pancreas is fibrotic, it also presents a high signal. Therefore, ultrasonography is limited in the measurement of pancreatic fat.

Computed tomography (CT) is widely used to study all the organs in the abdomen. The CT value of adipose tissue is negative, so the density of the pancreas with adipose infiltration is lower than that of the normal pancreatic parenchyma. Compared with the spleen, fatty pancreas presented low signal. The difference between pancreatic and spleen attenuation on CT was used to quantify pancreatic fat. Although CT can quantify pancreatic fat, and is economical and convenient, it still has defects. Low-density masses or cysts of the pancreas sometimes show the same signal as adipose deposition on CT. In addition, the unclear boundary between adipose cells and pancreatic tissue may lead to inaccurate quantification [11].

Magnetic resonance imaging (MRI) is a safe, accurate and repeatable non-invasive tool for fat quantification. Adipose tissue has a characteristic short T1 and long T2 signal on MRI. MRI signal intensity of normal pancreatic parenchyma is similar to that of the liver, while the pancreatic margin after adipose infiltration is often accompanied by lobulated or nodular changes. Diffusion-weighted MRI can more clearly show the infiltrated adipose tissue in the pancreas. In recent years, with the development of MRI technology, it can not only observe whether the pancreas has fat infiltration, but also conduct quantitative analysis of the pancreatic fat. There are many methods to quantify pancreatic fat content by MRI, including chemical displacement-based methods, such as hydrogen proton magnetic resonance spectroscopy (1H-MRS), antiphase sequence and Dixon sequence based on water-lipid separation (including 2-point and 3-point Dixon sequences). Is currently the most commonly used 1 h - MRS, MRS, lipid, determination of main water peak and the area under the peak, it can use magnetic resonance phenomena and chemical shift effect for specific nuclei, compounds of quantitative analysis, is a kind of noninvasive study living tissue metabolism, biochemical change and compound the quantitative method, it is reliable in data analysis, space positioning accuracy, breathing exercises influence is small, high image signal-to-noise ratio, etc. However, recent studies have shown that 3-point Dixon technique (3P-Dixon) can more accurately quantify pancreatic fat than 1H-MRS. 3P-Dixon is a method to separate fat and water signals by using the inherent difference in the resonant frequency of water and fat. It can use the extra information to correct the phase error caused by the non-uniform magnetic field, so as to achieve high quality separation of water and fat. More importantly, it allows for correction of T2* decay in voxels. However, MRI is expensive and time-consuming, and is not commonly used in clinical practice.

Pathophysiological Mechanism of Pancreatic Fat Deposition

The pathophysiological mechanism of pancreatic fat deposition is still not fully understood, but most studies believe that it is related to necrosis of pancreatic acinar cells and infiltration of pancreatic fat and the increase in the number of adipose cells is the histological manifestation of pancreatic fat deposition [12]. Therefore, pathological tissue biopsy is the gold standard for its quantitative evaluation. However, because of its invasive nature, it is inconvenient to be widely used in clinical practice. At present, most of the studies used b-ultrasound, computed tomography (CT), hydrogen proton magnetic

