INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com ISSN 2230 – 8407

Review Article

FISH CANCER DEVELOPED BY ENVIRONMENTAL POLLUTANTS

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Article Received on: 18/08/12 Revised on: 22/09/12 Approved for publication: 12/10/12

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ABSTRACT

The pollution of rivers and streams with chemical contaminants has become one of the most critical environmental problems. Fish living in a polluted water reservoir use the contaminated water to rinse their gills; this results in the deposition of polycyclic aromatic hydrocarbons (PAHs) in the fish body. Contamination of foodstuffs by heavy metals such as arsenic, cadmium, chromium, nickel and lead has poses a potential carcinogenic threat to humans. Arsenic and cadmium appear to be the most harmful to the fish. Several cancers in fish appear to be the result of exposure to different environmental pollutants/chemicals. High frequencies of liver and skin cancers in brown bullheads are associated with high concentrations of PAHs and some metals in the environmental sediments. Taking these facts in view, the present article gives the emphasis on the fish cancer caused by various environmental pollutants, suggesting that fish species are truly suffer from different cancers/tumours.

KEYWORDS: Cancer/tumour, environment pollutants/chemicals, fish, pollution.

INDRODUCTION

The term "pollution" covers all types of contamination emitted to the ground, surface water, and atmosphere that could be further absorbed by plants, fish and farm animals. The sources of pollution include industrial waste, diesel exhaust (mostly in the vicinity of roads) and pesticide residues in food products. The pollution of rivers and streams with chemical contaminants has become one of the most critical environmental problems. An example of the effect of environmental pollution on nutrition is contamination of fish by polycyclic aromatic hydrocarbons (PAHs). Fish living in a polluted water reservoir (in the vicinity of an oil refinery) use the contaminated water to rinse their gills; this results in the deposition of PAHs in the fish body. Another example is contamination of foodstuffs by heavy metals. Although some metals are essential for human nutrition, others including arsenic (As), cadmium (Cd), chromium (Cr), nickel (Ni) and lead (Pb), have been found to pose a potential carcinogenic threat to humans. As its main dietary source is fish) and Cd appear to be the most harmful.

Fish are exposed from different environmental pollutants, including drugs and chemicals. The most important environmental pollutants/chemicals causing severe toxicity to fish are the 'heavy metals', such as Cd, As, copper (Cu), Cr, iron (Fe), Pb, manganese (Mn), mercury (Hg), Ni, Zn (Zinc), tin (Sn), etc. Not only this, but the high concentrations of PAHs and some metals in the environmental sediments cause the liver and skin cancers in brown bullheads. Further, the contaminants/pollutants are responsible for induction of chemical carcinogenesis in fish[1].

Fish can also suffer from various types of cancer. Several cancers in fish appear to be the result of exposure to different environmental pollutants/chemicals. For example, high frequencies of liver and skin cancers in brown bullheads are associated with high concentrations of PAHs and some metals in the environmental sediments. The data correlated with contaminant/pollutant exposure and laboratory induction experiments reinforce the idea of chemical carcinogenesis in wild fish population. Liver neoplasms/cancers in sauger and walleye fishes are associated with heavy loadings of extremely fine particulates which were produced when copper 'stamp sands' were reprocessed. Now, one in four of the St. Lawrence whales are dying from cancer, mostly intestinal cancer. When scientists examined their bodies, the autopsies revealed high levels of PAHs. Epidemics of liver cancer have been found in 16 species of fish in 25 different polluted freshwater and saltwater locations. The same tumours/cancers were found in bottom-feeding fishes in industrialized and urbanized areas[2].

In deed, it is essential to know how to examine the fish for tumours/cancers, to recognize gross signs of tumours and know how to prepare samples for histopathology. Therefore, the field biologist should develop skill in recognizing the presence of commonly occurring tumours/cancers in fish and in preparing samples for further diagnosis. Zebrafish are used to study development, toxicology and toxicopathology. The zebrafish is known for its rapid development in the laboratory. The greatest advantage of the zebrafish as a model system comes from its well-characterized genetics, genetic and developmental techniques and tools, and the availability of well-characterized mutants. It has been further cited that the experimental carcinogenesis using fish species as alternative models may be a new and an important field of research. Expansion of synthetic chemical producing industries during the 1940's coincided with a number of pollution-associated fish neoplasia epizootics, with PAHs as significant components of contaminated sediments in several cases. Epizootics of primarily liver and skin neoplasia in benthic species near coastal urban or industrial areas indicated the sensitivity of fish species to known mammalian carcinogens. The potential for the application of research findings to both human and environmental health issues make fish species attractive and valuable alternative models in the carcinogenesis and toxicity research[3].

