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Evidence Review for Adverse Health Effects of Drinking Optimally Fluoridated Water (2010-2017)

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Contents

Key Messages

- The existing literature (to May 10, 2017) indicates that mild dental fluorosis (generally unnoticeable white specks on teeth) is the only adverse effect experienced from the consumption of optimally fluoridated water (Health Canada recommends the optimal level of fluoride in water at 0.7 mg/L).
- Infant formulas mixed with optimally fluoridated water may increase the chance of the mild form of dental fluorosis if they are the child's main food source. If prevention of the mild form of fluorosis is desired then infant formula can be occasionally mixed with low-fluoridated bottled water.
- If prevention of the mild form of fluorosis is desired, early exposure to other forms of fluoride including fluoride toothpaste, fluoride rinse, and fluoride supplements should be monitored.
- Considering the dose-response relationship between the fluoride exposure and health effects, as a practice consideration it is important to fluoridate water at the optimal concentration, where a suitable trade-off is achieved (benefits are maximized and adverse effects are minimized).

Background

To reduce the burden of dental decay, community water has been fluoridated in parts of North America for more than 70 years.[1] According to the US Centers for Disease Control, community water fluoridation (CWF) is considered one of the top 10 public health achievements of the 20th century.[2] According to a position statement released by the Public Health Agency of Canada (PHAC), the advantage of CWF is that it benefits all residents of a community, irrespective of their age, oral health behaviours, socioeconomic status, education, employment, or access to dental care, making it a truly equitable public health practice.[3]

Fluoride occurs naturally in water and its concentration can vary widely. In the United States (US), the natural level of fluoride in ground water varies from very low levels of less than 0.1 mg/L to over 4 mg/L.[4] Water fluoridation is a process of optimally adjusting the concentration of fluoride in community drinking water to help reduce tooth decay in the populations served. Health Canada recommends an optimal level of 0.7 mg/L and a maximum acceptable concentration of 1.5 mg/L. While the benefits of CWF in caries prevention are well documented,[5] there is ongoing public debate regarding the continuation of CWF, given the availability of fluoride from other sources and concerns about adverse health effects.[6]

In 2010, Health Canada developed the "Guidelines for Canadian Drinking Water Quality: Guideline Technical Document – Fluoride", to provide a better understanding about the different aspects related to fluoride including any adverse health effects.[7] This technical document from this point onward is referred to as the 2010 Health Canada fluoride document. The 2010 Health Canada fluoride document summarized findings from reports and studies published in or before 2010, focusing on both effectiveness and adverse health effects related to consumption of fluoridated water. The main adverse effects examined in the 2010 Health Canada fluoride document included dental fluorosis, skeletal effects, cancers, reproductive/developmental effects, mutagenicity/genotoxicity, neurobehavioral effects, and urolithiasis (kidney stones).[7]

The full-text 2010 Health Canada fluoride document is available from the Health Canada website.

Following the release of the 2010 Health Canada fluoride document, research has continued looking for any relationship between fluoridated community drinking water and adverse health effects.

Purpose

Based on a request from public health units in Ontario, the purpose of this report is to provide a summary of the 2010 Health Canada fluoride document findings (Appendix A) and new evidence on adverse health effects of optimally controlled fluoridated community drinking water on humans, published since then.

It is important to note that the 2010 Health Canada fluoride document included all studies irrespective of the fluoridation level and source, and included human as well as animal studies.

The scope of the present report is *optimally* controlled fluoridated community drinking water and *humans*. Therefore, content from the 2010 Health Canada fluoride document that is beyond the present scope is not described here.

Methods

Public Health Ontario (PHO) Library Services completed a database search on May 10, 2017. Four electronic databases were searched (Ovid MEDLINE, Embase, CINAHL, and Dentistry) for literature from January 1, 2009 to May 10, 2017. Key search terms included, but were not limited to: fluoridation, community water, infant formula, risk, fluorosis, bone and cancer. Duplicate references were removed. In addition, a grey literature search was conducted to identify organizational guidelines, reports and position statements published after the 2010 Health Canada fluoride document.

Peer reviewed published articles were eligible if they represented primary findings from any study design, or syntheses of existing literature. Articles evaluating the effect of naturally fluoridated water (where the fluoride concentrations vary significantly) were not considered, as the intent was to assess the effect of optimally controlled fluoridated water. Also, no studies assessing the effect of fluoridated salt or milk were included in this review. In addition, with the focus on adverse health effects, any study assessing the benefits or effectiveness of fluoride in terms of reducing dental decay, was excluded.

Nine hundred articles were identified and 29 were included: two systematic reviews,[5,8] 20 cross-sectional studies,[9-28] five prospective cohort studies,[29-33] and two case control studies.[34,35] All the included studies were observational in nature. The two included systematic reviews were appraised using the Health Evidence Quality Assessment Tool (HE).[36] The Newcastle-Ottawa Scale (NOS)[37] was used to assess the methodological quality of the observational studies (n=27).

The grey literature search for organizational guidelines, position statements, and reports yielded six documents; one each from the Public Health Agency of Canada (PHAC),[3] Health Services Ireland,[38] Public Health England (PHE),[39] American Dental Association,[40] the Centers for Disease Control and Prevention (CDC),[41] and the EU Scientific Committee on Health and Environmental Risks (EUSCHER).[42] The grey literature was not appraised.

