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References


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Utility of Serum Fatty Acid Concentrations as a Marker for Acute Myocardial Infarction and Their Potential Role in the Formation of Ischemia-Modified Albumin: A Pilot Study

To the Editor:

Myocardial ischemia, which precedes acute myocardial infarction (AMI)1 is associated with changes in human serum albumin (HSA) that result in decreased divalent cobalt ion (Co2+) binding. This reaction the basis of the serum colorimetric Co2+/HSA binding assay, which is an indirect measure of ischemia-modified albumin (IMA).

Previously we showed that IMA was a useful diagnostic test for the diagnosis of myocardial ischemia in suspected acute coronary syndromes (ACS) patients (area under the ROC curve 0.95) (1). The IMA values are reversible between ischemic and nonischemic conditions (2). Furthermore, it is known that HSA is the primary binder of fatty acids, commonly known as free fatty acids (FFA), and that plasma concentrations of FFAs are increased during myocardial ischemia owing to a compensatory hyperadrenergic state. Considering these findings, we explored the hypothesis that FFA-induced conformational perturbations of HSA are the basis of the IMA test, and FFAs may themselves serve as a potential marker(s) of myocardial injury.

Using pooled serum specimens, we performed an in vitro study to test the effect of physiolog-
cal significance was assessed by expressed as mean electrophoresis esterification, and capillary-zone thin-layer chromatography, trans-using organic solvent extraction, IMA values. Oleate and arachidonic acid of fatty acids showed elevations in concentrations in non-AMI and AMI patients. Each group consisted of 13 serum samples.

Table 1. Quantitative serum concentrations for 6 FFA levels.a

<table>
<thead>
<tr>
<th>Fatty acid</th>
<th>Non-AMI group</th>
<th>AMI group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oleic acid</td>
<td>0.24 ± 0.14</td>
<td>0.52 ± 0.27</td>
<td>0.003</td>
</tr>
<tr>
<td>Palmitic acid</td>
<td>0.13 ± 0.06</td>
<td>0.26 ± 0.13</td>
<td>0.0027</td>
</tr>
<tr>
<td>Linoleic acid</td>
<td>0.13 ± 0.07</td>
<td>0.22 ± 0.13</td>
<td>0.0425</td>
</tr>
<tr>
<td>Stearic acid</td>
<td>0.06 ± 0.02</td>
<td>0.09 ± 0.03</td>
<td>0.007</td>
</tr>
<tr>
<td>Palmitoleic acid</td>
<td>0.02 ± 0.01</td>
<td>0.03 ± 0.02</td>
<td>0.048</td>
</tr>
<tr>
<td>Arachidonic acid</td>
<td>0.01 ± 0.003</td>
<td>0.02 ± 0.01</td>
<td>0.058b</td>
</tr>
</tbody>
</table>

* Values are mean ± 2 SD, and showed significant increases (P < 0.05) except for arachidonic acid in the AMI compared to non-AMI patients. Each group consisted of 13 serum samples.

b Statistically not significant.

Letters to the Editor

nate additions at a comparable fatty acid/HSA molar ratio of about 8 produced a significant increase in the percentage IMA values by 32.3 ± 0.8 and 37.9 ± 0.5, respectively. Serum FFA concentrations of persons with and without AMI were 1.03 ± 0.45 mmol/L and 0.77 ± 0.34 mmol/L, respectively (P < 0.018), and in the same 2 groups the IMA values were 119.4 ± 37.3 U/mL and 88.6 ± 19.3 U/mL, respectively (P < 0.005). The ratios of mean values of FFA (1.34) and IMA (1.35) for AMI and non-AMI individuals are virtually identical, suggesting a temporal and proportional relationship. The correlation coefficient between FFA and IMA values in our test patients was 0.3293 (P = 0.012), indicating a statistically significant positive relationship. In the analysis of individual FFAs, 5 fatty acids, oleic, palmitic, linoleic, stearic, and palmitoleic acid, showed statistically significant elevations in AMI patients compared to non-AMI individuals (Table 1). Several potential cardiac markers for the diagnosis of ACS syndrome continue to be investigated (4). Our study shows that total FFA concentrations as well as specific FFAs are increased in AMI and may have potential diagnostic value. Changes in IMA values during AMI are likely caused by reversible conformational changes in HSA that are associated with FFA fluxes. The formation of IMA during ACS has been attributed to the modifications that may occur in N-terminal region of albumin, because Co2+ is thought to bind primarily to this site. However, a recent study has shown that the Co2+ binding site(s) are not located at the N-terminus (5). Because N-terminal sequence analysis of purified HSA obtained from ischemic patients with high IMA values did not show N-terminal modifications (1), other sites are likely involved, leading to perturbations in the conformation of albumin. Our study suggests a plausible but not a causal relationship between FFA and IMA, and a potential role for measurement of total FFA and specific FFAs in ACS.

Author Contributions: All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

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Potential Conflict of Interest form.

Potential conflicts of interest:

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Editor’s Note: Inverness Medical Innovations has notified their customers that effective June 30, 2009 that they will discontinue the sale and distribution of the Albumin Cobalt Binding Test due to insufficient demand to sustain production.

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References


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Use of a Resident On-Call Database to Characterize Communication Failures in Communicating Critical Laboratory Results

To the Editor:
The Clinical Laboratory Improvement Amendments require that laboratories have a procedure for reporting “imminent life-threatening results” to caregivers. Although this system has improved timely intervention, inability to reach care providers undermines its impact (1). Prior analysis of critical result reporting practices has identified qualitative factors that lead to delays in critical result reporting, such as patient location, missing provider information, patient heterogeneity, and nonideal “panic” values (2). However, we have not found reports quantifying sources of communication failures in critical result reporting. Here we report sources of communication failures in reporting critical results in our healthcare system, which has 950 beds equally divided between a university and county hospital.

In our system, more than 99% of the time, critical results are called to a care provider by a medical technologist. If this method is unsuccessful, the technologist elicits assistance from the laboratory medicine resident on call to ensure that the value is communicated and appropriate action taken. In 2004 our Clinical Pathology residency program began maintaining an online database of all calls to the on-call laboratory medicine residents or fellows (3), providing us with a unique opportunity to quantitatively identify sources of communication failures in critical result reporting. This database allows assessment of the causes of communication failure, and subsequent hypothesis-driven design of appropriate interventions.

During the period reflected in our dataset, August 2004 through January 2006, the clinical laboratories performed about 4 million billable tests (generating 15 million reportable results) annually. Of these results, about 100 000 (0.7%) were critical results. Critical limits are defined for 61 tests; 15 of these tests accounted for approximately 90% of total critical results. Positive blood cultures, the only microbiology critical result among these 15, accounted for approximately 7% of the total. Inpatients accounted for approximately 80% of orders for tests with critical limits and approximately 98% of critical results.

Our 18-month dataset contained 6700 calls to on-call laboratory medicine residents and fellows. Calls regarding critical values were accrued by searching the “Call Classification”, “Specific Re-