

Citrulline as a alternative for the Arginine in stimulating Growth Hormone

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ABSTRACT

Objective: children attending the specialized centre for endocrinology and diabetes and the children hospital in medical city who suffer from short stature.

Subjects And Methodes: human Growth hormone (GH) is a hormone that is essential for normal growth and development in children. It promotes proper linear bone growth from birth through puberty. There are many methods for stimulation growth hormone, the major method is the by glucagon IM and arginine infusions. This test is very important for assessment pituitary gland in children and adult for the produce and secretion growthhormone.40 child suffer short stature fromattending the specialized centre for endocrinology and diabetes and the children hospital in medical city. Citrulline it is amino acid that is used today in medicine as a cure for hypotonic in adult and blood pressure reduce inchildren.citrulline convert to arginine in the urea cycle and body. In this research used citrulline for the stimulation growth hormone alternative for arginine children and camper with stimulation by glucagon.

Setting: This study was performed during November 2023to February 2024.subject were selected from among the were diagnosed by the growth scale and to know the value of the growth hormone.When reviewing,the child must be fasting the basil blood is drawn and then the child will be injection by glucagon 0.03 mg\kg and then after 2 hours,the secondwithdrawal is done to see the extent of stimulation. after a period of two weeks to a month, the process is repeated for the same child using the citrulline oral at 0.33 gm\kg.And measured the s. glucose, s. creatinine,blood pressure and BMI. Aim of this study: Test the citrulline as a substitute for arginine in a growth hormone stimulation test and find out how efficient it is with stimulation compered to glucagon.

Result: The results showed for 40 children that the highest rate of stimulation with glucagon is 5.662 ng\ml from 0.965 ng\ml as a basil and the highest stimulating rate with citrulline is 3.258 ng\ml from1.036 ng\ml as a basil, which means that there is a significant difference between the two cases and that the glucagon Best as a catalyst of citrulline. The ratio of the efficiency of the citrulline compared to the glucagon is 57.7%.

Conciustion: This study has been proven the citrulline can be used as stimulation for growth hormone with the need for other research to know the optimal dose and appropriate time for the highest stimulation.

Keywords: Citrulline, Arginine, Growth Hormone

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1. INTRODUCTION

1-1- GROWTH HORMONE:

pituitary gland is one of the important glands in the human is responsible for the secretion and regulation of many hormones. One of the most important of these hormones is the growth hormone, which is responsible for bone growth and protein production in the muscle cells and the production of energy in the breakdown of fat. HGH is the polypeptide hormone

consist from single chain polypeptide with 191 amino acid,. HGH is the main function. And the responsible for the many metabolic function of the body(1) peaks at night and the peaks are in close association with slow.

GH is known play role to be raise a metabolic hormone which stimulates lipolysis and decrease the controls (GH) release done by hypothalamus tightly. the somatostatin inhibits and GH releasing hormone (GHRH. the peaks of GH secretion at night in deep sleeping (2). GH is the raise a metabolic hormone by the increase lipolysis and decrease carbohydrate metabolism which blood glucose levels mention (3). GH response to increase the production of IGF-I, and help uptake amino acid and increase protein synthesis in the body (4). the catecholamines and insulin in regulate glucose and fat metabolism GH Is the secondary role play in this metabolism (5). the compare with individuals with adequate GH levels obvious reductions in lean body mass and raise body fat (6)

The Peak spikes of GH release at deep sleeping around 10 p.m. Midnight, and 2 a.m. the growth hormone secretion at night time because the most of GH effects are mediated by many hormones, this causes the GH secretion in night the hormone mediated GH effect, somatomedins, IGH-1 and IGH-2. the action of GH is spread out more evenly during the day at result this (7).

