Scholars LITERATURE

La Prensa Medica Argentina

Research Article

DOI: https://doi.org/10.47275/0032-745X-180
Volume 106 Issue 2

Oxidative Stress in the Male Rats Treated with Metronidazole

Afyaa Sabah Nasir[1], Shaymaa Hussien Jaber[2], Methak Aded-musim Goda[1] and Basim A Almayahi[1]*

[1]Department of Ecology, Faculty of Science, University of Kufa, Iraq
[2]Department of Biology, Faculty of Science, University of Kufa, Iraq

Abstract

Metronidazole is a major antibiotic that is widely used for treating many parasitic illnesses so that many studies have recorded several beneficial effects for the drug. The present study is designing to determine its effect on the hematological blood parameters and antioxidant enzymes in the male white rats. Treatment of rats with metronidazole into two doses include 125 and 250 mg/kg for 30 days, the results show increment in the red blood corpuscles (RBCs), hemoglobin concentration (Hb) and the count of total blood cells (WBCs) but no change in the Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Volume (MCV) and Mean Corpuscular Hemoglobin Concentration (MCHC) values relative to their respective controls. Also, the results show elevated in the antioxidant enzyme (SOD) while reduced in the antioxidant enzyme catalase (CAT) while a significant increase in the malondialdehyde (MDA) in comparison with the control group. In conclusion, metronidazole has many useful effects on the hematological blood parameters and antioxidant enzymes in the male white rats but for a limited time.

Keywords: Superoxide dismutase; Catalase; Malondialdehyde; Metronidazole

***Correspondence to:** Basim AAlmayahi, Department of Ecology, Faculty of Science, University of Kufa, Najaf, Iraq; E-mail: basimnajaf@yahoo.com

Citation: Nasir SA, Jaber SH, Guda MA, et al. (2020) Oxidative Stress in the Male Rats Treated with Metronidazole. Prensa Med Argent, Volume 106:2. 180. DOI: https://doi.org/10.47275/0032-745X-180.

Received: December 17, 2019; **Accepted:** January 08, 2020; **Published:** January 13, 2020

Introduction

Metronidazole (MTZ) is a 5-nitroimidazole tranquilize generally utilizedinveterinaryandhumandrugsforthetreatmentoftrichomoniasis, giardiasis, amebiasis and anaerobic bacterial contaminations [1]. Notwithstanding its enemy of protozoal and bactericidal properties, MTZ is thought to have some immunomodulatory impacts and is normally used to treat incendiary inside sickness (IBD) in the two pooches and felines [2,3]. MTZ is quickly consumed through the gastrointestinal tract with the most extreme fixations in both serum and tissues. It is used in the liver and is discharged for the most part through the kidneys in pee and to a lesser degree through the intestinal divider with the dung of the creatures [4]. Be that as it may, MTZ is anything but a nontoxic medication and has been appeared to quickly cross the blood cerebrum obstruction [5]. Metronidazole is additionally utilized in the treatment of dermatological conditions (Rosacea), where it is showcased by Galderna under the exchange name Rozex and Metrogel [6]. Metronidazole can without much of a stretch be acquired off the counter (OTC) in the drug store and here and there in the open market in Nigeria. It is showcased by Pfizer under the exchange name Flagyl in the US, by Sanofi-Aventis all-inclusive under the equivalent tradename Flagyl [7]. Metronidazole, taken up by dispersion, is specifically consumed by anaerobic microscopic organisms and delicate protozoa. Once taken up by anaerobes, it is non-enzymatically decreased by responding with diminished ferredoxin, which is produced by pyruvate oxidoreductase [8]. This decrease makes the creation of dangerous items anaerobic cells and considers amassing in anaerobes [9]. The metronidazole metabolites are taken up into bacterial DNA and structure unsteady particles. This capacity possibly happens when metronidazole is in part diminished and because this decrease typically happens just in anaerobic cells, it has generally little impact upon human cells or oxygen consuming microscopic organisms [10]. The greatest paradox of aerobic respiration is that oxygen, which is fundamental for vitality creation, may likewise be negative since it prompts the generation of responsive oxygen species [11]. At the point when levels of responsive oxygen species (ROS) overpower the body's cell reinforcement protection framework, oxidative pressure (OS) happens. The mitochondrion is the powerhouse of breath. Thus, it is the real site of ROS age, which is delivered through the nicotinamide adenine dinucleotide-subordinate oxidoreductase pathway [12]. The present investigation aimed to evaluate the lethal impacts of MTZ in male rats by estimating the hematological parameters and antioxidant enzymes.

