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Inter-Relationship
Between
Serum concentration of Glucose , Glucagon and Insulin
During The First Two Days
In Healthy Newborns

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THESIS

Submitted for partial Fulfilment for Master Degree in Pediatrics

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1997

TO

MY FAMILY

بسم الله الرحمن الرحيم

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Abbreviations

Title	=
ADP	Adenosine Diphosphate
ATP	Adenosine Triphosphate
CCK	Cholecystokinine
CO_2	Carbon dioxide
c-AMP	Cyclin Adenosine Monophosphate
FFA	Free fatty acid
GIP	Gastrin inhibitory peptide
GLUT	Glucose transporter
H_2O	Water
HMP	Hexose Monophosphate Pathway
IGF	Insulin like growth factor
Mg^+	Magnesium
NAD	Nicotinamide adenine dinucleotide phosphate
NMR	Nuclear Magnetic Resonance
PEPCK	Phospho-Enol Pyruvate Carboxy Kinase
RNA	Ribose nucleic acid
SGA	Small for gestational age
TCA	Tricarboxylic acid cycle
UDP-G	Uridine diphosphate glucose
UTP	Uridine triphosphate

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Introduction And Aim of The Work

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Introduction
and
Aim of The Work

After birth newborn infant must adapt from a continuous supply of nutrients rich in glucose to intermittent enteral feeding of breast milk which is low in carbohydrates rich in fat ***(Swenne et al., 1994)*** .

The newborn is dependent on its own ability to produce glucose to meet the needs of the growing central nervous system . Thus during the early neonatal period the newborn undergoes a period of relative starvation and is at risk of developing hypoglycemia as the ability to form glucose from other substrates is not yet fully developed ***(Girard et al. , 1992) .***

Before and shortly after birth the concentration of glucagon , glucocorticoids and catecholamines increase ***(Girard and Sperling , 1983) .***

Shortly after birth , the concentration of glucocorticoids and catecholamines decrease , but increased concentration of glucagon persists beyond the initial post-natal period ***(Delameter et al. , 1974) .***

A role for glucagon for the initiation and maintenance of neonatal glucose production has therefore been suggested .

The aim of this work is to study the relationship of serum concentration of glucose , glucagon and insulin during the first two days of life in healthy newborns .

Review of The Literature

Glucose

Carbohydrates are saccharides , the molecule of which three or more carbon atoms combined together with hydrogen and oxygen. Glucose is one of the simplest forms of carbohydrate which is so called monosaccharides that also include galactose and fructose , glucose is the most important among them .

Blood glucose is mainly derived from 2 sources either exogenous or endogenous .

Exogenous glucose :-

The ingested carbohydrates are exposed to the action of several enzymes in the gastro-intestinal tract , through the action of these enzymes carbohydrates are split to their constituents monosaccharides . Starch , glycogen and maltose are converted to glucose , lactose to glucose and galactose and sucrose to glucose and fructose .These monosaccharides are practically absorbed completely in the small intestine . Absorption of two types :

Specific absorption : involving phsphorylation .

Non specific absorption : by diffusion resulting from osmotic forces across the mucous membrane .

The major portion of absorbed monosaccharides passes into the portal blood by which it is carried to the liver .

Endogenous :

Glycogenolysis : the polymerized storage form of glucose .

Gluconeogenesis : the formation of glucose from precursors including lactate , pyruvate , amino acids { especially alanine }and to a lesser extent from glycerol by hydrolysis .

Metabolic pathway of glucose :

1. Glucose is converted to glycogen for storage in the liver by a process called glycogenesis .

2. Glucose may be utilized for energy production through a process of oxidation whereby it is converted to CO2 and water , it may be degraded under anaerobic condition to lactic acid in a process called glycolysis .

3. Glucose may be utilized for synthesis of other compounds such as :

   a. **Fatty acids :** by a process called lipogenesis , takes place both in the liver and in peripheral tissues ***(Rittinberg and Bloch , 1945)*** .

   b. **Amino acids :** non- essential amino acids deliver their carbon skeleton from glucose or its metabolites .

   c. **Other carbohydrates** ; *these includes* :

      i- Ribose and deoxyribose required for synthesis of nucleic acid .

      ii- Mannose , glucoseamine , galactoseamine and neuraminic acid which form parts of muco - polysaccharides and glycoproteins .

      iii- Glucoronic acid which is also involved in mucopolysaccharides and detoxification reaction .

Glucose utilization :

The major sequence of catabolic reactions whereby glucose is degraded in most tissues to CO_2 and H_2O may be divided to aerobic and anaerobic phases . An initial anaerobic series of reaction take place , continuing directly in an aerobic series in the presence of oxygen . The anaerobic phase of glucose metabolism occurs whether oxygen is present or not , so glycolysis can take place under an anaerobic conditions but this limits the amount of energy produced per molecule of glucose oxidized , under certain condition glucose is broken down via another pathway which is H.M.S. or pentose shunt .

Anaerobic glycolysis { Embeden - Myerhof pathway } :

Glucose is first phosphorylated to glucose -6- phosphate which is converted to fructose -6- phosphate by phosphohexoisomerase ***(Meyerhof and Kocholaty , 1943)*** followed by another phosphrylation with ATP catalyzed by the enzyme phsphofructokinase to fructose 1-6 diphosphate ***(Taylor , 1952)*** . Fructose 1-6 diphosphate is split into 2 trioses : glyceraldhyde -3- phosphate and dihydroxy acetone phosphate which are inter converted by the enzyme phosphotriose isomerase ***(Meyerhof and Kocholaty , 1943)*** . Glycolysis proceeds by the oxidation of glyceradhyde -3- phosphate to 1,3 diphosphoglycerate and dihydroxy acetone phosphate is also oxidized to 1,3 diphosphoglycerate in the presence of Mg^{++} .

