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Short-Communication

Evaluation of Herbalife Nutritional Supplements in the Hepatic Function of Rats

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ABSTRACT

The intake of nutritional supplements among people who aim for weight loss has increased all over the world given the fact it is easily acquired without the need of a medical prescription.The goal of this study was to research the presence of toxicity due to the intake of Herbalife protein supplements and shakes in an animal model. Twenty-one male Wistar rats were divided in three groups: control, shake and protein. The shake and protein groups received 100 mg/kg/day of the supplement whereas the control group received 0.5 mg/kg/day of water. Supplementation regimen lasted two months and after this period laboratory exams and histological analysis were performed in order to evaluate hepatic lesions. The groups showed no differences in values of GGT, alkaline phosphatase, AST, ALT, cholesterol, HDL or triglycerides. All the toxicity reports related to Herbalife supplements are over longer periods of time of intake than the period established in this model. There are no reports on how the response of rats to this kind of supplementation works. The mechanism of hepatotoxicity in humans suggests an immune-mediated reaction. The presented model could not show the expected toxicity, it is reasonable to conclude that there is a direct relation between hepatic lesions in humans and the intake of Herbalife supplements.

INTRODUCTION

The indiscriminate use of nutritional supplements or formulas that promise fast weight loss has raised safety concerns on the consumption of such products for the last 10 years. Part of these concerns lies in the facility to sell these products and the difficulty to track them down once they are not pharmaceutical controlled substances and consumers themselves become sellers. In 2006 Hofman reported the association between an acute hepatitis case and the intake of Herbalife® supplements (Hofman *et al.,* 2006). Since then the number of reports on possible associations between these two situations have increased. The difficulty to establish this causal relation is owing to the fact that the components of the formulas as well as the way these formulas are prepared in the innumerable manufacturing facilities all over the world are unknown. Herbalife products are distributed in over 60 countries worldwide, many times by consumers who become sellers, and they are classified as nutritional supplements and herbs. They come in form of shakes, powdered supplements, cosmetics, energetic bars and capsules for weight control (Bunchorntavakul and Reddy, 2013). The goal of this study was to research the possible hepatotoxicity of Herbalife® protein supplements and shakes in an animal model.

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MATERIALS AND METHODS

This is a randomized trial performed with adult Wistar rats which were separated in three groups: control group, Herbalife® shake group and Herbalife® protein supplement group. The study was approved by the Animal Research Ethics Committee of Faculdade de Medicina do ABC under the number 08/2008. Twenty-one adult male rats were divided in three groups of seven animals each. They were kept under the same conditions of water and an ad libitum diet over a two-month period. The control group received 0.5 ml/kg/day of water, the shake group received 100 mg/kg/day of Herbalife® shake and the protein group received 100 mg/kg/day of Herbalife® protein supplement. All animals were gavage fed with the dosage recommended by the manufacturer during the period of two months. After two months, in order to evaluate the possibility of hepatic dysfunction, the following laboratory exams were performed: gamma-glutamyl transferase, AST, ALT, alkaline phosphatase, total cholesterol, HDL and triglycerides. The results of the continuous variables were expressed as the mean and standard deviation. The variance analysis between the groups was performed by means of ANOVA test and the accepted alpha value was 5 %.

RESULTS AND DISCUSSION

Table 1 (tab.1) presents the values found for the studied variables. Levels of GGT, AST, ALT, alkaline phosphatase, total cholesterol, HDL and triglycerides showed no difference through the variance analysis between the groups. There was no difference in terms of weight gain between the groups. Human beings, in their constant search for effortless weight loss, have been developing innumerable formulas to meet this unattainable goal throughout time. The development of promising weight-loss formulas labeled as nutritional supplements instead of medication has enabled their viral distribution among all social classes in both hemispheres. There is no strict control on local distributors or even a pharmacovigilance control that would help track down adverse effects or contamination events during the production process. First reports on hepatotoxicity involving these formulas were brought to light in no time at all. In 2008 Manso *et al* started writing case reports in Spain on the hepatotoxicity attributed to the intake of Herbalife® supplements (Manso *et al.,* 2008). The family of supplements is big and their formulas contain protein, carbohydrate, green tea, aloe vera, extracts from the plant guarana (*Paulinia capuana)* and other undescribed substances (Manso *et al.,* 2011). Schoepfer *et al* reported a series of 10 cases of toxicity related to the consumption of Herbalife® products. Investigation was carried out through the completion of a questionnaire, and in 5 out of those 10 cases the hepatic biopsy was made necessary revealing necrotic and subacute cholestatic hepatitis (Schoepfer *et al.,* 2007). Stickel *et al* showed contamination by the *Bacillus subtilis* in a report on acute hepatotoxicity after the intake of such supplements (Stickel *et al.,* 2009).

Consumers in general use more than one of those products along with medications they may be routinely taking. Researchers have been struggling to establish a causal relation between hepatic lesions and the association of Herbalife® products.

Owing to this difficulty one of the tools used to establish this causal relation is the WHO Causality Assessment Criteria which determines the analysis by means of three principles: reasonable time relation to the intake of the dietary supplement; exclusion of other causes of hepatic disease; reversal of the symptoms and the signs of hepatic disease after the intake interruption (Meyboom,1997) .

Moreover, the length of time of intake seems to have a relation with the development of hepatic lesions in humans where the physiopathological mechanism is no clearly established. Elinav *et al* , in a series of 11 patients and an average time of intake of 11.9 months, observed a mechanism of hepatocellular lesion in hepatotoxicity cases that needed biopsy, which suggested immune-mediated mechanism of action due to the presence of autoantibodies in some samples (Elinav *et al.,* 2007) .

In a recent study our team of researchers used the same animal model with the green tea supplement which has been used as a possible weight loss agent worldwide. There have been reports on hepatotoxicity since 1999 and they follow the same pattern of hepatocellular lesion and biliary stasis; however, it was upon the cathepsin action[2] and the generation of reactive oxygen species associated with the fasting period. Differences between groups in terms of laboratory and histologic parameters could not be observed (Feder *et al.,* 2011).

The model developed with the shake and protein supplements failed in showing this relation.

Table. 1: Group analysis and laboratory data.

	Shake	Protein	Control	p
AST (U/l)	109.8 ± 61.4	112.7 ±32.4	158.8 ±79.7	0.28
ALT (U/l)	52.7 ±11.1	52.7 ±10.5	67.7 ±42.5	0.50
GGT (U/l)	3.3 ±3.1	3.6 ±4.6	3 ±3.3	0.86
Alkaline Phosphatase (U/l)	168.2 ±39.1	134.8 ±14.9	128 ±41.4	0.10
Cholesterol(mg/dl)	49.2 ±7	57.8 ±6.6	53.7 ±10.8	0.21
HDL(mg/dl)	19.7 ±4.9	18.3 ±6	18.5 ±6	0.89
Triglycerides(mg/dl)	127.3 ±89	166.6 ±56.7	113.3 ±34.9	0.28

Results expressed in means and standard deviations.

All the analyzed studies include human cases and reports on animals are quite rare. Nevertheless, determining the exact composition of the supplements is still a major concern for the reasons here stated. The allotted period of time for this animal model study is sufficient to establish this relation.

Maybe the immune response, suggested as responsible for hepatocellular lesions, is not the same in humans and rats, and so this model would not have the same evolution characteristic of hepatic lesion as it is observed day by day. The conclusion is that more human models that establish this relation should be developed. However, it is impossible to turn a blind eye on the risks of consumption of these supplements when it comes to the development of hepatic lesions either owing to immune mediated response or the long-term consumption, or still given the possible contamination of the products during the production line.

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