Evidence of Subcutaneous Tissue Lipolysis Enhancement by Endogenous Cortisol in Critically Ill Patients Without Shock

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Abstract. Background/Aim: Cortisol is involved in many aspects of adipose tissue metabolism. A positive association between plasma cortisol and lipolysis has been observed. Critically ill patients exhibit 'lipemia of sepsis'. The aim of the present study was to study, in septic ICU patients, adipose tissue lipolysis in relation to tissue cortisol using microdialysis (MD). Patients and Methods: We studied 17 mechanically-ventilated patients (9 men; mean±SD age=63±19 years) with a diagnosis of severe sepsis. Upon ICU admission, an MD catheter was inserted under sterile conditions into the subcutaneous adipose tissue of the upper thigh. On days 2, 3 and 4, MD samples were collected six times per day for glycerol (used as an index of lipolysis) and tissue cortisol determinations. The mean of these six collections was used for analysis (normal values for adipose tissue glycerol <200 μmol/l). Statistics were carried-out with analysis of covariance (ANCOVA) and linear regression. Results: More than half of the samplings (19/31) indicated accentuated lipolysis with above-normal MD glycerol levels. By ANCOVA, MD glycerol (log values) was associated with MD cortisol (log values) (p=0.012) and was not associated with age or day of sampling. Furthermore, MD glycerol (log values) was positively correlated to MD cortisol (log values) (r=0.490, p=0.012). Discussion: Changes in interstitial/tissue cortisol may not be reflected in (total) plasma cortisol concentration. Thus, it is interesting that we observed, albeit weak, an association between tissue lipolysis (via MD glycerol levels) and MD cortisol, verifying (although modestly so) the well-known association between lipolysis and cortisol.

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hospitalized, mechanically ventilated, critically ill patients admitted to the 25-bed medical-surgical adult intensive-care unit (ICU) of a university hospital between March 2008 and July 2012. The hospital’s Ethics Committee approved the study (Approval number: 2/02-02-2011) and informed consent was obtained from patients’ relatives. Critically ill patients analyzed in the current study have been shared in other publications by our research group (3, 12, 13, 10, 14, 15, 4). Inclusion criteria were: mechanical ventilation and severe sepsis (16). Severe sepsis was defined according to the International Sepsis Definitions Conference (11). Patients were not enrolled in the study if one of the following exclusion criteria was present: age less than 18 years; glucocorticoid administration prior to ICU admission; mechanical ventilation for more than 48 hours before ICU admission; no need for intubation and mechanical ventilation during ICU stay; do-not-resuscitate clinical conditions; brain-death upon ICU entry and HIV infection. Patients with septic shock were excluded from the present study. Upon ICU admission an MD catheter (CMA 60; CMA Microdialysis AB, Stockholm, Sweden) was inserted under sterile conditions into the subcutaneous adipose tissue of the upper thigh, as previously described (3, 12, 10, 17, 13). On day 2 (n=12), day 3 (n=8) and day 4 (n=11), MD samples were collected six times per day for determinative of MD glycerol (used as an index of lipolysis) and MD cortisol. The mean of these six collections was used for analysis (normal values for MD glycerol <200 μmol/l (12, 17, 4). Statistics were carried out with analysis of variance, analysis of covariance (ANCOVA) and linear regression.

Results

The mean±SD APACHE score on ICU admission was 14.5±4.6; the SOFA score was 4.9±2.8. Four patients died. Above-normal MD glycerol levels were measured in more than half (19/31) of the samples.

The mean±SD MD cortisol levels of patients with accentuated lipolysis (i.e. those with above-normal MD glycerol; 1.20±1.36 μg/dl) and those without lipolysis (i.e. those with normal MD glycerol; 0.52±0.43 μg/dl) were not significantly different (ANOVA p=0.088). However, by ANCOVA, MD cortisol (log values) was associated with MD glycerol (log values) (p=0.012) and was not associated with age or day of sampling. Furthermore, we found a significant positive correlation of MD glycerol (log values) with MD cortisol (log values) (r=0.490, p=0.012) (Figure 1).

Discussion

In the present study, we demonstrated that the tissue level of endogenous cortisol is related to local lipolysis, as reflected by its relationship to the level of tissue glycerol, in critically ill patients without shock.

Patients in a critical state exhibit increased lipolysis, as reflected by high subcutaneous MD glycerol levels, but few studies of tissue lipolysis in such patients have been published. Martinez et al. evaluated MD glycerol in 11 critically ill patients (18) (this small number of patients is a major limitation); they observed higher MD glycerol concentrations in their five patients with sepsis, but not in their six patients with circulatory failure, compared to healthy individuals.

In a recent study, we noted increased lipolysis in critically ill patients receiving glucocorticoids (4). In fact, our previous work indicates that in patients with septic shock, lipolysis is modified by exogenous norepinephrine in early critical illness, whereas this effect becomes less prominent later on, and at that time, an effect of exogenous glucocorticoids becomes evident (7, 8).

Regional tissue blood flow distribution must play a role in the association of MD cortisol and MD glycerol in critically ill patients. In an earlier MD study, we did not observe any significant correlations between MD cortisol and MD glycerol (10) but the study group comprised mostly of patients with septic shock, whereas in the present study, patients with septic shock were excluded.

A limitation of the study is that we measured MD glycerol. Glycerol in the MD fluid (19) may not be the ideal marker for assessing lipolysis; free fatty acids would have been a more obvious choice. However, MD is fraught with technical difficulties when working with lipophilic substances (such as free fatty acids); these difficulties are related essentially to poor recovery rates (20).

Changes in interstitial/tissue cortisol may not be reflected in (total) plasma cortisol concentration (21, 10). Thus, it is interesting that we observed an association between tissue lipolysis (via MD glycerol level) and endogenous tissue cortisol (MD cortisol), verifying the well-known association between lipolysis and cortisol (9).
References


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