BRIEF REPORT

Insulin-like growth factor 1 and dehydroepiandrosterone levels in alcoholic liver cirrhosis

Werner Dammermann, Benedikt Seckinger, David Füller, Stefan Lüth and Florian Hentschel

Department of Gastroenterology and Hepatology, Brandenburg Medical School (Theodor Fontane), Brandenburg, Germany

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Correspondence
Dr. med. Florian Hentschel, Zentrum für Innere Medizin II, Hochschulklinikum Brandenburg der MHB, Hochstr. 29, 14770 Brandenburg an der Havel, Germany.
Email: f.hentschel@klinikum-brandenburg.de

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Introduction

Sarcopenia is a common phenomenon in liver cirrhosis (LC), where it is closely correlated to morbidity and mortality.\(^1,2\) Suspected reason for sarcopenia in LC is a lack of anabolic hormones, but this has only been demonstrated for insulin-like growth factor 1 (IGF-1) and for testosterone in male patients.\(^3,4\)

In this study, we prospectively measured the levels of two anabolic hormones in a mixed group of male and female cirrhotic patients: IGF-1 as an example of an anabolic peptide, and dehydroepiandrosterone (DHEA) as an example for a steroid that is present in both sexes. We then correlated the results to the Child–Pugh scores of our patients and to a group
of healthy controls, the hypothesis being both would be lower in the LC group and within this group even lower with higher scores.

**Methods**

Blood samples were drawn from 22 patients with LC. All were alcohol-induced and, at the time of being included, abstinent. Nine were female, 13 were male, mean age was 64 ± 14 years. We additionally drew samples from 8 healthy controls. One was female, 7 were male, mean age was 63 ± 10 years. DHEA and IGF-1 levels were measured using commercial ELISA kits (Test kit 1: EQ6154-9601, Euroimmun AG, Luebeck, Germany. Test kit 2: AB108873, Abcam PLC, Cambridge, UK). Test kit 1 is highly specific for DHEA, with cross-reactivity for DHEA-S or 16 hydroxydehydroepiandrosterone sulfate (16-OH-DHEA) below 0.05%. Detection limit of test kit 2 was 42.7 ng/mL IGF-1.

Sarcopenia was assessed in all patients and controls using the SARC-F questionnaire (Strength, Assistance in walking, Rise from a chair, Climb stairs, Falls). All individuals with SARC-values ≥ 4 were counted as sarcopenic. Additionally, all individuals underwent a handgrip strength test. Here, values ≤ 18 kg for women or 25.5 kg for men were counted as sarcopenic. For LC patients, Child–Pugh Scores were calculated out of existing clinical data.

All procedures followed were in accordance with the standards of the responsible committee on human experimentation (Study No. SAKL E-01-20 190 412) and the Helsinki Declaration of 1964 and later versions. Informed consent or substitute (Study No. SAKL E-01-20 190 412) and the Helsinki Declaration of the responsible committee on human experimentation for it was obtained from all patients included in the study.

**Results**

Mean IGF-1 level in the control group was 202 ± 115 ng/mL (Fig. 1a). Mean IGF-1 levels in the LC group were significantly lower compared to controls at 101 ± 39 for Child A patients (P = 0.03), and 75 ± 40 for Child B patients (P < 0.001). Levels in all Child C patients were below the detection limit of 42.7 ng/mL (P < 0.001). Mean DHEA level in the control group was 5.6 ± 3.8 ng/mL (Fig. 1b). Mean DHEA levels in the LC group were 12 ± 5.9 ng/mL (P = 0.6) for Child A patients, 13.5 ± 10.8 ng/mL (P = 0.3) for Child B patients, and 25 ± 14.7 ng/mL (P = 0.006) for Child C patients.

Sarcopenia, as defined by SARC-values ≥ 4, was present in 1 out of 8 controls (12.5%), 1 out of 6 Child A patients (16.67%), 6 out of 11 Child B patients (54.54%), and 4 out of 5 Child C patients (80%). Sarcopenia, as defined by Handgrip strength values ≤ 18 kg for women or 25.5 kg for men, was present in 1 out of 8 controls (12.5%), 2 out of 6 Child A patients (33.3%), 7 out of 11 Child B patients (72.75%), and 4 out of 5 Child C patients (80%) (Table 1).

In sarcopenic individuals of any definition, the median IGF-1 level was 48.7 ng/mL (min 47.2; max 476.2), median DHEA level was 12.1 ng/mL (min 2.8; max 45.3). In non-sarcopenic individuals, median IGF-1 level was 104.7 ng/mL (min 47.2; max 195.4), median DHEA level was 8.9 ng/mL (min 2.4; max 24.2) (Fig. 2).

**Discussion**

It is generally suspected that sarcopenia in liver cirrhosis is due to decreased levels of various anabolic hormones. In this study, we tested that hypothesis on two exemplary hormones: IGF-1 was chosen as a peptide that is unrelated to sex hormones. DHEA was chosen as a steroid that is not only a progenitor of male and female sex hormones alike, but that also acts as an anabolic hormone in...
In contrast, levels of DHEA were surprisingly elevated in alcoholic liver disease. 

Because of the small sample size and skewed distribution, no inferential statistics procedures were performed.

Both mechanisms are possible in principle, but none of them is proven. Additionally, none of them would explain the ineffectiveness of the raised DHEA levels in averting sarcopenia in liver cirrhosis.

To put it into perspective, this is a short report on a preliminary study, and as such, it has limitations. First, it is based on a small single cohort, so there is the possibility of pseudo-significance. Secondly, to keep the group consistent, we intentionally limited it to alcohol-induced LC. So theoretically, it is possible that a different cohort of non-alcoholic cirrhosis patients would show different results. Also for consistency, we limited it to two representative hormones and did not test for their metabolites. We have already started a more extensive prospective study that will hopefully clarify these points.

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Figure 2 Insulin-like growth factor 1 (IGF-1) and dehydroepiandrosterone (DHEA) levels in sarcopenic and non-sarcopenic individuals. Because of the small sample size and skewed distribution, no inferential statistics procedures were performed.
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