Saudi Journal of Biological Sciences xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Saudi Journal of Biological Sciences

journal homepage: www.sciencedirect.com

Original article

Susceptibility of mice strains to oxidative stress and neurotransmitter activity induced by *Plasmodium berghei*

Esam M. Al-Shaebi [a], Walid F. Mohamed [b], Saleh Al-Quraishy [a], Mohamed A. Dkhil [a,c,*]

[a] Department of Zoology, College of Science, King Saud University, Saudi Arabia
[b] Department of Biological and Geological Sciences, Faculty of Education, Ain Shams University, Egypt
[c] Department of Zoology and Entomology, Faculty of Science, Helwan University, Cairo, Egypt

ARTICLE INFO

Article history:
Received 1 December 2016
Revised 3 January 2017
Accepted 26 January 2017
Available online xxxx

Keywords:
Mice strain difference
Oxidative stress
Neurotransmitters
Plasmodium berghei

ABSTRACT

This study investigated the susceptibility of female C57Bl/6 and Swiss Albino mice to oxidative stress and neurotransmitters activity induced by *Plasmodium berghei*. On day 9 p.i. with *P. berghei* infected erythrocytes, the mice reduced in weight. This weight loss was markedly higher in SW mice and reached about −14%. Also, the infection was able to cause oxidative damage to the brain tissue. Catalase activity as well as glutathione, malondialdehyde and nitric oxide levels were different in the two mice strains. Moreover, the brain content of neurotransmitters, epinephrine, norepinephrine, dopamine and serotonin in mice brain was higher in SW mice than B6 mice. We concluded that, the strain of mice is one factor that could alter the response of mice to *P. berghei* infection.

1. Introduction

Cerebral malaria (CM) remains a very dangerous complication of infection causing a high mortality rate (Mehlhorn, 2014). According to the latest world health organization report, there were 214 million cases of malaria in 2015 and 438,000 deaths (WHO, 2015). In human, CM is due to *Plasmodium falciparum or Plasmodium vivax* infection and cause several neurodegenerative diseases (Apoorv and Babu, 2016).

Plasmodium berghei infection of mice is a widely used model of experimental cerebral malaria (Martins et al., 2016). Concerning the oxidative damage and changes in brain content of neurotransmitters, there is no available information about the strain difference effect on susceptibility of mice to *P. berghei* infection. However, there is a clear change in sex difference to susceptibility of mice to *P. berghei* infection (Dkhil et al., 2016).

Scheller et al. (1994) studied the susceptibility of different strains of mice to hepatic infection with *P. berghei*. Also, Randall et al. (2008) reported a significant heterogeneity between CBA/CaH and C57BL/6 mice infected with *P. berghei*.

The current study aimed to investigate the oxidative damage and neurotransmitters activity induced by *Plasmodium berghei* in C57Bl/6 and Swiss Albino mice.

2. Materials and methods

2.1. Mice strains

Both of Adult females C57BL/6 and Swiss albino mice were obtained from the animal facility of King Faisal hospital at Riyadh. Animals were maintained in a specific pathogen-free condition at the Department of Zoology animal housing facilities in strict accordance with the institutional and national official guideline for the project number RG-198. *Plasmodium berghei* were passaged in mice and just as parasitaemia reached about 20%, parasitized blood was taken to infect C57BL/6 (B6) and Swiss albino (SW) female mice. All infected mice received an intraperitonial injection of 1×10^6 *P. berghei*-infected erythrocytes. Parasitemia was calculated in blood smears stained with Giemsa. Cell number was estimated using a Neubaer-chamber.

2.2. Tissue preparation

Twelve mice of each strain were sacrificed by cervical decapitated on day 9 Postinfection (p.i.). Brains were rapidly excised from

Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

* Corresponding author at: Zoology Department, College of Science, King Saud University, P.O. Box: 2455, Riyadh 11451, Saudi Arabia.
E-mail address: mohameddkhil@yahoo.com (M.A. Dkhil).

http://dx.doi.org/10.1016/j.sjbs.2017.01.057
1319-562X/

skulls; weighed then stored at −80 °C for biochemical studies. In each group; six brains were used for the histological study and each brain of other 6 mice were divided into two halves. The first half was used for oxidative stress experiment and the second half was used for determination of neurotransmitters contents.

2.3. Oxidative stress biomarkers

According to Tsakiris et al. (2004), the isolated brain tissues were homogenized in ice-cold medium containing 50 mM Tris–HCl and 300 mM sucrose, pH 7.4. This brain homogenate was used for biochemical investigations.

Brain glutathione (GSH) level was estimated by the method of Ellman (1959). The method depends on the reduction of Ellman's reagent with GSH to give a yellow compound; the reduced chromogen directly proportional to GSH concentration. The absorbance was measured at 405 nm.

The level of nitric oxide was determined according to the method of Green et al. (1982). Briefly, in an acid medium and in the presence of nitrite the formed nitrous acid diazotise sulphanilamide is coupled with *N*-(1-naphthyl)ethylenediamine. The formed azo dye contained a bright reddish-purple color was measured at 540 nm.

