Biomedicine & Pharmacotherapy 102 (2018) 375–384

Contents lists available at ScienceDirect

Biomedicine & Pharmacotherapy

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

Pretreatment with taurine prevented brain injury and exploratory behaviour associated with administration of anticancer drug cisplatin in rats

Olatunde Owoeye[a,*], Isaac A. Adedara[b], Ebenezer O. Farombi[b]

[a] Department of Anatomy, College of Medicine, University of Ibadan, Ibadan, Nigeria
[b] Drug Metabolism and Toxicology Research Laboratories, Department of Biochemistry, College of Medicine, University of Ibadan, Ibadan, Nigeria

ARTICLE INFO

Keywords:
Cisplatin
Taurine
Neurobehavioral
Acetylcholinesterase activity
Brain damage

ABSTRACT

The neurotoxicity associated with cisplatin treatment is one of the major side effects compromising the efficacy of the anti-cancer treatment. The present study investigated the possible protective effects of taurine, an intracellular amino acid, on cisplatin-induced brain injury and exploratory behaviour using five groups of ten female rats each. Group I received drinking water only. Group II orally received taurine alone at 200 mg/kg whereas Group III received cisplatin alone intraperitoneally at 10 mg/kg. Groups IV and V were treated with taurine at 100 and 200 mg/kg respectively for sixteen consecutive days and a single intraperitoneal injection of cisplatin on day 13 to induce neurotoxicity. Endpoint analyses using video-tracking software revealed that cisplatin administration alone caused neurobehavioral deficits evinced by marked decrease in the total distance travelled, average speed, total time mobile, total mobile episode, number of crossing and absolute turn angle. Furthermore, cisplatin alone significantly suppressed brain antioxidant defense mechanisms, elevated nitric oxide and lipid peroxidation levels whereas it increased acetylcholinesterase activity in the treated rats. However, rats pretreated with taurine exhibited significant improvement in behavioural performance and brain antioxidant status with concomitant decrease in acetylcholinesterase activity and oxidative stress indices when compared with cisplatin alone group. Histologically, taurine pretreatment prevented cisplatin-induced neuronal death in the cerebral and cerebellar cortices, caudo-putamen and hippocampus as well as abrogated cisplatin-mediated decrease in the dendritic arborization and mean diameter of the somata of pyramidal neurons in the treated rats. In conclusion, taurine may be a possible protective supplement to reduce cisplatin-induced side-effects including neurotoxicity in patients undergoing cisplatin treatment.

1. Introduction

Cis-diamminedicholoroplatinum (Cisplatin) is a chemotherapeutic agent used to treat solid tumours of children and adults. Cisplatin has a wide spectrum of use in various tumor events, including the lung, kidney, ovary, testis, bladder, head, neck, and endometrium (Pabla and Dong 2008). Despite the satisfactory anti-cancer efficacy, cisplatin chemotherapy is associated with serious side effects such as neurotoxicity [1–3]. Indeed, cisplatin-induced neurotoxicity often lead to dose reduction or early cessation of chemotherapy which consequently affects patient life [4, 5]. Cisplatin reportedly penetrated into the human brain resulting in a significant concentration of cisplatin in the cerebrospinal fluid [6]. Moreover, Cisplatin reportedly elicited neurotoxicity via mechanisms involving increased reactive oxygen species production, 8-oxoguanine DNA damage, inflammation, mitochondrial dysfunction, and apoptosis in the nervous system [7–10].

Unfortunately, there is no standard clinical method for the early detection and comprehensive assessment of cisplatin-induced neurotoxicity presently known [11]. The American Society of Clinical Oncology is currently concerned about developing a guideline for the prevention and treatment of chemotherapy-induced neuropathies in cancer survivors [12]. Thus, the understanding of the mechanisms by which cisplatin triggers neurological damage is essential for improving approaches to therapeutic interventions. Since oxidative damage associated with the side effects of cisplatin can be ameliorated or mitigated by anti-oxidative [9,13], this study considered the use of a compound, taurine, reported to possess anti-oxidative, anti-inflammatory and anti-apoptotic properties to mitigate cisplatin-induced toxicity in brain of rats.

Taurine (2-aminoethanesulfonic acid) is a free intracellular amino acid, present in high concentrations in the mammalian brain and can be ingested especially from sea foods [14]. The biosynthesis of taurine in human occurs primarily in the liver via oxidation and decarboxylation of the amino acid, cysteine [15]. Taurine reportedly crosses the blood –

* Correspondence author.
E-mail address: o.owoeye@mail.ui.edu.ng (O. Owoeye).

https://doi.org/10.1016/j.biopha.2018.03.051
Received 15 January 2018; Received in revised form 7 March 2018; Accepted 9 March 2018