Pathophysiology 24 (2017) 39–44

Contents lists available at ScienceDirect

Pathophysiology

journal homepage: www.elsevier.com/locate/pathophys

Folic acid protects against lead acetate-induced hepatotoxicity by decreasing NF-κB, IL-1β production and lipid peroxidation mediataed cell injury

Eman S.H. Abd allah [a,*], Dalia M. Badary [b]

[a] Medical Physiology Department, Faculty of Medicine, Assiut University, Assiut, Egypt
[b] Pathology Department, Faculty of Medicine, Assiut University, Assiut, Egypt

ARTICLE INFO

Article history:
Received 14 November 2016
Received in revised form 19 January 2017
Accepted 4 February 2017

Keywords:
Lead acetate
Hepatotoxicity
Folic acid
Inflammation

ABSTRACT

Folic acid plays an important role in cellular metabolic activities. The present study was designed to investigate the protective effect of folic acid against lead acetate-induced hepatotoxicity. Twenty four male Wistar albino rats were randomly divided into four groups, six animals each. Negative control group received the vehicle, positive control group received 1 mg/kg folic acid for five consecutive days/week for 4 weeks orally, lead-exposed group received 10 mg/kg lead acetate intraperitoneally (IP) for five consecutive days/week for 4 weeks, and lead-treated group received 10 mg/kg lead acetate IP and 1 mg/kg folic acid orally for five consecutive days/week for 4 weeks concurrently. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and γ- glutamyltransferase (GGT) were measured. Hepatic total peroxide and interleukin-1β (IL-1β) were also investigated. Histopathological studies using hematoxylin-eosin (H&E) and periodic acid shiff's (PAS) were carried out. The expression of nuclear factor kappa B (NF-κB) was evaluated using immunohistochemistry. Serum AST, ALT and GGT and hepatic total peroxide and IL-1β were significantly increased in lead-exposed group and were positively correlated with hepatic lead level. Moreover, lead-exposed rats showed hydropic degeneration, nuclear vesiculation, high lymphocytic infiltration, depletion of glycogen content and NF-κB expression. Concomitant folic acid administration resulted in a significant alleviation of biochemical and structural alteration-induced by lead. This was associated with reduction of hepatic total peroxide and IL-1β and reduction of NF-κB expression. In conclusion, folic acid protects against lead acetate-induced hepatotoxicity by decreasing NF-κB, IL-1β production and lipid peroxidation mediataed cell injury.

1. Introduction

Lead, a poisonous heavy metal, is considered one of the most widely occupational and environmental hazards. Contaminated water and polluted air and soil are the main sources of lead [1]. Workers in paint, ceramic, glass, battery and ammunition industries are the most susceptible to lead poisoning. Lead poisoning results in multiorgan toxicity. Liver is considered the largest repository of lead followed by renal cortex and medulla. The mechanism of lead-induced hepatotoxicity is not clearly determined; however oxidative stress was suggested to be the main mechanism of lead toxicity [2].

Folic acid, also known as vitamin B9, is important for DNA synthesis and cell division. In addition, it possesses anti-oxidant activities; it scavenges free radicals and thereby preventing cellular damage [3]. Moreover, folic acid interacts with nitric oxide synthase and reduces the formation of superoxide [4]. It has been shown that folic acid has a hepatoprotective effect against ischemic reperfusion injury through its anti-oxidant effect [3]. To our knowledge, the protective effects of folic acid against lead acetate-induced hepatotoxicity have not been determined. Thus, the present study was conducted to examine the protective effects of folic acid against lead-induced hepatotoxicity and the possible mechanisms underlying these effects.

* Corresponding author at: Physiology Department, Faculty of Medicine, Assiut University, Assiut, Egypt.
E-mail address: eman_sayyed2@yahoo.com (E.S.H. Abd allah).

http://dx.doi.org/10.1016/j.pathophys.2017.02.002
0928-4680/

Table 1
Initial and final body weights, % of change in body weight, liver weight and liver to final body weight ratio (%) in different experimental groups.

Variables	Negative control group	Positive control group	Lead-exposed group	Lead-treated group
Initial body weight (g)	127.5 ± 2.1	126.6 ± 2.5	134.2 ± 6.7	133.3 ± 5.7
Final body weight (g)	162.5 ± 2.2	158.3 ± 2.1	103.3[a,b] ± 3.3	131.6[a,b,c] ± 6.5
% of change in body weight	27.7 ± 3.6	25.3 ± 3.5	−22.4[a,b] ± 3.2	−1.3[a,b,c] ± 1.9
Liver weight (g)	5.4 ± 0.08	5.3 ± 0.06	4.7 ± 0.25	5.2 ± 0.23
Liver weight to final body weight ratio (%)	3.3 ± 0.04	3.4 ± 0.02	4.6[a,b] ± 0.3	3.9 ± 0.19

Note: Data presented as means ± SEM ($n = 6$ in each group).
[a] Significantly difference vs the negative control group ($p < 0.05$).
[b] Significantly difference vs the positive control group ($p < 0.05$).
[c] Significantly difference vs the lead-exposed group ($p < 0.05$).

