COMMENTARY

Pesticides, Fresh Water Fish, Liver Flukes and Nitrosamines: A Story of Cholangiocarcinoma Development in Thailand

Viroj Wiwanitkit

Abstract

Cholangiocarcinoma is a common hepatobiliary carcinoma in Thailand. It is believed that both chronic exposure to liver fluke infestation and nitrosamine exposure are the two main underlying factors leading to the carcinogenesis. Here, the author further extrapolates and proposes a new hypothesis based on the environmental ecological data that the stimulation of fresh water fish by contaminated pesticide in water reservoirs might be a possible background of the high prevalence of cholangiocarcinoma in Thailand

Key Words: Cholangiocarcinoma - pesticides - fresh water fish - liver flukes - nitrosamines - Thailand

Asian Pacific J Cancer Prev, 10, 939-940

Introduction

Cholangiocarcinoma is a common hepatobiliary carcinoma in Thailand (Sripa and Pairojkul, 2008). This cancer usually manifests as a severe jaundice disease. Unluckily, the patients usually develop silent progression of tumor for a long time before the finalized severe hyperbilirubinemia due to obstruction of the biliary tract. The exact pathogenesis of this cancer is still controversial. Similar to other cancers, both environmental and genetic factors are mentioned to play roles. It is believed that both chronic liver fluke infestation and nitrosamine exposure are the two main underlying factors leading to the carcinogenesis.

In Thailand, the local people in northern and northeastern regions have a common problematic behavior, eating raw or uncooked fresh water fish (Sripa et al., 2007; Kaewpitoon et al., 2008a; 2008b). This is the main cause of getting liver fluke infestation. Focusing on the liver fluke life cycle, the infective stage metacercariae of liver fluke lives in the small fresh water fish in cyprinoid group and the infectious larvae will enter into the human who ingests uncooked fish. After entering into the human body, the parasite will move to chronic settle down in the biliary tract and cause chronic irritation. In addition to the parasite, many Thai local dishes are poorly prepared and contaminated with a well known carcinogen, nitrosamine (Hummel et al., 2008; Mitacek et al., 2008). The nitrosamine is confirmed for its carcinogenicity in the hepatic system. Therefore, in the local Thai people in rural areas, exposure to both liver fluke and nitrosamine can contribute to the carcinogenesis (Pairojkul et al., 1991; Srivatanakul et al., 1991a; 1991b).

However, there is still a question on the carcinogenesis

process of cholangiocarcinoma. Liver fluke, itself, is not a carcinogen and not all Thai local dishes add nitrosamine ingredient. Also, why the problem has just emerged for few decades is still unexplained. Therefore, it is still questionable whether there are any other sources of nitrosamine in the present day. Here, the author further extrapolates and proposes for a new hypothesis based on the environmental ecological data that the stimulation of fresh water fish by contaminated pesticide in water reservoi

Environmental Ecological Considerations

It is accepted that the concept of cancer prevention in the present day extends from the limited human beings focus to biome focus. Human and his/her environment must be concerned. Many pollutants can facilitate the carcinogenesis process. The author firstly hypothesized that there might be a possible additional source of nitrosamine in the system of carcinogenesis for cholangiocarcinoma. There might be a naturally contaminated nitrosamine in the fish before getting parasitic infestation or eaten by human beings. This is according to the principle of accumulation of toxic substance in food chain.

Of interest, there are many recent publications reporting on the high nitrogen species in the water reservoirs (Konda and Pásztor, 2001; Rabalai, 2002; Pilati et al., 2009). This is confirmed for the correlation to the contaminated pesticide in the water reservoirs (Gardner et al., 1998; Gammon et al., 2005). Also, the fresh water fish which live in those problematic reservoirs are exposed to nitrogen species including nitrosamine and accumulate in their flesh. There are reports that fresh water fish

chronically expose to nitrosamine can develop cholangiocarcinoma (Bailey et al., 1994; Diekmann et al., 2004). However, in real situation, the fresh water fish do not live for a long time because they are usually caught for eating by human beings.

Implications for Cancer Prevention

It can hereby be seen that there might be a complex chain of problems leading to the finalized problem of cholangiocarcinoma. At present, the campaign of "no eating of raw fresh water fish" is in use and effective in cancer prevention. This is also accompanied with screening for liver fluke infestation and prompt treatment. However, this might not be sufficient. Additional campaigns to avoid using nitrosamine additive in local foods are also needed. Nevertheless, it should also be noted that there is a need to extend the interest to the environmental problem, the excessive usage of pesticide and contamination of the pesticide into the water reservoir since these activities might lead to the accumulation of natural nitrosamine in fresh water fish which might be a big problem for eating.