resonance spectroscopy (1H-MRS) and other imaging methods to determine the content of pancreatic fat. B-ultrasound is simple to operate, but it is not considered as a reliable method for fat quantification due to its dependence on the subjectivity of the operator. Because of its special radiation, CT is not easy to be widely accepted and used in routine examination. Magnetic resonance imaging (MRI) is considered to be a safe, accurate and repeatable fat quantitative tool due to its noninvasive, radiation-free and high-resolution advantages. Applications of Mr To fat quantification include 1H-MRS, antiphase and chemically shifted water-fat separation techniques (including 2-point and 3-point Dixon). 1 h MRS is suitable for the quantitative of liver fat, has been considered the NAFLD (NAFLD) detection method of the "gold standard", it can be used to measure the fat cells related to the number of protons, fat fraction value can be used to directly calculate the spectrum, identify and proton density is directly related to the content of three acyl glycerin molecules, and, more importantly, it can eliminate the effects of the iron deposit. However, the pancreatic parenchymal tissue area is less than the minimum sampling volume used for 1H-MRS and is therefore not suitable for noninvasive assessment of pancreatic fat content. With the development of imaging technology, Dixon sequence of water-fat separation in MRI is a more accurate quantitative method of pancreatic fat. MRI imaging of soft tissue has advantages, but the fat of the strong signal often interferes with the diagnosis of lesions, the contrast of signals to inhibit fat increase lesions, and Dixon technology is a kind of using water, grease the resonant frequency of the inherent difference method, to separate water and fat signal by different phase difference between the different time of water, grease, can be independent of fat signals figure fat (like) and water figure (like) water, calculated using the formula fat score value. In recent years, Dixon technology has been greatly improved in noise and artifacts. The commonly used Dixon sequence includes 2-point Dixon sequence and 3-point Dixon sequence, while the 2-point Dixon sequence ignores the attenuation of T2* signal, and the mixed T2* signal tends to underestimate the fat fraction value, while the 3-point Dixon sequence (3P-Dixon) can correct the T2* attenuation effect in voxel to obtain more accurate fat/water separation. In addition, 3p-dixon sequence has the following advantages in the quantitative determination of pancreatic lipids :(1) the scanning time is relatively short; (2) The area of interest can be accurately placed in the pancreas; (3) Dixon reconstruction applies noise deviation correction to increase the noise ratio of the image; The proton density fat fraction diagram will be reconstructed automatically. Therefore, 3P-Dixon technique is currently the optimal method for quantifying pancreatic fat content.

In recent years, more and more scholars have begun to pay attention to the relationship between pancreatic fat content and the occurrence and development of T2DM. Some researchers believe that pancreatic fat deposition is involved in insulin resistance and abnormal insulin secretion and is an important pathogenesis factor leading to T2DM. However, some researchers have found that the relationship between the two is not obvious. And more in a previous study for study abroad, and focuses on discussion on simple obesity, pre-diabetes and diabetes new pancreatic fat deposition in the crowd and the relationship of T2DM in China has been diagnosed with type 2 diabetes in the study, and has its own characteristics in Chinese patients with T2DM, such as beta cells secrete a function is poor, early phase insulin secretion is damaged more serious; In addition, the proportion of overweight or obese people is more than 50%, and the visceral fat content of the same BMI is higher than that of European and American people.

Study on Type 2 Diabetes

Diabetes is by genetic factors, environmental factors, behavior factors and immune dysfunction such as joint action on the body caused by sugar, fat, protein, and a series of metabolic disorder characterized by chronic hyperglycemia, accompanied by insufficient insulin secretion and dysfunction, and chronic injury, cause multiple organ dysfunction and even failure of endocrine metabolic disease. With the progress of society and the change of lifestyle, the prevalence rate of diabetes is increasing year by year. According to the data of the International Diabetes Federation, by 2015, 1 person in 11 people in the world is suffering from diabetes, and 90% of them are T2DM. It is estimated that by 2035, the number of people with diabetes will increase by 55% to 600 million. The total number of diabetics in China ranks the second in the world, exceeding 40 million, and is expected to reach 60 million by

2025. The rapid increase of the prevalence of T2DM in China is mainly related to the following reasons: (1) Obesity: Obesity caused by excessive diet and reduced exercise is an important risk factor for T2DM. About 60%-80% of T2DM patients were obese before the onset of T2DM, and the degree of obesity is in direct proportion to the incidence of T2DM. Studies have shown that the ratio of muscle to fat changes as people age and become less physically active. From 25 to 75 years of age, muscle tissue will gradually decrease from 47% of body weight to 36%, and fat will increase from 20% to 36%. Therefore, the prevalence of T2DM in obese elderly people will increase significantly. (2) Dietary factors: Excessive intake of refined flour and sucrose in food will increase the incidence of T2DM. This study shows that proteins, vitamins and some trace elements in food play an important role in promoting insulin biosythesis, enhancing the function of pancreatic beta cells and energy metabolism in the body, and the refined food will lose a large number of these nutrients. (3) Mental factors: With the increase of life and work pressure, people's mental pressure has increased significantly in recent years. Studies at home and abroad have confirmed that mental factors play an important role in the development of diabetes. When in nervous tension, emotional excitement and various stress states, will cause growth hormone, norepinephrine and glucagon and other glycemic hormone secretion in large quantities. The flow chart of diabetes risk factors is shown in Figure 1:

