IJCMBS THE INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND BIOLOGICAL SCIENCES e-ISSN: 2791-8815

Review Article

Negative Effects of Aflatoxin B1 on Sperm

Aflatoksin B1'in Sperm Üzerine Negatif Etkileri

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Received: 08.07.2022
Accepted: 21.07.2022

Cite as: DOGAN. V Negative Effects of aflatoxin B1 on Sperm IJCMBS 2022;2(3):215-18 doi.org/10.5281/zenodo.6835093

Abstract

Aflatoxins are secondary metabolites that produced by *Aspergillus* fungi which are soilborne and involved in the decomposition of plant materials in nature. *Aspergillus* species find opportunity to produce aflatoxins in high humidity and temperature conditions such as tropical and subtropical environment. Therefore, in changing climatic conditions caused by global warming, geographical distribution of these fungi to have changed day by day, and find out an opportunity to grow in different feed materials. Aflatoxin B1 (AFB1) is the most toxigenic mycotoxin in these group and threatens both human and animal health due to its carcinogenic and mutagenic properties. In cattle, commonly known adverse effects of AFB1 depending on the chronic exposure such as decreasing milk production and quality, reducing the feed efficiency in beef cattle, increase susceptibility to diseases following suppression of the immune system, compromise ruminal functions, disruption of ruminal microorganism growth and functions.

In this study, the negative effects of AFB1 on bull sperm has been examined. Topics such as negative effects of AFB1 on sperm proteomes, increase in the reactive oxygen species, changes in sperm DNA and plasma membrane integrity are discussed.

Key Words: Aflatoxin, Aflatoxin B1, Sperm

ÖZ

Aflatoksinler, toprak kaynaklı olan ve bitkisel materyallerin çürümesinde görev alan Aspergillus türü mantarlar tarafından üretilen sekonder metabolitlerdir. Aspergillus türleri, tropikal ve subtropikal ortamlar gibi yüksek nem ve sıcaklık koşullarında aflatoksin üretme fırsatı bulmaktadır. Bu nedenle, küresel ısınmanın neden olduğu iklim değişikliklerine bağlı olarak aflatoksin üreten mantarların coğrafi yayılışları değişmekte ve farklı yem materyallerinde üreme imkanı bulmaktadırlar. Aflatoksinler içerisinde en toksik olanı aflatoksin B1'dir (AFB1) ve karsinojenik ve mutajenik özelliğinden dolayı insan ve hayvan sağlığını tehdit etmektedir. Aflatoksin B1'e uzun süre maruz kalmaya bağlı olarak sığırlarda; süt veriminde ve kalitesinde azalma, besi sığırlarında yemden yararlanmada düşme, immun sistemin baskılanması ve buna bağlı olarak hastalıklara karşı duyarlılıkta artış, karaciğer fonksiyonlarının baskılanması, rumen fonksiyonlarında azalma, rumen mikroorganizmalarının gelişme ve fonksiyonlarının sekteye uğratılması gibi etkileri yaygın olarak bilinmektedir.

Bu çalışmada, AFB1'in boğa spermi üzerindeki olumsuz etkileri incelenmiştir. Boğa spermindeki proteomlar, reaktif oksijen türlerindeki artışlar ve plazma membran bütünlüğündeki değişiklikler, sperm DNA'sında meydana gelen değişiklikler gibi konular ele alınmıştır.

Anahtar Kelime: Aflatoksin, Aflatoksin B1, Sperm

Highlights

- AFB1 impairs the spermatozoa acrosome reaction and capacitation.
- AFB1 reduces PARK7 expression in spermatozoa and increases ROS generation.
- DNA fragmentation in spermatozoa is increased in males exposed to AFB1.

Introduction

Aflatoxin contamination in various feed materials such as corn, maize, sorghum, rice and wheat are common worldwide (1-3). Aflatoxin contamination of corns cause economic losses in U.S. corn industry between US$52.1 and US$1.68 billion (4). Estimates of the economic losses caused by mycotoxin contamination vary, nevertheless, neither of these estimates contain human health impact of aflatoxin contamination.

