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OCHRATOXIN A (OTA) AND BALKAN ENDEMIC NEPHROPATHY (BEN)

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Abstract

OTA as the aetiological agent of BEN could not be treated as the exclusive agent responsible for BEN, because OTA is already estabilished all around world including neighbourhood areas surrounding BEN endemic regions. His presence in tissues-organism of animals who took OTA and which were used for cooking or other procedure by men, diminished after 2-3 hours of cooking and as a result it could not be determined in substrate-beans. Seeing the existing close correlation of high aflatoxin concentration and B and C hepatitis in incidence of primary liver carcinoma, maybe it should be taken as an example of synergism of two factors which could be explored in strictly localised regions of BEN with adequate valid methods and possible exploration of all existing etiologic agents (soil related or other).

Actual aethiology hypothesis of BEN includes genetic, toxic and virous ones and amongst them for the last 20 years the toxic hypothesis represents the most significant one. Seeing that OTA is present all over the world, as in the substrates contaminated with the molds and in most common producers of OTA, Asp. ochraceus, Pen.viridicatum as well as in animal's products (pigs, poultry) in these regions, they determine pathologic changes in kidneys (liver as well) and as such are connected aethiologically with BEN. Such a hypothesis is quite understable, when other hypothetic role of genetic and virous agents-causes could not be connected with BEN (1, 2, 3).

From this point of view, there are not unexpected investigations from BEN regions in countries of former Yugoslavia, where OTA presence was found in the great number of grains and the beans, as well as in human blood and blood and tissue of animals who ingested OTA by food (4-24).

It is known, that OTA in animals is resposible also for other derrangements, leading to the noneconomic animal production. In the

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same time, the presence of OTA in animal products represents danger for the people consuming these food.

Investigations on OTA presence were done on animals and blood and other samples. The main goal of all these investigations was to determine correlation and the causal connection between the presence of OTA in food, the quantities and the changes in organs of people and animals and to determine if such a connection exists in the more and significant measure on BEN regions. Numerous investigations have been done and are cited in relevant literature (Ožegović L., Pepeljnjak, 26).

These investigations were in relation to mass loss of turkey poults in Britain in 1960 (called «X disease of turkeys») later determined as poisoning with toxins from peanut, respectively mycotoxin aflatoxin, with later liver lesions and intoxication with Asp. flavus toxin-aflatoxin pure toxin with incidence of livre carcinoma. These continued investigations of aflatoxin hepatotoxicity concering aethiology of primary liver cancinoma in humans especially concentrate on certain regions where the peanuts and products alike are the only protein source of nutrition. Legislation and investigations on toxicity for individual species and cathegories of animals and for people led to the new knowledges of the way sof production and the toxinogenic species and varieties of Asp. flavus, from methods and ways of production and measurements of decreasing concentrations in these products to new approaches to detoxification of indigested aflatoxin (25). Aflatoxin is not only one mycotoxin regarded for regional increased frequency of carcinoma in people. Same approach goes for fumonisin, who is presumably responsable for incidence of carcinoma of oesophagus and stomach in certain regions of the world.

Subsequent investigations proved that the initial euphorya on the exclusively role of aflatoxin in the aethiology of liver carcinoma in people was premature seeing that in certain regions with high incidence of liver carcinoma and high content of aflatoxin present and corn, there was high incidence of hepatitis B and C too, thus proving the fact that the primary liver carcinoma is the result of mutual activities of aflatoxin and hepatitis viruses. Not surprising seeing that in these regions factors included besides mycotoxin aflatoxin and B and C hepatitis concerned powerty and malnutrition. Theory-hypothesis of OTA aethiology of BEN is really not whitout good reason, because this nephrotoxin is really present in grains and food-products of animals fed with such a contaminated food, but this hypothesis is confronted by the fact, that in the great part of the world, especially in Danmark and Poland, as well as in many other regions in Balcans, in spite of really high concentrations of OTA in grains, there is BEN nonexisting. That includes OTA presence in almost every region of former Yugoslavia.

OTA presence was proved in humans outside BEN regions who never showed any BEN clinical signs but subclinical course more than 20 years course . Critical appreciation on the OTA presence in food and the quantity of the food people are taking on a dayly basis and eventual connetion with BEN is of great interest. By counting on these parameters (OTA food concentration / necessary OTA quantities to cause kidney damage), the day average dose of contaminated food was estabilished: 95 μg/kg of corn or 85 μg/kg of bean meaning 6kg of corn or 6,6kg of beans as a toxic OTA dosage (14).

It is well known, that the food preparation procedure on daily basis has influence on present OTA activity. People from BEN regions do not consume OTA contaminated food uncooked and cooking procedure diminishes the quantity and activity of present OTA: by length of food preparation and by temperature used in this cooking process. 2 - hours post cooking period shows small OTA presence in cooked beans (experimentally with the toxic strain of Asp. ochraceus) and no activity present (32).

According to these results, with existing possibility of taking small quantities of OTA and its slower or faster desintegration in organism and later newfilling with further dosages, still there is too much «space» to the dosage what should be absolute toxic. Although it is relative in respect to every individual organism and his possibilities to degrade mycotoxins, depending on its actual metabolism. Although, OTA presence in great concentrations in grains or other food in wide regions of the world is in relations to certain factors; agricultural procedures, climate factors, abilities to metabolise mycotoxin (s), it represents a problem unsolved.

The reason for these expressed manifestations should be present and «the cause» should be common to all BEN localitions. If we bear in mind lever carcinoma and its etiology (hepatitis B and C as well as aflatoxin) we should ask ourselves is OTA responsibile for BEN? In the case of liver carcinoma and aflatoxin and the connection with the virus of hepatitis B and C viruses, it is obvius that one of these two factors is «trigger» and the other is «killing» factor or «executor». If the hypothesis of OTA signifanse is looked at the same way, we should ask ourselves which is the «trigger» for BEN in OTA presence and which is the other trigger agent, strictly bound to restricted BEN regions. Otherwise speaking, we should continue our investigation of all relevant and possible causes-agents which could work in synergism, if the hypothesis of OTA is still one of possible factors of BEN.

Apstrakt

OTA kao uzročnik BEN ne može biti smatran isključivim agensom odgovornim za to oboljenje, jer OTA je utvrđen u cijelom svijetu, pa i u neposrednom susjedstvu područja u kojem je BEN endemičan. Osim njegove prisutnosti u tkivima – organima životinja, koje su uzimale OTA, a takvi produkti se uzimaju od ljudi isključivo pripremanjem hrane (djelovanje topline i eventualno dodanih začina), žitarice i grah se također kuhaju – pripremaju, a dokazano je da toplina kuhanja graha uništava OTA već nakon 2 sata kuhanja. Prema tome način ishrane stanovništva produktima u kojima se nalazi OTA isključuje njegovo toksično djelovanje i ne može se OTA smatrati uzročnim agensom BEN. Možda bi se iz sličnosti primarnog karcinoma jetre u područjima u kojima je utvrđena visoka koncentracija aflatoksina i virusa hepatitisa B i C mogla uzeti kao primjer sinergizma djelovanja dva moguća agensa, što bi u područjima BEN trebalo utvrditi s obzirom da je BEN vezan uz strogo i usko ograničena područja u kojima nisu odgovarajućim validnim metodama istraženi svi mogući etiološki agensi, vezani možda uz tlo ili drugi uzrok – uzročnik.

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