The prevalence of T2DM and its complications is a major threat to global health. The main harm of diabetes does not originate from itself, but from various acute and chronic complications during its development, including diabetic ketoacidosis, retinopathy, diabetic nephropathy, cardio-cerebrovascular disease, diabetic neuropathy and diabetic foot, which almost involve all organs of the body. Although with the development of modern medical technology, the blood sugar of most patients has been well controlled, but still cannot effectively prevent and treat the complications caused by diabetes. Due to the high incidence and severity of complications of diabetes, its mortality rate has become the third largest after tumors and cardiovascular diseases, and has become a major public health problem.

Type 2 diabetes mellitus is a common metabolic disease, main show is insulin hyposecretion and insulin resistance, from normal glucose tolerance to low glucose tolerance, diabetes, the evolution of the process, the first is insulin resistance, then the islet beta cells of first phase insulin secretion reduced or disappeared, the second is the first 2 phase secretion increased, peak backwards or spikes, the last is the first 2 basic secretion also gradually lost. Changes in islet cell function play an important role in the onset and progression of type 2 diabetes. In the high glucose clamp test, the insulin secretion test showed two phases: one phase secretion and two-phase secretion. When glucose infusion increases blood glucose within 1-3min, it will lead to a rapid increase in blood insulin level, which will lead to the rapid release of insulin stored in the cell endocrine granules. Its characteristic is that insulin level rises rapidly and then drops rapidly, with sharp and sharp waveform, and then returns to the baseline level in about 10min. After 10-20 minutes of glucose stimulation, insulin secretion gradually increases again, and peaks again 2-3 hours later. Insulin decreases gradually until blood glucose returns to normal. At this time, part of the insulin comes from the secretory particles stored in the original beta cells, and the rest comes from the newly formed insulin, which accounts for about 20% of the secretion of the beta cells. This is called the second secretory phase of insulin, also known as the delayed secretory phase. It mainly reflects the synthesis and secretion function of cells after glucose stimulation, and has certain effect on inhibiting glucagon secretion.

Insulin phase secretion can inhibit the fat decomposition, glucagon secretion, the production and output of liver sugar, has an obvious restriction effect on the release of free fatty acids into the blood, and can also significantly reduce the rise of postpranational blood glucose and late hyperinsulinemia. The decrease of insulin secretion in the first phase is closely related to the occurrence and development of type 2 diabetes. In the early stage of the disease, the deficiency of insulin secretion has already occurred, and the decrease of insulin secretion peak value plays a predictive role in the occurrence of type 2 diabetes.

EXPERIMENTAL STUDY ON ISLET CELL ANTIBODY AND CELL FUNCTION IN CHILDREN WITH DIABETES MELLITUS

General Data Collection

Gender, age and course of diabetes were recorded, elevation, weight, blood pressure, waist

circumference and hip circumference were measured, and BMI and waist-hip ratio were calculated [13].

Determination of Pancreatic Fat

Each subject underwent a 3.0T MR abdominal scan, which included T1WI, T2WI, T2 lipoprotein pressure and T2* corrected 3-point Dixon sequence. 3P-Dixon scanning parameters: Repeat time (TR): 9.25ms, echo time (TEs): 2.46, 3.68, 7.36ms, layer thickness 6mm, matrix 256×176, inversion Angle 10°, excitation frequency 1, bandwidth 280 kHz, visual field 400mm × 400mm. Subject will be in supine position, T1WI and 3-point Dixon sequence shall be held for 15 s and 30 s respectively (subject will receive breathing training before examination). After 3P-Dixon sequence scanning, 5 groups of derived images were obtained, including in-phase, anti-phase, aqueous phase, fat phase and fat fraction graph. The ROI of Dixon's FF chart is drawn independently, that is, the pancreatic head, body and tail, and the average fat fraction (FF) of the pancreas is calculated.