Aflatoxins are the secondary metabolites produced by fungi, *Aspergiluus flavus, A. parasiticus* and *Penicillium* species (5-7). Aflatoxins consist four main compounds called Aflatoxin (AF) B1, B2, G1 and G2 (6). Aflatoxin M1 and M2 which are found in milk and dairy products are hydroxylated forms of AFB1 and AFB2, respectively (8). According to the International Agency for Research on Cancer, AFB1 is classified as Group 1 carcinogen to humans (9).

In cattle, long term exposure to aflatoxins can reduce production performance, interrupt liver function, increase the susceptibility to diseases following suppression of immune function (10). The negative effects of aflatoxins such as production performance have been observed by researches using pure aflatoxins because it allows control of the dose applied and more contamination prevention. However, in nature, different fungi species can growth in the feedstuffs depending on the environmental conditions. Therefore, mycotoxins may cause more severe damage due to the synergistic or additive effects of different types of mycotoxin as well as other metabolites and their fungal sources (11-13). Applebaum et al (1982) observed that the pure AFB1 administration to dairy cows did not affect the milk productions whereas impure AFB1 administration reduced the milk production in dairy cows (14). Due to the synergistic or additive effects of different mycotoxin types, or aflatoxins, may exert their deleterious effects more severely in vivo or in vitro.

Aflatoxin B1 may have toxic to the male reproductive system in animal as well as human. The negative effects of AFB1 on male reproductive system are sorted as pathological changes in testis and epididymis, decreases in the number of leydig cells, and in the number of spermatogenesis, spermatocytes and spermatids (15). In addition, AFB1 exerts it's negative effects on human are reported as poor sperm quality and infertility (16).

Effect on sperm capacitation and acrosome reaction

The acrosome reaction is a prerequisite process of spermatozoa for fertilization. Acrosome-reacted spermatozoa are being capable to pass through the zona pellucida subsequently bind the oocyte plasma membrane and fuse with the oocyte (17). All mammalian spermatozoa including human undergo a series changes during their ascent in the female reproductive tract, is called capacitation (18). The acrosome reaction requires to release of hyaluronidase and acrosin enzymes (17). Ataman et al., (2014) have observed significant increase in semen hyaluronidase activity in rams exposed to aflatoxin from 3 week of the trial (19). Researchers had discussed on increase in semen hyaluronidase activity could be arise from an increase in the rate of abnormal or nonviable spermatozoa or could be explained by the transfer of hyaluronidase from the serum into the seminal plasma as a result of chronic intoxication. In contrast, chronic exposure to AFB1 of mammals in dose dependent manner cause low serum testosterone (20, 21). In another hand, the high testosterone levels in sheep results in high serum hyaluronidase levels (22). Therefore, the increase in hyaluronidase activity in semen could not be related to the transfer from the serum into the seminal plasma.

Komsky-Elbaz et al., (2018) reported that AFB1 causes significant decrease the proportion of sperm that reacts to Ca^{++} ionophore and underwent induced acrosome reaction in sperm obtained from the epididymis tail (23). In another study, the ubiquitin-proteosome systems (UPS) that involved in capacitation, acrosome reaction and zona pellucida penetration, have been found affected by the AFB1 (24).

Effect on mitochondria

Alterations in mitochondrial functions caused by the environmental substrates such as aflatoxins are associated with dysfunction male and female infertility (25). The mitochondria involve in ATP synthesis, reactive oxygen species (ROS) production, calcium signaling and apoptosis. Impairment of mitochondrial functions in cells exposed to AFB1 induce apoptosis following activating ROS generation by the mitochondria (29). Komsky et al., (2018) observed that AFB1 induced alterations in mitochondrial membrane potential in spermatozoa (23). In addition, AFB1 reduced expression of PARK7, a protein involved in cell protection against mitochondrial damage and high levels of ROS generation (24, 26). These results suggest that AFB1 reduces fertilization rate via mitochondrial damage. The ubiquitin C-terminal hydrolase L3 protein is located in the mitochondrial sheath and shows reduced expression in male infertility (24).

