

# EVOLUTION OF RELATIONSHIP BETWEEN INCREASED DEMAND OF INSULIN SECRETION AND INCREASED LEVEL OF PROINSULIN IN BLOOD OF PATIENT OF DIABETES MELLITUS 2

**Article Review By Dr. Madhumati Varma, India**

*(DNB Family Medicine, MMSc in Diabetology Student of Texila American University)*

*Email:- madhumativarma@gmail.com*

## SOURCE

Thomas G K Breuer 2010, 'Proinsulin levels in patients with pancreatic diabetes are associated with functional changes in insulin secretion rather than pancreatic b-cell area', European Journal of Endocrinology (2010) 163 551–558, viewed [www.eje-online.org](http://www.eje-online.org)

## REVIEW OF LITERATURE

The Insulin resistant triggered by high proinsulin to insulin ratio which is associated with NIDDM( 1 ). Elevated intact proinsulin seems to indicate an advanced stage of  $\beta$ -cell exhaustion and is a highly specific marker for insulin resistance. It might be used as arbitrary marker for the therapeutic decision between secretagogue, sensitizer, or insulin therapy in type 2 diabetes( 2 ). In DM2, insulin processing deficient. There is an increased proinsulin:insulin ratio( 3 ). Changes in proinsulin levels are associated with diabetes.

Random proinsulin levels and the proinsulin-to-C-peptide ratio represent dynamic markers of the state of  $\beta$ -cell function that complement immune markers in identifying relatives who are at high risk of contracting type 1 diabetes( 4 ). Proinsulin is a very sensitive marker of beta cell exhaustion and may therefore be useful for therapeutic decision-making in type 2 diabetes ( 5 ). IDDM in humans and in non-obese diabetic (NOD) mice is a T-cell-dependent autoimmune disease in which the  $\beta$ -cells of the pancreatic islets are destroyed.

Several putative  $\beta$ -cell auto antigens have been identified, but insulin and its precursor, proinsulin, are the only ones that are  $\beta$ -cell specific.(6), his assay allows for a pathophysiological

staging of type 2 diabetes based on beta-cell secretion. It could be confirmed by a large epidemiological study (IRIS-2, 4,265 patients) that intact proinsulin is a highly specific marker for insulin resistance. It could also be shown in other studies that successful resistance treatment with insulin or glitazones led to a decrease in elevated proinsulin levels and, thus, to a decrease of cardiovascular risk, while the levels remained high during sulfonylurea therapy.

Therefore, patients with increased fasting intact proinsulin values should be treated with a therapy focusing on insulin resistance. Assessment of beta-cell function by determination of intact proinsulin may facilitate the selection of the most promising therapy and may also serve to monitor treatment success in the further course of the disease.( 7).

## **KEYWORDS**

Insulin, Proinsulin ratio, Endocrinology, Ampullary Cancer, Venous Blood, Immune System

## **INTRODUCTION**

In a healthy population, glucose is controlled by Insulin. When secretion of Insulin increased on in circumstances like stress, operation, resection of some part of pancreas with resection and B cells, destruction of due to auto antigens, increase release reserve insulin form of proinsulin which increase resistance of periphery of receptor of insulin on cells which prohibits enter glucose in cell for utilization and this develops Insulin resistance other name called Diabetes type 2.

This study was done after pancreatectomy where reduced mass of pancreas but not effect to increase level of proinsulin but when increase demand of insulin secretion of increases that time increase level of proinsulin in blood and increase ratio of Proinsulin on Insulin which indicate Insulin resistant Diabetes Mellitus 2,Proinsulin is immature insulin precursors and insulin is mature .after somatostatine infusion improves Hyperproinsulinemia and ratio of proinsulin to insulin and also in .

Diabetes type 2 show advance stage of B cell exhaustion and marker of insulin resistance and indicate treatment of sensitizer therapy or insulin. Proinsulin, a major  $\beta$  cell protein, is the only autoantigen that is almost exclusively expressed in  $\beta$  cells

## ARTICLE SUMMARY

The study shows that when reduces b cell mass which results decreased insulin secretion but increase proinsulin concentration both total and intact results impairment of insulin secretion an action of insulin. Proinsulin ratio increase mostly in obese patient and high risk of DM 2. The proinsulin increase when increase demand of secretion of insulin in DM 2.