Materials and Methods

Metronidazole tablets a product of Rhone-Poulenc, U.K., manufactured by Alexandria Pharmaceutical Co. Egypt).Adult male rats weightingbetween 230 -250 g were breed in the animal house at Kufa university. animals were kept in ventilated cages at room temperature (28-30°C) and normal commercial diet and water ad libitum.Thirty male rats (*Rattus norvegicus*) were kept for one week for acclimatization before the experiment and randomly divided into three groups each group have ten rats: Group one administrated tab water to keepas control group, Group two administrated metronidazole at

dose 125 mg/kg and Group three administrated metronidazole at dose 250 mg/kg. Drugs were prepared with tab water and given daily to the animals by oral gavage for 30 days.Blood collecting after last dose of metronidazole by heart puncture, each rat was anaesthetized by the mixture of 0.1 ml of xylazine and 0.5 ml of ketamine, blood kept in gel tube for15 minutes in room temperature after this blood was separated by centrifuged at 3000 rpm for 10 minutes, the sera obtained were kept in deep freeze for biochemical analysis [13]. The hematologic indices were determined according to standard methods. The tests included RBCs, Hb, WBCs, MCH, MCV and MCHC. the hematological parameters were measured using a fully automated hematology analyzer (Beckman Coulter, Germany; Ac.T 5diff CP) according to the manufacturer's instructions.Measurement of SOD activity by ELISA Kit (Elabscience, U.S.A.).The quantitative determination of CAT concentration in serum through the enzyme linked immunosorbent assay using ELISA kit (Elabscience, U.S.A.).Measurement of MDA activity by ELISA Kit (Elabscience, U.S.A.) is an enzyme immunoassay.Statistical Analysis: Data were expressed as mean±S.E. and Statistical Analysis was carried using computerized SPSS program version with one-way ANOVA [14].

Results

Where: (*) is the significant difference P<0.05 between control and treated groups.

Discussion

Metronidazole as a chemotherapeutic happens in numerous structures and is generally utilized in dentistry, for example in periodontal treatment, and endodontic treatment [15,16]. This examination has uncovered that metronidazole caused a critical increment in the RBC and Hb esteems. This proposes metronidazole can possibly invigorate erythropoietin discharges from the kidneys with a resultant increment in the rodent of RBC generation (erythropoiesis) which could, at last, incite polycythemia, since it has been accounted for those estimations of RBC and related parameters lower than ordinary extents are demonstrative of frail conditions while higher qualities are suggestive of polycythemia [17]. It could likewise show that there was an upgrade in the oxygen-conveying limit of blood and the measure of oxygen conveyed to the tissues since RBC and hemoglobin are significant in moving respiratory gases [18]. The huge increment in the TWBC check actuated by metronidazole proposes an improvement in the insusceptible framework. The comparative report was given by Adewusi and Afolayan [19]. Metronidazole caused non-huge changes in the MCV and MCH values which could be a sign of nonappearance of macrocytic pallor since expanded MCV an MCH esteems are known to be characteristic of macrocytic pallor, Likewise, metronidazole caused non-critical change in the MCHC esteem which propose and nonappearance of innate spherocytosis since MCHC qualities are known to be raised in genetic spherocytosis [20]. Free radicals are exceptionally responsive intermediates delivered in typical cell digestion. The oxygen radical producing frameworks are available in a wide range of cells including endothelial cells, adipocytes and germ cells. In a sound condition, there is a harmony between the receptive oxygen species (ROS) development and the end. Be that as it may, when ROS cell overproduction overpowers characteristic cancer prevention agent limit, oxidative pressure happens pursued by most likely the harm to the biomolecules of typical cells and tissues [21]. To ensure against the conceivably harming impacts of ROS, cells are outfitted with a few cancer prevention agent proteins, for example, Superoxide dismutase (SOD) and Catalase (CAT) which kill the harming impacts of ROS by inactivating them. The synergistic activities of the cancer prevention agent catalyst framework are basic in assurance against oxidative harm. These cancer prevention agent chemicals, subsequently, fill in as the barrier arrangement of the cell. In any case, the cancer prevention agent barrier framework might be overpowered by different obsessive or ecological factors with the goal that a small amount of ROS may escape annihilation and structure progressively receptive hydroxyl radicals [22]. Prior, a few creators have announced MTZ-actuated oxidative worry in the testis [23,24]. The consequences of the present examination additionally uncover huge modifications in the exercises of testicular cancer prevention agent compounds, "utilitarian markers and LPO level demonstrating the MTZ-instigated oxidative worry in the body (Tables 1 and 2). The degree of LPO items have been generally utilized as a list of oxidative pressure, the critical increment in the degree of LPO is as per the discoveries announced in rodents following organization of 15 mg/kgBW/day, 200 mg/kgBW/day and 400 mg/kgBW/day of MTZ for about two months, the raised LPO level, as demonstrated by expanded action of MDA in the assortment of MTZ-treated mice, is suggestive of the layer harm of the body cells [25]. Close to this, the OH-radical has been proposed to be an initiator of LPO, thusly, the expanded degree of LPO saw in the present investigation, is additionally showing rise of OH-radical which, itself is a ROS and harms the cell layer (Tables 3 and 4). It is additionally detailed that hydrogen peroxide (H_2O_2) builds lipid peroxidation [26]. Accordingly, the expanded LPO level as saw in the present investigation may be because of the extreme age of H_2O_2 which a superoxide anion is and causes the tissue damage. The cancer prevention agent protein action in the high portion of MTZ-treated gathering shows an expanded movement of SOD while diminished action of catalase. The outcomes propose that expanded action of SOD is likely encouraging higher change of the created ROS, i.e., superoxide anion ($O_{2.}$) to hydrogen peroxide (H_2O_2) [27].