Statistical Data Processing

All data were processed and analyzed with SPSS22.0 statistical software. Measurement data are expressed as mean ± standard deviation (x ± s). T test and analysis of variance were used for comparison between measurement data sets. Normal distribution data were analyzed by Pearson correlation analysis, while non-normal distribution data were analyzed by logarithmic conversion or SQRT conversion. P<0.05 was considered statistically significant.

DISCUSSION OF ISLET CELL ANTIBODY AND CELL FUNCTION IN PEDIATRIC DIABETIC PATIENTS

Study on Cell Function in Children with Diabetes

(1) Group, according to the results of the ICA positive pediatric diabetes fasting and postprandial blood glucose were higher than the ICA negative patients, patients with ICA positive meal after 1, 2 h, serum insulin, C peptide were significantly lower than that of the ICA negative patients, insulin, c-peptide area below the ICA patients with negatie, prompt the ICA positive beta cell function in patients with pediatric diabetes under the ICA negative patients. The specific experimental data are shown in Table 1 and Figure 2:

(2) As shown in table 1, fasting and 1, 2 and 3h after meals in children with ICA positive diabetes were higher than those with ICA negative (P> 0.05). Postprandial l, 2h insulin and c-peptide of ICA positive patients were significantly lower than those of ICA negative patients (all P <0. 05), fasting and 3h postprandial insulin and c-peptide were also lower than those of ICA negative patients (P>0. 05).

Study on Insulin Levels in Groups A and B

(1) After eating 80 grams of instant noodles, 81 diabetic children were tested for blood glucose levels in each group: the blood glucose levels of group A on an empty stomach and 120 minutes after a standard meal were 6.26 and 12.9 mmol/L, respectively, while the blood glucose levels at two points in group B were respectively 12.2 and 19.9 mmol/L, there was no significant difference in age, gender, BMI, waist circumference, SBP, DBP, fasting insulin levels between the two groups, but TC standard meals 0, 30, 60, 120 min blood glucose, blood true insulin and 30, The difference between 60 and 120 minutes insulin is significant. The area under the insulin curve of group A was significantly higher than that of the high blood sugar group, especially true insulin. The β-cell secretion function calculated with true insulin can explain 43% of blood glucose changes in group A, 55% of blood glucose changes in group B, and insulin sensitivity can explain 13% of blood glucose changes in group A, and can explain 13% of blood sugar changes in group B. Explaining 5.9% of the change in blood glucose, that is, the contribution of insulin deficiency to blood glucose level is 3.8 times that of insulin resistance in group A, while the former is 9.7 times of the latter in group B. The experimental data is shown in Table 2 and Figure 4:

All cases were divided into group A (FPG <8.92mmol/L) and group B (FPG≥ 8.89mmol /L) according to the level of fasting blood glucose (FFG), and the contribution of cell function and insulin resistance to the blood glucose level was evaluated in the two groups. Results the sensitivity of insulin and true insulin in group B was 65.5% and 64% of that in group A. After adjusting the effect of insulin resistance, the cell function in group B was only 1/5-1/7 of that in group A. Insulin swabs and cell function, measured by insulin, contributed half to glucose levels in group A, while cell function contributed eight times as much to glucose levels as insulin resistance in group

B, as shown in Figure 5.

CONCLUSION

According to this study, controlling blood glucose to a near normal level can significantly reduce the ocular and renal complications of diabetes. However, at present, the glycemic control of diabetic patients at home and abroad is not ideal, mainly because of the blindness in making treatment plans in clinical treatment. Because there is no simple and practical method to estimate the extent to which the increase of blood glucose in patients is caused by insulin resistance and depends on the functional damage of their islet B cells, it is difficult to use insulin sensitizers and insulin secretory agents rationally. It would be possible to improve the situation if certain parameters could be found to approximate the effects of insulin resistance and insulin deficiency. In order to analyze the relationship between insulin resistance and cell failure and blood glucose level, we explored the possibility of using empty source blood glucose as the parameter of drug selection for hypoglycemic therapy to control blood glucose more effectively.

