Title: THE TRIPHASIC EEG RESPONSE TO INSULIN-INDUCED HYPOGLYCEMIA IN HEALTHY SUBJECTS

Authors: RN Sakamoto, M.D., SA Chalew, M.D.[1], RJ McCarter, Jr. Ph.D.[2], MJ Matjasko, M.D. and AA Kowarski, M.D.[1]

Affiliation: Departments of Anesthesiology, Pediatrics (1) and Social and Preventive Medicine (2), University of Maryland School of Medicine, 22 South Greene Street, Baltimore, Maryland 21201.

Introduction: Current popular tight control of diabetics can result in an increased incidence of hypoglycemia[1]. The anesthetic management of diabetics can include the preoperative and intraoperative administration in insulin. Convenient methods for detecting hypoglycemia during anesthesia could improve the quality of anesthetic care of the diabetic patient.

A variety of computerized quantitative EEG monitors are commercially available. Computerized EEG (CEEG) monitoring may be useful in detecting hypoglycemia in anesthetized diabetic patients. In this study we attempt to initially characterize the CEEG changes due to insulin-induced hypoglycemia in healthy awake subjects.

Methods: Subjects were five healthy nondiabetic (3 females, 2 males), ages 16-35. This study complied with institutional standards regarding human studies; consent was obtained from each subject. After an overnight fast, an indwelling intravenous catheter was placed in a forearm vein and attached to a continuous glucose monitor. A heparin lock was placed in the other forearm for the insulin injection. Blood pressure (BP) and heart rate (HR) were recorded at 2.5 minute intervals with a Datascope automatic blood pressure monitor; respiratory rate (RR) and signs and symptoms were recorded every 5 minutes by an observer (RNS) present throughout each study. Except for periodic questioning about symptoms, subjects were asked to rest quietly with eyes closed.

CEEG monitoring was performed with a Lifescan monitor (Neurometrics, San Diego) with leads placed bifrontally and bimastoidally and referenced to FPZ. Raw EEG 2 second epochs were recorded onto magnetic tape and later analyzed for total power (amplitude ^{2},uV_2) and % total power in four frequency bands (0.5-3Hz delta, 3-8Hz theta, 8-12Hz alpha, 12-30Hz beta).

After baseline vital signs and EEG were recorded for 10 minutes, 0.075 units/kg of regular insulin was administered as an IV bolus. Glucose (G) was continuously monitored and recorded on computer. EEG artifact rejection due to subject movement was performed by the observer present.

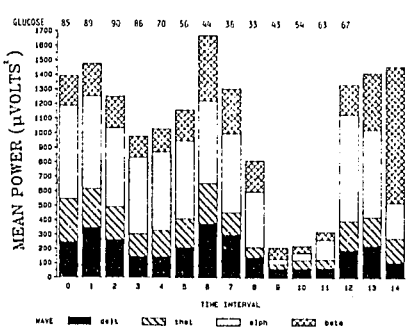
CEEG data was divided into 5 minute intervals for analysis. For aggregate analysis the natural log of power was derived. Analysis of variance of repeated measures was performed; the model evaluated the natural log of the power as a function of time interval (TI), $(TI)^2$, and $(TI)^3$. Changes in vital signs with time were evaluated statistically by analysis of variance of repeated measure differences between variables means at baseline and subsequent time intervals were tested by the Waller-Duncan multiple range method, with the signficance level set at 0.05.

Results: Normal intersubject variability in total power at baseline was noted. All subjects experienced symptomatic hypoglycemia of 38+6mg/dl occurring within 30-40 minutes of insulin administration followed by spontaneous recovery; none of the subjects required the administration of extra glucose. Aggregate and individual CEEG studies demonstrate a consistent triphasic EEG response. Phase I occurs 20-35 min. post-insulin injection (i.e. just prior to the blood G nadir) and is characterized by significant increases in total power and power in each frequency band. In Phase II, total power andpower in each frequency were significantly reduced; this phase coincided with rising blood G levels. Total and frequency associated power returned to baseline levels in Phase III with return of blood G to nonhypoglycemia levels (> 60mg%). Figure 1 shows the total power and frequency specific power for one hemisphere of one subject and is representative of the bihemispheric changes observed in all of the subjects.

RR increased from 15±5 (mean ±1SD) breaths/min. at baseline to 24±4 at the G nadir, gradually returning to baseline with recovery of G levels. Increased RR coincided with Phase I and ended with the beginning of Phase III. A significant increase in HR occurred during Phase I; mean BP fell significantly below baseline coinciding with the nadir of CEEG power and the initial portion of Phase III.

Discussion: In this study of health unanesthetized subjects, insulin-induced hypoglycemia to approximately 38mg% resulted in a characteristic sequence of changes in EEG activity as a recorded by CEEG analysis. This study suggests the feasibility of continuous CEEG monitoring to detect hypoglycemia in the anesthetized patient. Further studies are planned using unanesthetized diabetics and anesthetized healthy and diabetic subjects.

Figure 1:



References:

[1] Unger RM: Meticulous control of diabetics: benefits, risks and precautions. Diabetes 3:497-483, 1982.