This study show three principle pointes

- 1) There is absolute or relative increase of proinsulin in blood with patient of secondary Diabetes.
- 2) When the function of b-cell declines level of proinsulin increases in blood,.it is measured by HOMA index camper to B-cell area
- 3) There is not strong relation between Insulin resistance and proinsulin level in blood..

Proinsulin Insulin ratio improves after Somatostatin, Metformin, Thizoliinedione, relative reduction of proinsulin level but increase proinsulin/insulin ratio after sulphonylureas. The study shows lower proinsulin level indicate HOMA index improvement but b-cell mass negligible. There is positive relationship between proinsulin and insulin resistance. The fasting insulin level in both Matsuda Index of insulin sensitivity and HOMA index of insulin resistance moch close to proinsulin based parameter. Hyperproinsulinema is more close to functional defect rather than b-cell mass.

## ARTICLE STRUCTURE

The article was initiated with Abstract in which clearly mentioned introduction, Patients and methods, Results, Conclusions. Idea well formed which author wanted to explain that Hyperproinsulinaemia is has direct relation with defects in insulin secretion rather than reduction in b-cell area. Introduction explained about mature insulin and immature proinsulin. Ratio of Proinsulin/insulin normal in healthy people and increased ratio in secondary diabetes or in insulin resistance and DM type 2 but not related to mass of pancreas reseated.

Next explained types of taken spacemen and patients with diseases of pancreas which done resection of pancreas like chronic pancreatitis, pancreatic carcinoma, pancreatic adenoma or ampullary cancer and number of patient. There was paragraph of experimental procedures where clearly mention how to take a sample of venous blood for glucose tolerance.

The was next heading patients and methods ,study design, pancreatic tissue processing, morph metric analysis , calculations and statistical analysis where explained kit of ELISA for proinsulin .C-peptide and ,taken sample for histopathology and seen in microscope .etc Calculations and statistical analysis explained HOMA index was calculated for b-cell function linear or non-linear regression functions correlation analyses carried.

There was presented result between different type of patent proinsuline in graph form and quantitative analysis. Finally main objective of proinsulin /insulin ratio increase in insulin resistanc Diabetes type2 .rather than reduce b-cell mass discussed in discussion paragraph. At the end declaration of interest, funding, acknowledgements, references are written clearly

## **AUTHORITY**

This article published in European Journal of Endocrinology (2010),It is authentic journal and Thomas G K Breuer worked up this project in Ruhr-University Bochum, 44789.This article is authentic article and several references used which showed it unbiased authenticity. Author has academic background I working in university. There work in academic qualified study on patient in with patient and laboratory. It is valuable. This article as authority very strog academic of nature because is related to University of Germany and funded by authentic source and acknowledged.

## **ACCURACY**

Source of information on study carried out I academic University of Germany is correct and accurate. But there is no literature review, conclusion mentioned in article. There is clear and good explanation about methodology, discussion, introduction. There are reference which shows accuracy. This project funded by Deutsche

Forschungsgemeinschaft (DFG grant no. Me2096/5-1 to J J Meier) and the Ruhr-University of Bochum (FoRUM grants to J J Meier and acknowledged by Birgit Baller, Kirsten Mros, Heike Achner and Gudrun Muller .

## **PERIOD**

Article Received on 21 June 2010. Accepted at 2 August 2010 so it is recent article.

It is published in European Journal of Endocrinology (2010).Which as resent article .This study is 4 years earlier published but received in june 2010.It shows is resent article.

## **RELEVANCY**

This study done with a group of academic specialist in University. It is more relevant as done with funding and acknowledgement of authorized body and in academic and university level. There is references which interlinked and correlated to eah other and study well organized relevant as done in University and academic level and published in relevant authentic journal of Endocrinology.

## **OBJECTIVITY**

The article gives information is evidence based due to reference provided to use in study .There in no literature review. There objectivity clearly mentioned and acknowledge. This is very nicely explained objectivity to proinsulin and relation with Diabetes type 2.

Stability- About the stability of the article based on its publication. This is the source of academic database of the University and that is why it is stable database.

Analysis of graph/Image/Table – Brief analysis of the Graph/image/table

Following graphs and chart explain nicely

-Correlation analyses between the fasting insulin

-Concentrations and the Matsuda index of insulin sensitivity, Correlation analyses between total proinsulin ,

-Intact proinsulin, Correlation analyses between total proinsulin .

