Dynamic Chiropractic

HEALTH & WELLNESS / LIFESTYLE

Water Disinfection By-Products: Trihalomethanes and Carcinogenicity -- Should DCs Care?

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Chiropractic and environmental health are a good mix. The full breadth of the health issues continues to widen in the face of increasing recognition of health hazards in our environment and lives. The doctor of chiropractic has new roles to play outside of the neuromusculoskeletal realm when counseling, advising and referring patients. The sphere of concern and activity seems to be pushing outward, as DCs are cross-trained in other health disciplines. Water disinfection byproducts are another example of a group of potentially lethal man-made environmental chemicals being consumed by every one of our patients.

"The presence of trihalomethanes in drinking water has been the subject of increasing public concern since the 1970s."[1] Specific concerns over the potential adverse effects related to cancer and developmental abnormalities have been the point of public and scientific debate.2 As a consequence of public concern, the Environmental Protection Agency (EPA) is taking action. The EPA has prepared an 85-page summary of proposed drinking water regulations related to disinfectants and disinfection byproducts (DBPs) containing 122 references and available off the Internet.[2] The following is a brief overview of the topic of DBPs and trihalomethanes, using selected examples. In doing so, a basic review of the facts is presented regarding their sources, routes of exposure, toxicology and epidemiological relationship to carcinogenicity. The authors are intending to inform and educate treating doctors of chiropractic on yet another health issue that may adversely effect their patients, families and themselves. The next time you advise a patient to drink eight glasses or more of water a day, you might think of adding the words "filtered" first.

Sources

Key factors identified as affecting the formation of DBPs include the type of disinfectant, application point in the treatment process, type and concentration of organic matter in the water being treated, pH, temperature, and contact time with disinfectant.[2,3,4,5,6]

Chlorine is the principal disinfectant used to purify 98% of the drinking water in the modern world.[3,7,8] Bromine may alternatively be used in water disinfection with or without chlorine.[5] Disinfection of water against waterborne disease is achieved through chlorination. "Chlorination starts at the point where pH >5 and Cl concentration in the mg 1-1 range, complete and instantaneous disassociation is observed."[9] Free chlorine is toxic to waterborne organisms.

Basic water treatment methods include coagulation, sedimentation, filtration, chemical oxidation and disinfection.[4] Critical to the formation of DBPs is the total organic compounds (TOCs) in the water; this varies depending on the location of chlorination in that process and treatment methods used. Chlorine or bromine is added to the water at potentially multiple points in the disinfection treatment process. Free chlorine or bromine may then interact with TOCs to produce a wide array

of organo-compounds: trihalomethanes (THMs), halogenated acetic acids (HAAs), halogenated acetonitriles, haloketones, halophenols, aldehydes, chlorinated furones, and others (see table 1).[4,5,10,11] As a consequence of water treatment methods, DBPs have been identified in variable concentrations in different communities.[2]

Table 1: Potential Disinfection Byproducts (DBPs).

Trihalomethanes	Haloalkenes
Chloroform Bromodichloromethane Dibromochloromethane Bromoform	1,1 Dichloropropanone 1,1,1 Trichloropropanone
Haloacetic Acids	Chlorophenols
Monochloroacetic acid Trichloroacetic acid Monobromoacetic acid Dibromoacetic acid	2,4 Dichlorophenol 2,4,6 Trichlorophenol
Haloacetonitriles	Aldehydes
Dichloroacetonitrile Trichloroacetonitrile Bromochloroacetonitrile Dibromoacetonitrile	Trichloroacetaldehyde Formaldehyde Acetaldehyde
	Others
	Chloropicrin Cyanogen chloride 3 Chloro 4(dichloromethyl) Hydroxy 2 (5H) furanone

Exposure Routes

Humans are primarily exposed to DBPs, specifically THMs, through consumption of drinking water.[2,12] Other routes of exposure include dermal and respiratory pathways from bathing and swimming pool use.[13,14]

Toxicokinetics

DBPs are rapidly absorbed and distributed by the blood compartment to many tissues.[15,16] Mathews et al. (1990) found radioactively tagged DBPs within 24 hours of their ingestion, in blood, plasma, adipose, intestine, kidney, liver, muscle, skin and stomach. The highest levels were found in the liver. Biotransformation varies with the chemical characteristic of the DBP. THMs, such as chloroform, follow two pathways: one, first-order kinetics with elimination of parent compound through the lung; and two, metabolism in the liver by P450 enzyme oxidation, and to a lesser extent in the kidney and other tissues.[13]