SOME ENVIRONMENTAL POLLUTANTS CAUSING FISH CANCER

(a) N-Methyl-N'-Nitro-N-Nitrosoguanidine (MNNG)- It is a direct-acting carcinogen that induces neoplasms/cancers of

gastrointestinal tract in rats, hamsters and dogs on oral administration. Liver neoplasms are also reported, as well as fibrosarcoma with subcutaneous injection and multiple organs involvement with intraperitoneal injection. Carcinogenic effects of selected N-nitroso carcinogens have been studied in a small number of fish species. As a group, N-nitroso carcinogens cause liver neoplasia in essentially all fish species studied in detail, when exposure occurs in early life stages[4]. In addition to liver neoplasia, MNNG causes neoplasia in gill, pseudobranch, thyroid, gonad, pancreas, gas bladder, mesothelium, scale, skin, olfactory epithelium, connective tissue, skeletal muscle, notochord, blood vessels and pigment cells of medaka[4-6]. Channel catfish given subchronic aqueous exposure to MNNG beginning at 6 months of age develop neoplasia in skin, fin, gill, thymus, bone, oropharynx and generalized lymphoid system[6]. In rainbow trout, only epithelial neoplasms occur in MNNG-treated fish, with liver, stomach, swim bladder and kidney targeted in trout given aqueous exposures as embryos or fry[7]. Cancers/neoplasms occur only in stomach in rainbow trout fed MNNG, beginning at 2 months of age[8]. A high incidence of thyroid neoplasia is reported in *Rivulus* following immersion exposure of young fry to MNNG[9]. The MNNG also causes osteosarcoma of ribs and vertebrae in coho salmon treated as embryos[10].

Embryos and fry were both quite responsive to MNNG; however, juvenile zebrafish were remarkably refractory to MNNG-induced neoplasia. The main target organs in zebrafish treated as embryos with MNNG were liver and testis, with hepatocellular adenoma the most prevalent hepatic neoplasm. A variety of mesenchymal neoplasms occurred in zebrafish following embryo exposure to MNNG, including chondroma, haemangioma, haemangiosarcoma, leiomyosarcoma and rhabdomyosarcoma. Testis and blood vessel were primary target organs for MNNG following fry exposure, with seminoma, haemangioma, haemangiosarcoma, and various other epithelial and mesenchymal neoplasms occurring[8]. The zebrafish is a responsive, cost-effective lower vertebrate model system to study the mechanisms of carcinogenesis[3,8].

With exposure of either juvenile or adult medaka, cancers were primarily induced in gills, connective tissues, skin, and olfactory and reproductive systems. Within the skin, cancers were variable and included melanoma[11-12]. Vascular tumours were the most common type of cancer in one study, but many other tissues were affected[4]. Multiple tissue involvement was mentioned in another juvenile exposure study, but only data on gill cancers were given[13]. Despite the preceding variations, the tissue distribution of cancers suggests direct action of MNNG on aqueously exposed tissues. The reported distribution of cancers in rainbow trout exposed to MNNG was different from medaka, with no apparent relationship to exposure age or route. With embryos, fry, or adults exposed aqueously or by injection or diet, cancers were seen in liver, stomach and kidney, with a low incidence in swim bladder[14]. However, in two of these reports, histologic examination was restricted to those same tissues. Liver cancers were relatively common in rainbow trout, whereas in medaka they were absent, not reported, or occurred at rates no higher than controls[4]. In a separate report of 9,802 exposed (various compounds) and control medaka, 40 cases of lymphoma were seen[15], and the lack of a significant difference between control and treated groups indicated that the cancer may be spontaneous in this species. However, the tumour biology of lymphosarcoma in catfish is unknown, and an 8.8% incidence of lymphosarcoma in *Poeciliopsis* strain *P. monacha* exposed to DEN was seen[16].

Most of the cancers were spermatocytic seminomas containing spermatocytes and spermatids. Fewer seminomas were comprised strictly of spermatogonia. As previously reported in medaka, oocyte differentiation was observed in seminoma or adjacent testis of certain zebrafish. And interestingly, spermatocytic seminoma occurs in female medaka as well as male, in the case of both spontaneous and carcinogen-related gonadal neoplasia[17]. Benign or malignant thyroid neoplasia is the most common histologic type of epithelial neoplasia reported in medaka following fry treatment with MNNG; and seminoma is the second most frequent histologic type of epithelial neoplasia seen in medaka given fry bath treatment with MNNG[5]. The MNNG and other N-nitroso carcinogens induce pigment cell neoplasia in medaka, Nibe croaker and *Xiphophorus*[8,11].