Table 1: Effect of metronidazole in the levels of the physiological blood parameters in the rats after 30 days.

Groups	RBCs (x10^6/µL)	Hb (g/dl)	WBCs (x10^6/µL)
125 mg/kg	9.63 ±0.23	15.20 ±1.25	11.02±0.47
250 mg/kg	10.58*±0.13	16.31*±0.08	12.13 *±0.55
Control	9.10±0.08	15.14±4.04	11.04±1.13

Values are the Mean±SE, n=10

Table 2: Effect of metronidazole in the levels of the blood indices in the rats after 30 days.

Groups	MCV (FL)	MCH (Pg)	MCHC (g/dl)
125 mg/kg	56.21±1.03	20.02±0.07	33.70 ±0.17
250 mg/kg	58.01±5.13	20.32±2.08	33.01±0.05
Control	55.28±0.08	20.50±4.04	33.14±1.13

Table 3: Effect of metronidazole in the levels of the antioxidant enzymes in the rats after 30 days.

Groups	SOD(ng/ml)	CAT(ng/ml)
125 mg/kg	0.17±0.02	64.01±3.01
250 mg/kg	0.15*±0.13	69.32*±2.08
Control	0.28±0.08	60.07±4.04

Table 4: Effect of metronidazole in the level of the malondialdehyde in the rats after 30 days.

Groups	MDA(ng/ml)
125 mg/kg	28.33±7.23
250 mg/kg	35.21*±5.13
Control	25.10±6.08

Conclusion

In conclusion, this examination has demonstrated that metronidazole could have some gainful possibilities on the blood science of pale skinned person rodents. Be that as it may, its impact on human blood science and cancer prevention agent proteins however for restricting time by the by, thinking about these discoveries in creature model, metronidazole is hence prescribed as a nourishment supplement.