The author hereby would like to summarize for the necessary point for control and prevention of cholangiocarcinoma as the followings

- 1. Control of usage of nitrosamine additive in food
- 2. Promotion for no eating of raw fresh water fish
- 3. Regular stool test for liver fluke infestation and antiparasitic drug distribution
- 4. Control of pesticide usage and monitor for pesticide contamination in water reservoir (Ozonoff and Longnecker, 1991).
- 5. Surveillance on the naturally contaminated nitrosamine in fresh water fish

The author hereby discusses and presents on an environmental-human beings model for explaining the problem of an infamous cancer in Thailand, cholangiocarcinoma. It can be seen that there might be a forgotten problem of pesticide usage that can induce accumulation of nitrosamine in fresh water fish.

References

- Bailey GS, Hendricks JD, Nixon JE, Pawlowski NE (1984). The sensitivity of rainbow trout and other fish to carcinogens. Drug Metab Rev, 15, 725-50.
- Diekmann M, Hutsch V, Nagel R (2004). On the relevance of genotoxicity for fish population I: effects of a model genotoxicant on zebrafish (Danio rerio) in a complete life cycle test. Aquatic Toxicol, 68, 13-26.
- Gammon DW, Aldous CN, Carr WC Jr, Sanborn JR, Pfeifer KF (2005). A risk assessment of atrazine use in California: human health and ecological aspects. Pest Manag Sci, 61, 331-55.
- Gardner HS Jr, Brennan LM, Toussaint MW, et al (1998). Environmental complex mixture toxicity assessment. Environ Health Perspect, 106 Suppl 6, 1299-305.
- Kaewpitoon N, Kaewpitoon SJ, Pengsaa P (2008a). Opisthorchiasis in Thailand: review and current status. World J Gastroenterol, 14, 2297-302
- Kaewpitoon N, Kaewpitoon SJ, Pengsaa P, Sripa B (2008b).

- Opisthorchis viverrini: the carcinogenic human liver fluke. World J Gastroenterol, 14, 666-74.
- Konda LN, Pásztor Z (2001). Environmental distribution of acetochlor, atrazine, chlorpyrifos, and propisochlor under field conditions. J Agric Food Chem, 49, 3859-63.
- Mitacek EJ, Brunnemann KD, Suttajit M, et al (1999). Exposure to N-nitroso compounds in a population of high liver cancer regions in Thailand: volatile nitrosamine (VNA) levels in Thai food. Food Chem Toxicol, 37, 297-305.
- Mitacek EJ, Brunnemann KD, Suttajit M, et al (2008). Geographic distribution of liver and stomach cancers in Thailand in relation to estimated dietary intake of nitrate, nitrite, and nitrosodimethylamine. Nutr Cancer, 60, 196-203.
- Ozonoff D, Longnecker MP (1991). Epidemiologic approaches to assessing human cancer risk from consuming aquatic food resources from chemically contaminated water. Environ Health Perspect, 90, 141-6.
- Pairojkul C, Shirai T, Hirohashi S, et al (1991). Multistage carcinogenesis of liver-fluke-associated cholangiocarcinoma in Thailand. Princess Takamatsu Symp, 22, 77-86
- Pilati A, Vanni MJ, González MJ, Gaulke AK (2009). Effects of agricultural subsidies of nutrients and detritus on fish and plankton of shallow-reservoir ecosystems. Ecol Appl, 19, 942-60.
- Rabalais NN (2002). Nitrogen in aquatic ecosystems. Ambio, **31**, 102-12.
- Sripa B, Kaewkes S, Sithithaworn P, et al (2007). Liver fluke induces cholangiocarcinoma. PLoS Med, 4, e201.
- Sripa B, Pairojkul C (2008). Cholangiocarcinoma: lessons from Thailand. Curr Opin Gastroenterol, 24, 349-56.
- Srivatanakul P, Ohshima H, Khlat M, et al (1991a). Endogenous nitrosamines and liver fluke as risk factors for cholangiocarcinoma in Thailand. IARC Sci Publ, 105, 88-
- Srivatanakul P, Ohshima H, Khlat M, et al (1991b). Opisthorchis viverrini infestation and endogenous nitrosamines as risk factors for cholangiocarcinoma in Thailand. Int J Cancer, 48, 821-5.