The pathogenesis of pediatric diabetes is not very clear, and it is generally believed that it is related to the autoimmune response caused by virus infection and other foreign factors. The ICA positive rate was as high as 60%-80% in newly diagnosed ID-DM, and gradually decreased with the prolonged course of disease. Weight management, insulin resistance and improvement of islet cell function should be emphasized in the treatment of early childhood diabetes. This study shows that obese patients have a significant phenomenon of insulin resistance. After weight loss, tissue sensitivity to insulin will be increased, blood insulin concentration will be reduced, compensatory secretion of pancreatic beta cells will be improved, and insulin resistance level will be reduced.

According to the findings of this study, fat cells in obese people are larger in size and accumulate more fat in the body. Fat cells are prone to hypoxia and easily cause inflammation and death of fat cells. The inflammatory factors produced can also cause insulin resistance in skeletal muscle, adipose tissue and liver by interference with insulin signal transduction pathways. When insulin resistance occurs, the beta cells compensate by producing more insulin to meet the body's needs, leading to hyperinsulinemia. The results of this study showed that the sensitivity of insulin and true insulin in group B was 65.5% and 64% of that in group A. After adjusting the effect of insulin resistance, the cell function in group B was only 1/5-1/7 of that in group A.

REFERENCES

1. Hunjan, M. K., Schoch, J. J., Anderson, K. R., Lohse, C. M., Marnach, M. L., & Hand, J. L. (2017) "Prenatal Risk Factors for Infantile Hemangioma Development", *Journal of Investigative Dermatology*, 137(4), pp.954-957.
2. Castrén, E., Salminen, P., Gissler, M., Stefanovic, V., PitkRanta, A., & Klockars, T. (2016) "Risk Factors and Morbidity of Infantile Haemangioma: Preterm Birth Promotes Ulceration", *Acta Paediatrica*, 105(8), pp.940-945.
3. Harryvan, T. J., Morsink, L. M., & Tushuizen, M. E. (2018) "A Middle-Aged Man with Jaundice and A Gastric Tumor", *Gastroenterology*, 155(6), pp.1699-1700.
4. Wong, K., Song, L. M., Gostout, C. J., Tucker, R. D., Morris, M. L., Bowers, W. J., & Cattau, E. L. (2016) "Electrosurgery in Gastrointestinal Endoscopy: Terminology Matters", *Gastrointestinal Endoscopy*, 83(1), pp.271-273.
5. Peng, Q. (2016) "Insulin Autoantibody Positive Distribution and the Changes of C Peptide and Related Biochemical Indices in Patients with Type 2 Diabetes Mellitus", *Laboratory Medicine*, 31(1), pp.9-12.
6. Huerta, P. (2017) "Nmdar-Reactive Lupus Autoantibodies Alter Spatial Memory, Place Cell Function and Dendritic Architecture of Hippocampal Neurons", *Biological Psychiatry*, 81(10), pp. S39.
7. Silalahi, B., & Okvita, N. (2016) "Jenis Dan Tingkat Serangan Cacing Parasitik Berdasarkan Perbedaan Tingkatan Umur Pada Insang Dan Saluran Pencernaan (Usus) Ikan Bawal Air Tawar (Colossoma Macropomum) Pada Kolam Budidaya Di Tanjung Morawa", *Journal of Diabetic Complications*, 3(1), pp.27-34.
8. Guan, S. S., Sheu, M. L., Yang, R. S., Chan, D. C., & Liu, S. H. (2016) "The Pathological Role of Advanced Glycation End Products-Downregulated Heat Shock Protein 60 in Islet β-cell Hypertrophy and Dysfunction", *Oncotarget*, 7(17), pp.23072-23087.
9. Xue, D., Liu, P., Chen, W., Zhang, C., & Zhang, L. (2019) "An Anti-Cd103 Antibody-Drug Conjugate Prolongs the Survival of Pancreatic Islet Allografts in Mice", *Cell Death & Disease*, 10(10), pp.1-11.
10. Beeck, A. O. D., & Eizirik, D. L. (2016) "Viral Infections in Type 1 Diabetes Mellitus-Why the β Cells", *Nature Reviews Endocrinology*, 12(5), pp.263.
11. Welsh, M., Jamalpour, M., Zang, G., & Kerblom, B. (2016) "The Role of the Src Homology-2 Domain Containing Protein B (Shb) in β Cells", *Journal of Molecular Endocrinology*, 56(1), pp. R21-R31.
12. Wesslen, N., & Hellman, B. O. (2017) "The Influx of Ca2+ into Pancreatic β-Cells and Its Regulation by Glucose", *Biomedical Research*, 7(5), pp.339-344.
13. Corches, C. L., McBride, A. C., Robles, M. C., Rehman, N., Bailey, S., Oliver, A., & Skolarus, L. E. Development, Adaptation and Scale-up of a Community-wide, Health