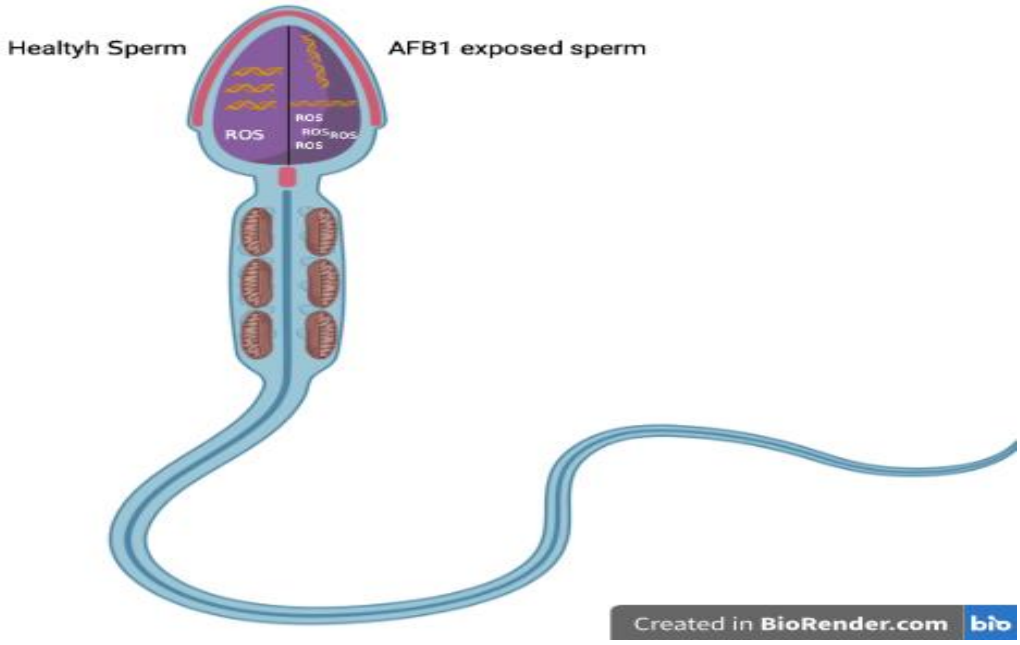

Figure 1: Effects of Aflatoxin B1 (AFB1) on sperm quality. Acrosome reaction is impaired, and apoptosis is induced following activated ROS generation. DNA fragmentation is increased.

DNA Fragmentation

Paternal components which are believed to be crucial for oocyte activation and zygote formation, are deliverd by spermatozoon. During fertilization, the proportion of sperm with DNA fragmentation is considered a practical parameter for characterizing semen quality (27, 28). DNA fragmentation reduces sperm fertilization and also effects embryonic development (29), but embryo can repair DNA damage of sperm origin. This process starts after fertilization (30). Komsky et al., (2018) reported DNA fragmentation in bull sperm exposed to AFB1 but no difference on the blastocyst formation between AFB1-treated group and control (23).

Cell membrane integrity is important on the cell viability. Komsky et al., (2018) reported that exposure of low concentrations of AFB1 (1 or 10 μM) reduced the viability of sperm (23). Ram spermatozoa exposed to AFB1 induced the higher rate of dead spermatozoa proportion in comparison with control group (19).

In conclusion, while aflatoxins are considered one of the risk factors for decrease in production performance such as milk production, feed efficiency in dairy and beef cattle, according to the data from the limited studies, they may also accepted as risk factor for male reproduction. These risk factors for male reproduction include decreasing sperm motility and viability, increasing the rate of fragmented DNA, and ROS in spermatozoa. Further studies are required for negative effects on male reproduction exposed to aflatoxins either alone or combined with other mycotoxins.

Acknowledgements: I thank the Institute of Medical Sciences, Ataturk University.

Ethical Approval: *This review does not require any ethical committee approval.*

Author Contributions: *Author Contributions: Concept: Veysel DOGAN Literature Review: Veysel DOGAN Design: Veysel DOGAN Writing manuscript: Veysel DOGAN Critical revision of manuscript: Veysel DOGAN*

Conflict of Interest: *The authors have no conflicts of interest to declare.*

Financial Disclosure: *Authors declared no financial support.*

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