Malondialdehyde level was determined according to the method of Ohkawa et al. (1979) by using 1 ml of trichloroacetic acid 10% and 1 ml of thiobarbituric acid 0.67% and were then heated in a boiling water bath for 30 min. Thiobarbituric acid reactive substances were determined by the absorbance at 535 nm.

The activity of catalase in brain homogenate was estimated by the method of Aebi (1984). In this assay, catalase combines with a known quantity of H_2O_2 and the reaction is stopped after exactly one minute with a catalase inhibitor. In the existence of horseradish peroxidase, the remaining H_2O_2 reacts with 3,5-dichloro-2-hydroxybenzene sulfonic acid and 4-aminophenazone to give a chromophore with a color intensity inversely proportional to the extent of catalase in the original sample, and then determined at 240 nm.

2.4. Estimation of neurotransmitters contents

The content of epinephrine, norepinephrine, dopamine and serotonin was determined according to the method of Ciarlone (1978).

2.5. Statistical analysis

Statistical analysis was achieved by using an unpairedStudent's *t* test. MS Excel 2007 (Microsoft, Rochester, NY, USA) and SigmaPlot 2011 (Systat Software, Inc, Chicago, IL, USA) were used for data analysis.

3. Results

P. berghei infection induced a significant difference ($P \leq 0.01$) in parasitemia between B6 and SW mice (Fig. 1). This clear significant difference with increased parasitemia in SW mice was detected on days 5–9 p.i. (Fig. 1).

On day 9 p.i. with *P. berghei* infected erythrocytes, the mice reduced in weight. This weight loss was markedly higher in SW mice and reached about -14% (Fig. 2).

Histological alterations were also observed between the two mice strains. In SW mice, there were more blood appeared in the haemorrhage area. Also, some more neural cells appeared vacuolated. Moreover, the Purkinje cells were destructed in SW mice more than B6 mice (Fig. 3).

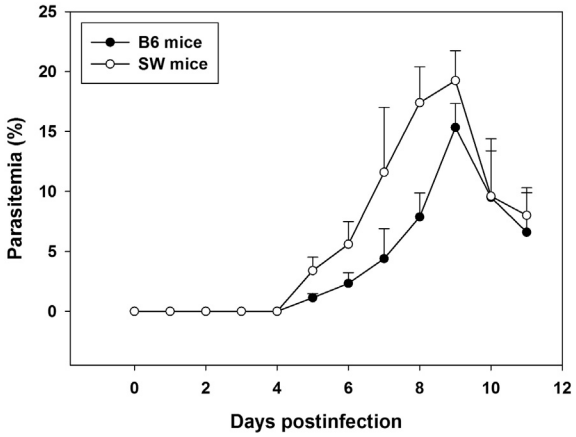

Fig. 1. Parasitemia of B6 and SW mice infected with *P. berghei*. Values are means ± SD.

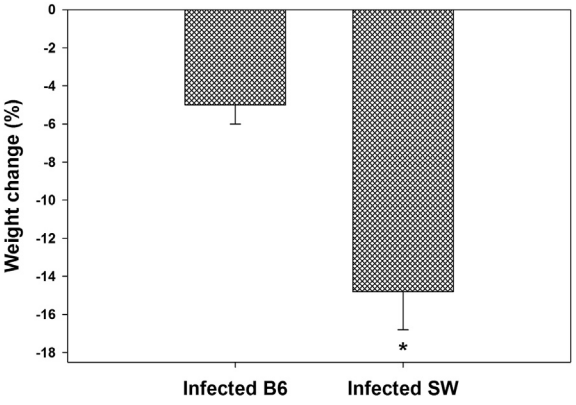

Fig. 2. Weight change in mice at day 9 p.i. with *P. berghei*. Values are means ± SD. *Significant change at $P < 0.01$ between B6 and SW mice.

The infection was able to cause oxidative damage to the brain tissue. Catalase activity as well as glutathione, malondialdehyde and nitrite/nitrate levels were different in the two mice strains (Table 1).

A change in the brain content of neurotransmitters was clearly observed through the significant alteration in epinephrine, norepinephrine, dopamine and serotonin. The brain content of these neurotransmitters in mice brain was higher in SW mice than B6 mice (Table 2).

4. Discussion

C57Bl/6 mice were found to be more susceptible to *P. berghei* infection thanSwiss albino mice. Strain specificity of the disease depend on genetically determined physiological factors as the rate of parasite proliferation (Brewer and Powell, 1965) or host's immune responses, restricting parasite multiplication or producing auto-antibody and immunological injury (Voller, 1974; Mackey et al., 1980). Such strain specific factors which may be reflected by changes in the haemogram, organ weight or structural and functional lesions of organ systems can be compared with those in other animals and in human malaria (Sadun et al., 1966). In this study, the parasitemia, mice weight and the histopathological lesions in brains of B6 an SW mice were significantly different. In general, the infection induced weight loss due to the disturbances in the mice metabolism and the loss of mice appetite (Dkhil et al., 2016).

Please cite this article in press as: Al-Shaebi, E.M., et al. Susceptibility of mice strains to oxidative stress and neurotransmitter activity induced by *Plasmodium berghei*. Saudi Journal of Biological Sciences (2017), http://dx.doi.org/10.1016/j.sjbs.2017.01.057