-Correlation analyses between total proinsulin,

-Plasma concentrations of total proinsulin

## **RECENT ADVANCES RELATED TO THE TOPIC**

When glucose increases, it simulate proinsulin formation by increasing PC3 biosynthesis. This is endopeptidase that regulate proinsulin secretion while insulin resistance in DM type 2 increase obesity and increase resistance of insulin on periphery. n type 1 diabetes (T1D), there is an intense inflammatory response that destroys the  $\beta$  cells in the pancreatic islets of Langerhans, the site where insulin is produced and released.

A therapy for T1D that targets the specific autoimmune response in this disease while leaving the remainder of the immune system intact, has long been sought. Proinsulin is a major target of the adaptive immune response in T1D. We hypothesized that an engineered DNA plasmid encoding proinsulin (BHT-3021) would preserve  $\beta$  cell function in T1D patients through reduction of insulin-specific CD8+ T cells.

## **CONCLUSION**

The reviewed article 'Proinsulin levels insulin secretion rather than pancreatic b-cell area' has introduction, methodology, discussion and conclusion. The article has good academic background and stable article and accurate, but there is no literature review and conclusion. In a healthy population glucose is controlled by Insulin. When secretion of Insulin increased on in circumstances like stress, operation, resection of some part of pancreas with resection and B cells, destruction of due to auto antigens, increase release reserve insulin form of proinsulin which increase resistance of periphery of receptor of the insulin on cells which prohibits and enter glucose in cell for utilization and this develops Insulin resistance other name called Diabetes type 2.

There are study was done after pancreatectomy where reduced mass of pancreas but not effect to increase level of proinsulin but when increase demand of insulin secretion of increases that time increase level of proinsulin in blood and increase ratio of Proinsulin on Insulin which indicate Insulin resistant Diabetes Mellitus 2, Proinsulin is immature insulin precursors and insulin is mature .after somatostatine infusion improves Hyperproinsulinemia and ratio of proinsulin to insulin and also in .Diabetes type 2 show advance stage of B cell exhaustion and marker of insulin resistance and indicate treatment of sensitizer therapy or insulin. Proinsulin, a major  $\beta$  cell protein, is the only autoantigen that is almost exclusively expressed in  $\beta$  cells

## REFERENCE

- 1) Michelle, B. French (1997). Transgenic Expression of Mouse Proinsulin II Prevents Diabetes in Nonobese Diabetic Mice, *Diabetes* January vol. 46 no. 1 34-39, Retrieved from, <http://diabetes.diabetesjournals.org/content/46/1/34.short>,
- 2) Mykkänen, L.(1997). The relation of proinsulin, insulin, and proinsulin-to-insulin ratio to insulin sensitivity and acute insulin response in normoglycemic subjects. *Diabetes*. Dec;46(12):1990-5. Retrieved from ,[diabetes.diabetesjournals.org/content/46/12/1990.full.pdf](http://diabetes.diabetesjournals.org/content/46/12/1990.full.pdf).
- 3) Pfützner, A.(2004). Fasting intact proinsulin is a highly specific predictor of insulin resistance in type 2 diabetes. *Diabetes Care*. Mar;27(3):682-7. Retrieved from, [www.ncbi.nlm.nih.gov/pubmed/14988285](http://www.ncbi.nlm.nih.gov/pubmed/14988285)
- 4) Pfützner, A.( 2004), Role of intact proinsulin in diagnosis and treatment of type 2 diabetes mellitus, *Diabetes Technol Ther*. Jun;6(3):405-12. Retrieved by <http://www.ncbi.nlm.nih.gov/pubmed/15198846>
- 5) <http://care.diabetesjournals.org/content/27/3/682.abstra>
- 6) [www.raymondcheong.com/.../DB33%20-%20Diabetes,%20Insulin%20A](http://www.raymondcheong.com/.../DB33%20-%20Diabetes,%20Insulin%20A)
- 7) [http://www.alpco.com/pdfs/ALPCO\\_Proinsulin\\_ELISA\\_and\\_Diabetes\\_Research.pdf](http://www.alpco.com/pdfs/ALPCO_Proinsulin_ELISA_and_Diabetes_Research.pdf)