Monitoring of blood beta-hydroxybutyrate as a screening test for diabetic ketoacidosis at the emergency unit

Thesis

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INTRODUCTION

Diabetes is a chronic illness that requires continuing medical care and patient self-management education to prevent acute complications and to reduce the risk of long-term complications. Diabetes care is a complex matter that requires many issues, beyond glycemic control, should be addressed. A large body of evidence exists that supports a range of interventions to improve diabetes outcome ***(Tasali et al., 2008).***

The standards of diabetes care are intended to provide clinicians, patients and other interested individuals with the components of this care, treatment goals, and tools to evaluate the quality of care ***(Gaede et al., 2008).***

Diabetic ketoacidosis (DKA) is a life threatening complication of both type 1 and type 2 diabetes mellitus and is considered to be the most common hyperglycemic emergency in patients with diabetes mellitus ***(Dunger DB et al., 2004).***

Recent studies using standardized written guidelines for therapy have demonstrated a mortality rate of less than 5%, with higher mortality rates observed in elderly patients and those with concomitant life-threatening illnesses. Worldwide, infection is the most common precipitating cause for DKA, occurring in 30-50% of cases. Urinary tract infection and

pneumonia account for the majority of infections. Other precipitating causes are intercurrent illnesses (i.e., surgery, trauma, myocardial ischemia, and pancreatitis), psychological stress, and non-compliance with insulin therapy ***(Umpierrez GE et al., 2003).***

The presenting complaint suggestive of hyperglycemia may be polyuria, polydipsia. Ketone testing is performed at the emergency department if a urine sample could be procured. Diabetic ketoacidosis (DKA) has no universally agreed definition, physicians use standard clinical criteria (metabolic acidosis pH < 7.3 and/or bicarbonate < 15 meq/L, blood glucose > 200 mg/dl, urine ketones ≥ 2+) to define diabetic ketoacidosis ***(Naunheim et al., 2006).***

DKA is caused by an effective lack of insulin, leading to hyperglycemia and accumulation of ketoacids. Ketoacids are produced by the liver during states of low carbohydrate intake or availability as a side product of fat breakdown. The main ketoacid produced during the development of DKA is β -hydroxybutyrate (β -OHB) ***(Rewers Arleta et al., 2006).*** In diabetic ketosis (DK) and ketoacidosis (DKA), β-OH butyrate (β-OHB) is the major ketone body accumulated in blood. B-OHB is converted to acetoacetate and acetone which are excreted in urine. Serum β-OHB concentration is one of the best parameters reflecting the metabolic status in DKA ***(Turan Serap et al., 2008).***

In recent years, ketone-meters have been manufactured to measure capillary blood β-OHB by electrochemical method (Vanelli M et al., 2003), using the blood β-OHB meter (Optium, Abbott/Medisense Laboratories, Abingdon, UK) will gives a quantitative measurement of β-OHB in a range of 0.0–6.0 mmol/L from a single five microlitre prick capillary blood sample ***(Bektas F et al., 2004).***

AIM OF THE WORK

The aim of the study is:

1. To evaluate if bedside monitoring of blood beta-OHB levels can simplify management of DKA through elimination of superfluous laboratory monitoring.

2. To assess the effectiveness of a quantitative test of beta-hydroxybutyrate (B-OHB) against a commercial test for urine ketone bodies (UKB).

3. To determine if β-OHB levels measured using the bedside meter is correlated with laboratory values of pH, bicarbonate, blood urea nitrogen (BUN), and partial pressure of CO2 (pCO2) levels during treatment and resolution of DKA in pediatric patients.

4. To find whether blood beta-OHB meter is time and costs reducing in an intensive care unit and emergency department.

Diabetes Mellitus

Definition:

Diabetes mellitus is a group of metabolic diseases characterised by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The abnormalities in carbohydrate, fat, and protein metabolism that are found in diabetes are due to deficient action of insulin on target tissues. If ketones are present in blood or urine, treatment is urgent, because ketoacidosis can evolve rapidly. ***(ISPAD, 2009).***

The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels ***(American Diabetes Association, 2007).*** It is the most common endocrine – metabolic disorder of childhood and adolescence ***(Sperling, 2000).***

Diabetes mellitus has metabolic, vascular and neuropathic components that are interrelated; this makes DM a major health problem with long-term microvascular and macrovascular complications. The development and progression of diabetic complications are strongly related to the degree of glycemic control ***(Özmen and Boyuada, 2003).***

Classification:

WHO classified D.M. into clinical (normoglycemia, IGT/IFG, diabetes), and etiological types ***(Pickup and Williams, 2003).***

Table (1): Etiological classification of diabetes mellitus ***(ADA, 2007).***

I.	**Type 1 diabetes** (ß-cell destruction, usually leading to absolute insulin deficiency)
A.	Immune mediated
B.	Idiopathic
II.	**Type 2 diabetes** (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance)
III.	**Other specific types**
A.	*Genetic defects of ß-cell function:*
1.	Chromosome 12, HNF-1α (MODY3)
2.	Chromosome 7, glucokinase (MODY2)
3.	Chromosome 20, HNF-4α (MODY1)
4.	Chromosome 13, insulin promoter factor-1 (IPF-1; MODY4)
5.	Chromosome 17, HNF-1ß (MODY5)
6.	Chromosome 2, Neuro D1 (MODY6)
7.	Mitochondrial DNA
8.	Others
B.	*Genetic defects in insulin action:*
1.	Type A insulin resistance
2.	Leprechaunism
3.	Rabson-Mendenhall syndrome
4.	Lipoatrophic diabetes
5.	Others
C.	*Diseases of the exocrine pancreas:*
1.	Pancreatitis
2.	Trauma/pancreatectomy
3.	Neoplasia

4. Cystic fibrosis
5. Hemochromatosis
6. Fibrocalculous pancreatopathy
7. Others

D. Endocrinopathies:

1. Acromegaly
2. Cushing's syndrome
3. Glucagonoma
4. Pheochromocytoma
5. Hyperthyroidism
6. Somatostatinoma
7. Aldosteronoma
8. Others

E. Drug- or chemical-induced:

1. Vacor
2. Pentamidine
3. Nicotinic acid
4. Glucocorticoids
5. Thyroid hormone
6. Diazoxide
7. ß-adrenergic agonists
8. Thiazides
9. Dilantin
10. -Interferon
11. Others

F. Infections:

1. Congenital rubella
2. Cytomegalovirus
3. Others

G. Uncommon forms of immune-mediated diabetes:

1. "Stiff-man" syndrome
2. Anti–insulin receptor antibodies
3. Others

H. Other genetic syndromes sometimes associated with diabetes:

1. Down's syndrome
2. Klinefelter's syndrome
3. Turner's syndrome
4. Wolfram's syndrome