Tables and Figures

Table 1.
Blood glucose area, insulin area and C-peptide area were compared between the two groups

Goup		Blood glucose area	Insulin area	C peptide area
The ICA positive	5	65.22±17.88	29.27±7.47	0.60±0.47
The ICA negative	3	58.23±18.11	34.55±8.32	0.92±0.52
The control group	2	19. 65±28.57	80.80±24.63	5.83±1.56

Table 2.
Islet function in group A and Group B

	True insulin calculates the beta cell secretion function	Insulin sensitivity
Group A	43%	55%
Group B	13%	5.9%

Figure 1.
Flow chart of diabetes risk factors

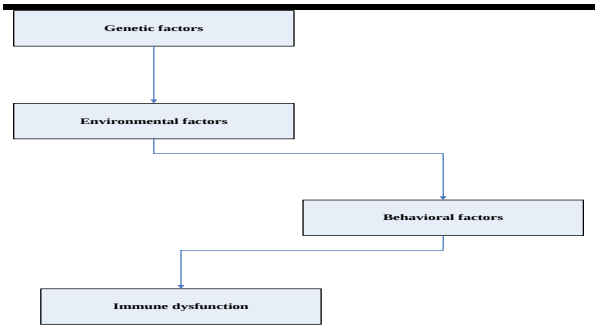

Figure 2.
Blood glucose area, insulin area and C-peptide area were compared between the two groups

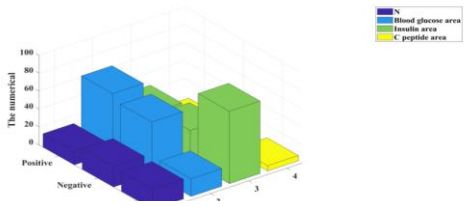

Figure 3.
Area data of blood sperm, insulin and C-peptide were compared between the two groups

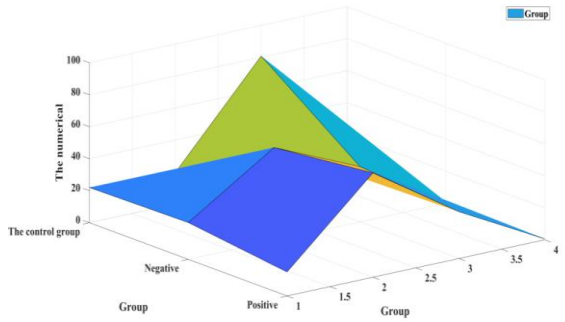

Figure 4.
Islet function in group A and Group B

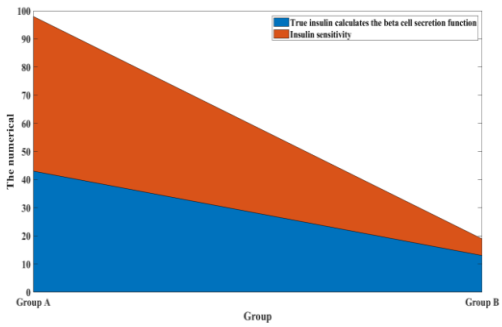

Figure 5.
Beta cell function contributes to blood sugar levels