(b) Diethylnitrosamine (DEN)- It is also called N-nitrosodiethylamine (DENA), which is one of the most potent carcinogens. In the 1970s, there was an increased frequency of liver cancer found in Norwegian farm animals. The farm animals had been fed on herring meal, which was preserved using sodium nitrite. The sodium nitrite had reacted with dimethylamine in the fish and produced DEN. Nitrosamines can cause cancers in a wide variety of animal species, a feature that suggests that they may also be carcinogenic in humans. DEN has been extensively used in medaka and rainbow trout, and has proved to be a potent inducer of hepatic neoplasms[7].

(c) Methylazoxymethanol Acetate (MAM-Ac)- This is a potent carcinogen with direct- and indirect- acting properties. It induces liver, kidney and colon cancers in rodents and nonhuman primates when administered by different routes[4].

(d) Some Indirect-Acting Carcinogens- Benzo(a)pyrene (B[a]P) is hepatocarcinogenic in rainbow trout, but its long-term exposures through the diet or intraperitoneally are required[18]. The racemic (±)-trans-B[a]P-7,8-dihydrodiol is a much more potent carcinogen in trout[19]. Reconstitution studies with purified enzyme and liver microsomes from BNF-treated trout indicate that CYPIA is the predominant subfamily involved in B[a]P and B[a]P-7,8-dihydrodiol bioactivation to the ultimate carcinogen 7S-trans-7,8-dihydrobenzo[a]pyrene-7,8-diol-anti-9,10-epoxide[7,19].

Topical administration of a PAH extract or B[a]P also induced epidermal papillomas in two species[4], and a solitary gill haemangioma was seen in a high-dose B[a]P exposure group; B[a]P) causes liver cancer in guppy and madaka[20].

Although pancreatic cancers occurred, the incidence in DMBA- and B[a]P- exposed medaka was not higher than controls. The pancreatic acinar carcinoma may represent a spontaneous rather than carcinogen-induced cancer in medaka[21]. One pancreatic adenoma was reported in PAH extract exposure studies[22]. A number of extrahepatic cancers were induced by DMBA in medaka, but the types were not specified[23]. However, the cancers were reportedly absent in guppy exposed to DMBA by intramuscular, intraperitoneal, or topical routes[24]. DMBA is a much more potent hepatocarcinogen in trout than B[a]P and produces tumours in kidney, swim bladder and stomach as well[25]. Preliminary evidence indicates that dibenzo(a,l)pyrene (DBP) resembles DMBA with respect to trout target tissues but is a more potent carcinogen, especially for liver and swim bladder[7]. It has been reported[26] that DMBA causes hepatocellular carcinoma (HCC), hepatic adenoma, renal acinar cell carecinoma, neurilemmoma and fibrosarcoma in guppy. It

also caused HCC and lymphosarcoma in *Poeciliopsis* species[7]. In *Cyprinodon variegates* also, DMBA caused HCC and hepatic adenoma[21].

N-methyl-N-nitrosourea (MNU) is an alkylating agent that methylates DNA bases primarily at nucleophilic sites (N_7 and N_3 alkylpurines). The primary mutagenic lesion of MNU exposure is believed to be O_6 methylguanine[27]. This carcinogen also induced a wide variety of tumours in *Xiphophorus* hybrids, including neuroblastomas, rhabdomyosarcomas, melanomas and fibrosarcomas, at high incidence, and various carcinomas at a greatly reduced incidence[28-29]. The papillary thyroid tumour induction by MNU has also been reported[30].

CONCLUSION

Contamination of foodstuffs by heavy metals such as arsenic, cadmium, chromium, nickel and lead has poses a potential carcinogenic threat to humans as well as fish. Arsenic and cadmium appear to be the most harmful to the fish. Accumulation of PAHs in the fish body causes the development of different cancers. Therefore, many cancers in fish occur due to the exposure of different environmental pollutants/chemicals. This article concludes that similar to other animal species, fish may also from different cancers/tumours. The present article further suggests the development of cancer model in fish for needful research studies.

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Source of support: Nil, Conflict of interest: None Declared