References

1. BerganT (1985) Antibacterial activity and pharmacokinetics of nitro imidazole. A review. Scand J Infect Dis Suppl 46: 64-71.
2. Groman R (2000) Metronidazole. Compend Cont Educ 22: 1104-1107.
3. PlumbDC(2002) Veterinary drug handbook. (4thedtn), Iowa State University Press, United States.
4. Finch RG, Snyder IS (1986) Antiprotozoan drugs. In: Modern pharmacology. (2nd edtn), Little, Brown Co, United States.
5. Gupta AK, Agarwal MP, Avasthi R, Bhadoria DP, Rohatgi N (2003) Metronidazole-induced neurotoxicity. J Assoc Physicians India 51: 617-618.
6. Oda S (2012) Histopathological and biochemical alterations of metronidazole-induced toxicity in male rats. Glob Vet 9: 303-310.
7. Ahmad A, Chaudhary M, Soni A, Payasi A, Dwivedi VK (2010) Comparative toxicity profile study of mebatic vs. ofloxacin, ornidazole and metronidazole drugs in rat model. Asian J Biochem 5:78-88.
8. Chukwu VO, Akudike CJ, Ezejindu DN, Augustine IC (2015) The protective effects of turmeric on liver enzymes of metronidazole treated adult male *Wistar* rats. IJASR 1: 255-258
9. Chandak S, Agarwal A, Shukla A, Joon P (2016) A case report of metronidazole induced neurotoxicity in liver abscess patient and the usefulness of MRI for its diagnosis. J Clin Diagn Res 10: TD06-TD07.
10. Eisenstein BI, Schaechter M (2007) DNA and chromosome mechanics. In Schaechter's mechanisms of microbial disease. (4th edtn), Lippincott Williams & Wilkins, United States.
11. Saleh RA, Agarwal A, Kandirali E, Sharma RK, Thomas Jr AJ, et al. (2002) Leukocytospermia is associated with increased reactive oxygen species production by human spermatozoa. Fertil Steril 78: 1215-1224.
12. Kumari M, Singh SP, Singh P (2018) Testicular oxidative stress and inducible nitric oxide synthase expression following metronidazole administration in the laboratory mouse. Free Radic Antioxid 8:32-39.
13. Kavakli HS, Koca C, Alici O (2011) Antioxidant effects of curcumin in spinal cord injury in rats. Ulus Travma Acil Cerrahi Derg 17: 14-18.
14. Al-RawiK (2000) Entrance to the Statistics. (2nd edition), Ministry of higher education and scientific research in Iraq, University of Al-Mosul, Iraq.
15. El-Nahas AF, El-Ashmawy IM (2004) Reproductive and cytogenetic toxicity of metronidazole in male mice. Basic Clin Pharmacol Toxicol 94: 226-231.
16. Ahmad A, Chaudhary M, Soni A, Payasi A, Dwivedi VK (2010) Comparative toxicity profile study of mebatic *vs*. ofloxacin, ornidazole and metronidazole drugs in rat model. Asian J Biochem 5: 1-11.
17. American Diabetes Association (2004) Nutrition principles and recommendations in diabetes. Diabetes Care 27: s36-s36.
18. Fararjeh M, Mohammad MK, Bustanji Y, AlKhatib H, Abdalla S (2008) Evaluation of immunosuppression induced by metronidazole in Balb/c mice and human peripheral blood lymphocytes. Int Immunopharmacol 8: 341-350.
19. Adewusi EA, Afolayan AJ (2009) Safety evaluation of the extract from the roots of Pelargonium reniforme Curtis in male wistar rats. AfrJ Pharm Pharmacol 3:368-373.
20. Oyedeji KO, Bolarinwa AF (2013) Effect of metronidazole on haematological parameters in male albino rats. IOSR JDMS 3: 61-63.
21. Droge W (2002) Free radicals in the physiological control of cell function. Physiol Rev 82:47-95.
22. Onopiuk B, Onopiuk P, Dabrowska Z, Dabrowska E, Pietruska M, et al. (2018) Effect of metronidazole on the oxidoreductive processes in the submandibular and parotid glands in experimental research. Oxid Med Cell Longev 2018: 1-9.
23. Raji Y, Kunle-Alabi OT, Olaleye SB, Gbadegesin MA, Awobajo FO, et al. (2007) Impact of α-tocopherol on metronidazole and tetracycline-induced alterations in reproductive activities of male albino rats. J Bio Sci 7:41-6.
24. Ligha AE, Bokolo B, Didia BC (2012) Antifertility potential of metronidazole in male Wistar rats. Pak J Biol Sci 15: 224-30.
25. Ligha AE, Paul CW (2011) Oxidative effect of metronidazole on the testes of Wistar rats. Aus J Bas Appl Sci 5: 1339-1344.
26. Said TM, Aziz N, Sharma RK, Lewis-Jones I, Thomas Jr AJ, et al. (2005)Novel association between sperm deformity index and oxidative stress-induced DNA damage in infertile male patients. Asian J Androl 7: 121-126.
27. Cavaletto M, Ghezzi A, Burlando B, Evangelisti V, Ceratto N, et al. (2002) Effect of hydrogen peroxide on antioxidant enzymes and metallothionein level in the digestive gland of Mytilus galloprovincialis. Comp Biochem Physiol C Toxicol Pharmacol 131: 447-455.