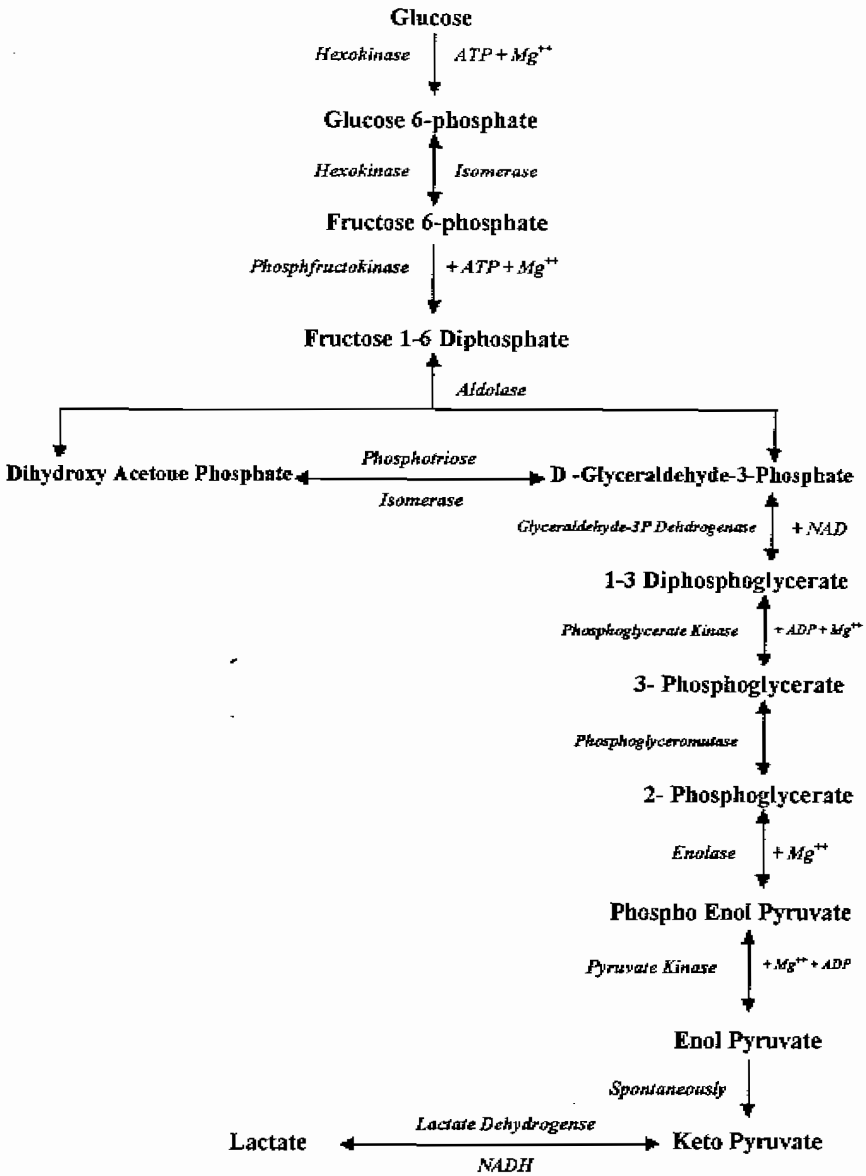

Figure (1) : Embden Myerhof Pathway of Glycolysis

The phosphoglycerate kinase enzyme transfers the carboxyl phosphate of the diphosphoglyceric acid to ADP forming ATP and 3- phosphoglycerate ***(Kuborwitz , 1944)*** . 3-phosphoglycerate is converted to 2- phosphoglycerate which undergo a reversible dehydration to phosphoenol pyruvate , the high energy phosphate of phosphoenol pyruvate is transferred to ADP to generate at this stage 2 mol. of ADP / mol. of glucose oxidized . Enolpyruvate formed is converted spontaneously to keto form of pyruvate ***(Meyerhof and Goseper , 1949)*** .

Pyruvic acid is aerobically oxidized to CO_2 and H_2O ***(Cabib , 1963)*** , under anaerobic conditions pyruvic acid is reduced to lactic acid by dehydrogenase and NADH , the reoxidation of NADH via lactate formation allows glycolysis to proceed in the absence of O_2 by regenerating sufficient NAD for the reaction catalyzed by glyceraldhyde-3- phosphate dehydrogenase .

Reaction of pyruvic acid :

Pyruvic acid is the end product of the glycolytic pathway . It can undergo a variety of reactions by which it gains entrance to the body proteins , fat as well as to the common metabolic pool , this is performed by one of the following ways :

1- Pyruvate reduction : pyruvate may act as a hydrogen acceptor being reversibly reduced to lactate .

2- Pyruvate carboxylation : in which pyruvate can accept a CO_2 forming oxalacetate .

3- Pyruvate decarboxylation : pyruvate is oxidatively decarboxylated to acetyl Co-A **{ active acetate }** , which is the starting point for the biosynthesis of fatty acids , cholesterol and ketone bodies **{ aceto - acetate and B - hydroxybutyrate }** .