1.2 Glucagon hormone1-2

Glucagon hormone is the important function the staying glucose homeostasis by the synthesis hepatic glucose stimulation, the pancreatic alpha cells is the responsible secretion in the islet of Langerhans s.(8)the function of glucagon is the stimulating insulin production from pancreatic beta cells for the raise plasma level of glucose concentrations, when low level plasma glucose concentrations represent, decrease glucagon secretion. as accordingly (9)

1-3 Citruiline

The citruiline name is the coming from Citrullus vulgaris (watermelon) in the 1930 s discovered.(10). CIT is the non-preotic amino acid because this not important in the scientific community (11) discovered small intestine releases of CIT which is largely taken up by the kidney In the early 1980 (12) and, amount to about 75% of the CIT taken up by the arginine secreta. Then, Castillo (13,14) were the first to represent the CIT and ARG in vivo kinetics at the whole-body level in healthy subjects.

the suggestion of which can be seen an ARG–CIT–ARG inter-organ cycle (15) as a mechanism for protection dietary ARG from increase liver degradation (because CIT is not taken by the liver(16))the protein homeostasis keeping. The end product of citruiline it NO syntheses reaction (17) The role of the intestine as a control of CIT production was further emphasized in situations where intestinal function is change (i.e. short-bowel syndrome, radiation-induced intestinal damage, coeliac disease. (18,19). In situations where ARG production is compromised, CIT becomes a conditionally essential amino acid(20), thus controlling dietary supplementation with ARG. The specificities of CIT and ARG

1.4 Growth hormone deficiency in children1-4

Dwarfism is a common disease, one of the most important causes GH deficiency. this disease is evident in children, where short stature is observed . Children with GHD causes may be divided in to congenital or acquired. The causes Congenital include multiple pituitary hormone because genetic mutation such as deficiency in the PROP1, HESX1, PIT-1 and LHX3/4 (21). Structural lesions causes example empty Sella, and sept-optic dysplasia midline.

The many causes to the acquired GHD, secondary to pituitary tumors, craniopharyngioma is the common being, and treatment example, hypothalamus-pituitary and irradiation namely pituitary surgery

(22). Infiltrative diseases example as Langerhans cell histiocytosis, sarcoidosis or tuberculosis are uncommon causes. traumatic brain injury has been qualified as a cause of children GHD(72). the most common cause of children onset GHD is idiopathic is by far. In this situation the most of children will have normal GH secretion when return tested on completion of growth. (24)

1-5 Growth hormone stimulation in institutions health in Iraq

Way is assumed that the health institutions specialized in examining the growth hormone according to the global evidence for the examination, which includes the stimulation procedure with two stimulating substances from the approved materials according to the high evidence separating the first and the second stimulus a specific time period, but most institutions adopt stimulation with one article for the weakness of the financial capabilities and not having lobbies for entry Patients for their dependence on the outpatient system

In the Specialized Center for Endocrinology and Diabetes in Baghdad, for example, and it is the largest center for endocrine diseases in Iraq, the substance is used only by stimulation and on the result of stimulation, the patient is diagnosed if he is suffering from a lack of growth hormone or not.

In other institutions affiliated with the Ministry of Health in Iraq, clonidine tab is used only as a stimulus. As for private institutions in Iraq, it uses clonidine tab only. The truth is that both methods are not sufficient by themselves to determine whether or not the patient has growth hormone deficiency, as the global evidence provides for the adoption of two diagnostic items

2. SUBJECTS AND METHOD

2-1 Subjects:

This study was performed during the period from September 2023 to January 2024 where 40 children from reviewers to specialized endocrine center in Baghdad and pediatric hospital in medicine city. these children review these centers for having development problems.

In these center measurement GH concentration before stimulation and after stimulation by glucagon after the diagnostic whether or not they suffer from growth problems due to a lack of growth hormone.

To find out whether or not a child has short stature, the height and weight of the child are taken and compared to the growth chart life.

The first and important step in the research is to choose the children who donate after taking the approval of their parents to work stimulation with the substance citrulline after stimulation with glucagon and it was done through a form that includes the child's name and general information and the signature of the child's Guardian on the form to agree to bring the child to the center for the purpose of conducting the stimulation after a one month from the first examination.

these same children were stimulated again after a period of not less than a week with citrulline as a stimulation material and compare the efficiency of stimulation with glucagon and citrulline.

3. RESULT AND DISCUSSION

3-1 Result of stimulation test

taking a group of 40 children reviewing the Specialized Center for Endocrinology and Diabetes and the Children's Hospital in Medical City who are suspected of suffering from a lack of growth and know if they suffer from a lack of growth hormone secretion from nothingness by conducting the stimulation process of the pituitary gland they were first stimulated with glucagon and after Almost a month, the stimulus was re-conducted by the citrulline research subject for the purpose of the coupler and knowledge of the efficacy of the citrulline in the stimulus. The results showed for 40 children that the highest rate of stimulation with glucagon is 5.662 and the highest stimulating rate with citrulline is 3.258, which means that there is a significant difference between the two cases and that the glucagon Best as a catalyst of citrulline.