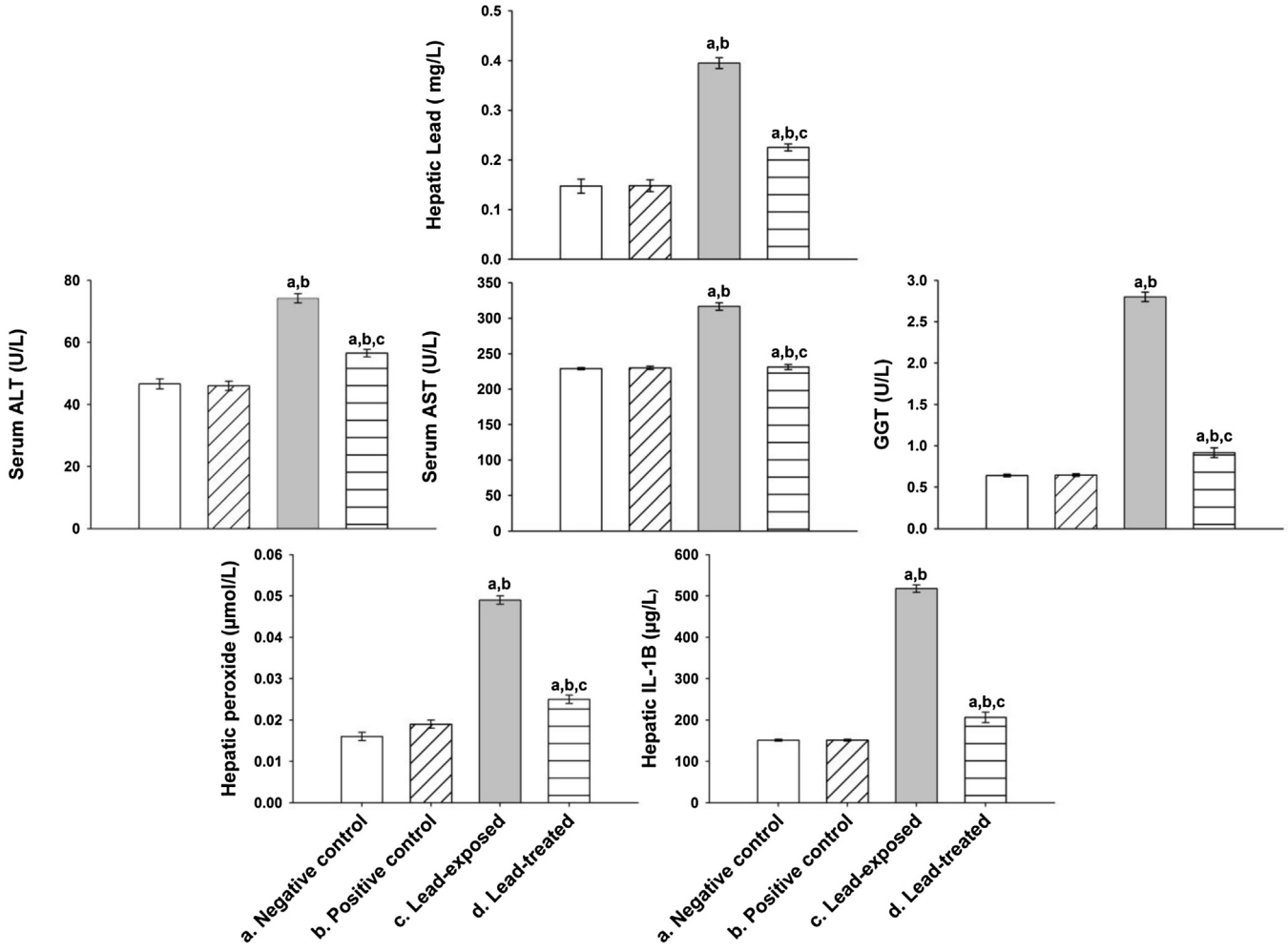

Fig 1. Levels of lead in the liver, serum ALT, AST and GGT and hepatic total peroxide and IL-1β in different experimental groups. Data presented as means ± SEM ($n = 6$ in each group).[a] Significantly difference vs the negative control group ($p < 0.05$).[b] Significantly difference vs the positive control group ($p < 0.05$).[c] Significantly difference vs the lead-exposed group ($p < 0.05$).

2. Material and methods

2.1. Drugs and chemicals

Lead acetate 3 hydrate (El Nasr Pharmaceutical chemical Co., Egypt) was freshly dissolved in saline (0.9%). Folic acid was purchased from Oxford laboratory (Mumbai) and was dissolved in saline (0.9%). Lead acetate dose was chosen according to Hamed et al. [5]. The dose of folic acid was chosen according to a previous study [6] in which therapeutic effects were observed and no toxicity was identified.

2.2. Animals

Twenty four adult male Wistar albino rats, weighing 120–150 g, were used. All animals were maintained under a natural light–dark cycle and room temperature and provided with standard laboratory chow and water *ad libitum*. The research protocol complied with the "Guidelines of Experiments on Animals" and was approved by the ethics committee at the Faculty of Medicine, Assiut University, Egypt.