Normal glucose values are associated with a lower risk of mortality in hospitalized patients

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Objective - Hyperglycemia is a common condition in hospitalized patients. The aim of the study was to investigate the relationships between glycemia upon admission and mortality in a heterogeneous group of adult patients.

Research Design and Methods - The three-year records released from a general hospital were associated to plasma glucose dataset of its general laboratory. A matched case control study was implemented (3338 cases-controls). All Patient Refined Diagnosis Related Groups and the Relative Risk of Death were the matching criteria. A multivariate conditional logistic regression model was used to evaluate the associations between death and glycemia.

Results - Higher in-hospital mortality was associated with hyperglycemia or hypoglycemia while the lower risk was observed for values between 78 and 101 mg/dl.

Conclusions - Our data confirm the relation between glycemia upon admission and mortality and suggest that slightly increased or decreased plasma glucose can be linked with increased mortality risks.
Hyperglycemia is a common co-morbid condition in hospitalized patients, independent of the diagnosis of diabetes, and is associated with adverse outcomes (1-4). Although there is strong evidence suggesting that tight glycemic control is intimately linked to an improved outcome in the intensive care unit (5), hyperglycemia in hospitalized patients is generally not considered a major therapeutic focus. It is important to determine target plasma glucose (PG) concentrations and glycemic thresholds associated with optimal benefits during hospitalization. The aim of this study was to investigate the relationship of PG on admission with in-hospital mortality and to identify the range of glycemic values associated with significant reductions of mortality risks in a heterogeneous group of adult hospitalized patients.

METHODS

Analyses included data released from 96,405 patients hospitalized for different pathologies at San Giovanni Battista Hospital of Turin, a large teaching general hospital excluding departments of Ophthalmology, Obstetrics and Gynecology, Pediatrics and Infectious Diseases, between October 1st 2003 and September 30th 2006. For every patient, administrative records were associated to the laboratory measurements dataset of PG. Of the 96,405 admissions, 26,409 (27.4%) were excluded because PG was not achieved upon admission to hospital. From this cohort, a matched case control study was implemented. Cases were defined as the in-hospital deaths. All patients discharged alive were considered as controls. Matching criteria were the All Patient Refined Diagnosis Related Groups (APR-DRGs) and their relative Risk of Death (RISKD)(6). APR-DRGs are DRG-based severity measurement systems taking into consideration: the principal diagnosis, age, interactions of multiple secondary diagnoses and combinations of non-operating procedures incorporated with the principal diagnosis. Among the 3,401 deaths, 63 records (62 with an APR-DRG 196: “Cardiac arrest, unexplained” and 1 with APR-DRG 130: “Respiratory system diagnosis with ventilator support 96+ hours”) were excluded from the study since were not find a surviving control. A total of 3,338 cases were thus matched with a random sample of controls within each matching stratum. This procedure led to a set of 6,676 patients, perfectly balanced for APR and RISKD distribution. All PG was determined in a central laboratory with a glucose analyser (Roche/Hitachi Modular D analyser: ACN 767, Indianapolis, IN). We performed a multivariate conditional logistic regression model to evaluate the associations between in-hospital mortality and a set of variables including demographic characteristics (sex, age, marital status, level of education) and clinical characteristics (type of admission, type of treatment and PG on admission). APR-DRGs and RISKD, as matching variables, were not included in the model. All the covariates were inserted in the model without any formal selection. PG measurements were added to the model as restricted cubic spline to investigate the association between in-hospital death and PG levels through a straight and smooth line outside the whole interval of values. Non linearity of the effects was eventually tested with a Chi-square type test. Values of PG minimizing the risk of death were determined using the inverse spline function and 95% confidence intervals were derived from bootstraps with 1000 runs. Data are reported as median and interquartile range and with 95% C.I whenever appropriate.

RESULTS

The whole population with PG available at admission presents 69,996 cases
(65:51-75 years, 42% female, 5% death); within these group we analysed a cohort of 3338 cases (death) versus 3338 controls (alive) (70:59-78 year vs 73:63-80; 40% vs 42% female; 99:82-128 mg/dl vs 107:85-144 PG on admission). The effect of PG adjusted by administration data was not linear as described in Figure 1. Accordingly, the minimal risk of in-hospital mortality was found at PG levels of 89:78-101 mg/dl. The adjusted ORs of deaths for PG on admission from 100 mg/dl to 200 mg/dl is 1.32 (1.22-1.43), while from 80 mg/dl to 60 mg/dl it is 1.06 (1.04-1.07).

DISCUSSION

A significant number of in-hospital patients display hyperglycemia, that can be the cause of admission or more frequently co-morbidity. Previous reports (7-9) have indicated the relationship between hyperglycemia and prognosis in critically ill patients. The main novelty of the present study is that even moderate glucose elevations or reductions are associated with increased in-hospital mortality in this heterogeneous population. In this study we have analysed a large cohort of patients hospitalized for multiple pathologies with a nested case-control study. Furthermore, our observations strongly suggest that, independently of the cause of hospitalization, a patient with an optimal PG between 78 and 101 mg/dl displays lower risks of death. Interestingly, this optimal glycemic range is closely related to normoglycemic values as defined by criteria of the ADA (10). The main limitation of this study is its retrospective nature. The retrospective design prevents concluding whether or not hypo or hyperglycemia was a cause of increased mortality or just a marker of increased risks of mortality, however we observe a strong association between hospital mortality and glycemic levels. Other limitations are: 1) missing data for 27.4% of all admitted patients (this data gap could be the consequence of the use of point of care procedures) in any case within this group the mortality rate was only 3.5%; 2) some specialties were excluded from the study because allocated in other hospitals; 3) we do not know the duration of hypo or hyperglycemia; 4) hypoglycemic values could result from diabetes therapy or critical diseases. However, these data confirm the importance of glycemic value on hospital admission (11). Lowest hospital mortality rates were observed among patients with PG concentrations between 78 and 101 mg/dl and even a moderate variation below or above these cut-off values may increase mortality in a heterogeneous group of patients.

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