Table 1: Comparison between difference groups in level of growth hormone

Group	No	Mean \pm SE of growth hormone (ng/ml)
Glucagon Basal	40	0.965 \pm 0.10 c
Glucagon stimulation 2hr	40	5.662 \pm 0.46 a
Citrulline basal	40	1.036 \pm 0.09 c
Citrulline stimulation 2hr	40	3.258 \pm 0.19 b
LSD value	--	0.725 **
P-value	--	0.0001
** (P \leq 0.01).		
Means having with the different letters in same column differed significantly.		

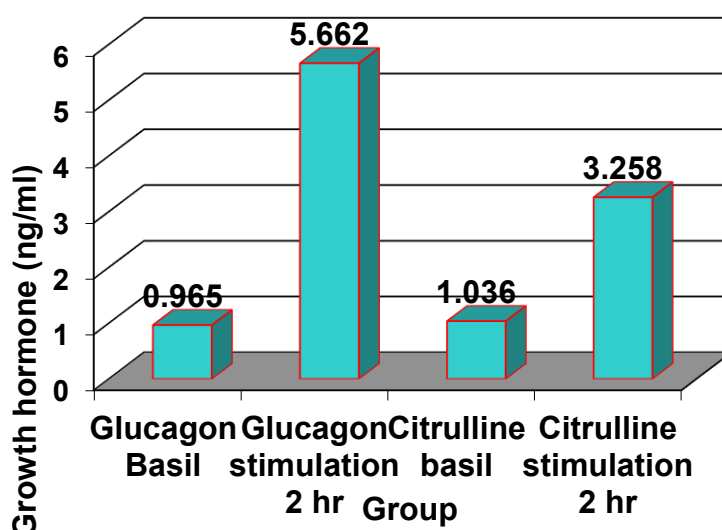


Figure 1. comparison between difference group in level of growth hormone

4. DISCUSSION

Glucagon stimulation test: This test is commonly used for the evaluation of growth hormone deficiency (GHD). Glucagon causes blood glucose to increase leading to insulin release and therefore indirectly stimulating GH and ACTH release through provocation of the hypothalamic-pituitary axis

A peak plasma GH concentration of $\geq 7 \mu\text{g/L}$ indicates a normal response to the test and no further investigations are required.

A peak plasma GH concentration of $< 5 \mu\text{g/L}$ is diagnostic of growth hormone deficiency but requires a second GH provocation test to confirm the diagnosis.

A peak plasma GH concentration of $5-7 \mu\text{g/L}$ may still be indicative of GH deficiency and requires further investigation. (25).

Glucagon method is the gold stimulation for growth hormone in this result the different between glucagon and citrulline is the efficiency of citrulline is the 57.7% from glucagon

The citrulline method first time trial of motivation, and there are no sources that can be used for the optimum dose and the best time to stimulation.,

In this study glucagon is the best stimulation from citrulline but the glucagon is the known optimum dose and time but the citrulline not known dose and time optimum because used the first time in the stimulation.

The dose of citrulline deboned to altricial of the drug. This drug used treatment patient suffered from hypotonic onebag contain 1gm.

The time stimulation by citrulline after 2 hours chose deboned similar to glucagon.

If I do other research that determines the best dose and time gives the highest stimulation perhaps, we will get excellent results of stimulation.

The nearly mothod used stimulation hormone by citrulline is the stimulation by arginine.

Arginine is a good stimulation and it is widely used and its results can be compared to citrulline but arginine cannot to be given orally and given only intravenously.

This study relied on giving citrulline instead of arginine, because it is faster absorbing than arginine and in the urea cycle, mainly the citrulline turns in to arginosuccinate and then arginine.

The difficulty of administering intravenous arginine to children in outpatient clinics in our health institution. This study aims to find an alternative that is given orally that is available and easy to administer and has no side effect.

The results indicate that the rate of stimulating citrulline compared to glucagon in the research is 57.7% which indicates that citrulline is a good catalyst for growth hormone.

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