Toxic metabolites may be formed by P450 enzyme reaction and then induce glutathione and other phase II enzymes to conjugate and detoxify hepatic and nephrotic cells, or result in additional activation and cell injury.[17] THMs such as chloroform and bromodichloromethane (BDCM) are eliminated via respiration, urine and feces.[13,16,17]

Toxicodynamics

Toxic metabolites may be formed during biotransformation of a number of DBPs and induce cell injury. Pegram and colleagues[17] reported that rodent and bacterium studies revealed evidence that chloroform and BDCM both induce cytotoxicity through glutathione (GSE) mediated pathways. In two-year rodent studies, cytochrome P450 enzyme induced reactive metabolites such as phosgene to be formed. Those same researchers also concluded, "Chloroform hepatotoxicity has been associated with covalent binding of reactive metabolites to tissue macromolecules."[16,18]

Snyder and Andrews18 discuss an indirect theory of carcinogenesis from recurrent injury to hepatic cells. The kidney was also identified as a target organ for phosgene generated from BDCM. Genotoxic metabolites derived from GSE-transferase interactions are believed to exert injury if generated intracellularly.[17] Daniel and colleagues[19] found increased organ weights in rats exposed to BDCM in their subchronic 90-day study. Overall reduced body weights were seen in treated rats; liver and kidney weights increased while brain weight decreased. Histopathologic evaluation revealed fatty changes, inflammation, and slight necrosis in hepatic cells and tubular necrosis in the kidneys. Dunnick & Melnick[20] reported DBPs, chlorodibromomethane, BDCM, and bromoform induced base-pair substitution mutations in bacterium studies. Evidence from their chronic two-year study on rats revealed P450 mediated oxidation to toxic dihalocarbonyl intermediates causing cellular injury and regenerative hyperplasia. Itoh & Matsuoka[21] found evidence that DBP compounds containing nitro and carbonyl groups could induce chromosomal aberrations in hamster cells.

Epidemiology

Numerous investigators have looked into the association of DBPs to adverse health effects in the areas of carcinogenesis and reproductive and developmental effects. Koivusalo and colleagues[22] found that "statistically significant risk" was observed for women to develop cancers of the bladder (relative risk RR: 1.48), rectum (RR 1.38), esophagus (RR 1.90), and breast (RR 1.11 -- see Figure 3). Stocker1 reported, "These trihalomethanes have shown evidence of genotoxicity in bacterial and mammalian cell systems in vitro and some evidence of carcinogenicity in rodents." King & Marrett[23] found evidence of increasing risk for bladder cancer with increasing concentration and duration of DBP exposure. Koivusalo and and colleagues[24] found minimal to significant increasing risk of cancers of the liver, pancreas, soft-tissue, Hodgkin's disease, non-Hodgkin's lymphoma, and leukemia due to drinking chlorinated water. McGeehan[25] in Colorado found increased risk of bladder cancer with prolonged exposure to chlorinated surface water compared with no exposure.

Table 2: Cancers potentially related to DBPs. Koivusalo, et al., 1997.

Site	Women (RR)	Men (RR)
Esophagus	1.90	0.92
Liver	0.84	1.11
Soft Tissue	1.46	0.93
Melanoma	1.27	1.02
Breast	1.11	0.00
Bladder	1.48	1.12
Non-Hodgkins	1.40	1.18

Glioma	1.35	0.94
Leukemia	1.08	1.02

Conclusions

While the jury is still partially out, the evidence is growing, both epidemiologically and mechanistically, to identify and understand the relationship between THMs and other DBPs and their role in increased cancer rates. Researchers have been quick to admit that ecological and environmental studies are fraught with difficulty when attempting to establish a clear cause-effect relationship of DBPs to cancer. The confounders are numerous and very difficult, if not impossible, to adjust for entirely. Increasing interest has been focused on alternative water disinfection methods; however, they too are not without drawbacks. It is clear that the risk of not using proper disinfection methods far outweighs the immediate consequences of waterborne infectious disease. The real risk of disease from chlorinated or bromonated water is not known. The EPA2 has estimated that "Cancer risks due to DBPs range from less than 1 case per year to over 10,000 cases per year," while cost estimates to reduce these risks range from $400,000 to $8 billion per case!

Chiropractic doctors should advise their patients and families to drink water that has been filtered, distilled, or at least left open to volatilize organics and increase the purity of the water. Water is essential to life, and disinfection methods are being adapted to minimize DBP formation in most communities. Everyone shares environmental health issues. Stand up and be educated on the risks to which your patients are exposed; give good advice and take pride in being a multitalented health practitioner.

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