Main Findings

Quality appraisal of included articles

All included articles from the peer review literature were appraised according to the criteria of the relevant quality appraisal tools used. Additional published critiques,[43,44] were considered to augment the quality assessment of two included articles.[18,20] No studies were removed based on their quality appraisal score. In general, the included studies accounted for key methodological parameters such as representativeness and size of the study sample, relevant confounders (such as age, gender etc.), assessment of outcome, and reported adequate follow up periods. However, due to the observational nature of the included studies and the risk factor being fluoride exposure exclusively through community water, it may be difficult to control for other forms of fluoride exposure in respective studies' participants. This is not a reporting issue, but a general limitation for such studies. Similarly, blinding was not possible due to the nature of exposure under consideration i.e., difficult to blind participants to fluoride exposure. Exposure in included studies was assessed either by record linkage or was self-reported. Self-report has the potential to introduce bias. Details about article screening and the quality appraisal scores are available upon request.

Organization of Findings

The evidence in this report is organized by adverse health outcomes that include: dental fluorosis, enamel opacities, hypo-mineralization, and bone health, cancers including bone cancers, reproductive, neurobehavioral effects, mutagenicity, hypothyroidism, and urolithiasis. Broadly, these outcomes align with the 2010 Health Canada fluoride document. For the purpose of comparison, this report includes the relevant background information from the 2010 Health Canada fluoride document for each outcome (see Appendix A).

Developmental defects of teeth

One Cochrane systematic review,[5] 12 primary studies, and two grey literature reports[3,39] assessed the effect of water fluoridation on developmental defects of teeth. Of the 12 primary studies, three each were conducted in Brazil[13,23,35] and England;[11,15,22] two each in Australia[10,26] and the US[16,24] and one each in Hong Kong[12], and Switzerland.[14]

DENTAL FLUOROSIS

Consistent with the 2010 Health Canada fluoride document, the prevalence of mild or worse forms of fluorosis continued to vary across recent studies.[13-15,22-24,26,35] Fluorosis presents as white specks on teeth and is generally unnoticeable.[3] Assessed by the Thylstrup Fejerskov (TF) index (the levels range from TF0 to TF5; Public Health England considers a level of TF3 as mild or mild to moderate), the two communities in Brazil, starting fluoridation (0.7 mg/L) in different years (in 1971 and 1997), observed the fluorosis prevalence among 12-year-olds (in 2007) at TF3 level as 0.67% and 1.51%, respectively. [13] In a study

done in Switzerland, 2.7% of 12-year-old children in a fluoridated community (0.8-1.0 mg/L) scored fluorosis level of TF3. [14] An Australian study showed approximately 9.9% of 8 to 12-year-old children who were exposed to fluoridated water during at least the first three years of life having a fluorosis level of TF2 or more. [26] Pretty et al. found that the prevalence of fluorosis at levels TF3 or greater was 10% in fluoridated communities of England. [15] The 2014 Public Health England's report (based on monitoring the effects of water fluoridation schemes on the health of people living in the areas covered) concluded that among 12-year-olds in fluoridated (1.0 mg/L) communities, the prevalence of TF2 was 9%; TF3 was 6%; and TF4 was 1%. [39]

Assessing fluorosis by the Dean's index (the levels are: normal, questionable, very mild, mild, moderate and severe), a Brazilian study reported 2.6% of 12-year-old children have a mild or moderate form of fluorosis in a fluoridated community.[35] Another Brazilian study reported approximately 10% having mild and 1.5% with moderate form of fluorosis among 12-year-old children regularly exposed to fluoridated water.[23] In a US study, 3.5% children had mild and 1.1% had moderate forms of fluorosis in a fluoridated community.[24] Bal et al. reported that in Australia, a water fluoridation concentration of 1.0 mg/L was associated with 6% mild and 1.5% moderate or severe forms of fluorosis among 7 to 11-year-old children.[10] Bal et al indicated that the relatively higher prevalence of fluorosis was related to the higher-than-optimal level of fluoride in drinking water and fluoridated toothpaste swallowing during early childhood. [10]According to the Cochrane systematic review, with a fluoride level of 0.7 mg/L in water, approximately 12% of people can have mild or worse dental fluorosis.[5]

Similar to the 2010 Health Canada fluoride document, a position statement from the Public Health Agency of Canada (2016) reported that the most likely adverse effect of CWF is mild dental fluorosis, which causes white specks on teeth and is generally unnoticeable.[3] In terms of levels, Health Canada (2010) concluded that a moderate level of dental fluorosis was the end-point of concern, and that the prevalence of very mild and mild dental fluorosis is of no concern. However, the Cochrane systematic review reported that mild or worse fluorosis might be an aesthetic concern.[5] Of note, the various sources of evidence are not consistent in defining the endpoint of concern when it comes to aesthetics (i.e. mild vs. moderate fluorosis).

In terms of self-perception about the aesthetic impact of dental fluorosis, a Swiss study by Buchel et al. reported that fluorosis in communities with fluoridated water did not represent an aesthetic problem nor a public health concern.[14] Interestingly, McGrady et al., in a UK study, found that teeth with a fluorosis level of TF1 and TF2 are ranked more favourably than TF0.[22] Fluorosis, not as an outcome but as an attribute, was studied by Joaloso et al., who found that the milder forms of fluorosis do not affect the eruption time of teeth. [16]

ENAMEL OPACITIES AND HYPO-MINERALIZATION

In regard to the developmental defects of enamel, enamel opacities and hypo-mineralization have been reported as adverse health effects.

A repeated cross-sectional study in Hong Kong assessed diffused enamel opacities on maxillary incisors using data from 1983, 1991, 2001 and 2010, when fluoridation levels were 1.0, 0.7, 0.5 and 0.5 mg/L,

respectively.[12] The prevalence of opacities for the four observed years was 89.3%, 48.5%, 32.4% and 42.1%. The prevalence decreased from 1983 to 2001, but increased again in 2010, although fluoridation levels remained the same. The authors concluded that this change did not fully correspond to the concentration of fluoride in the drinking water during the time of enamel development, but could be due to exposure to other forms of fluoride.[12]

A study conducted in Northern England reported an 11% prevalence of molar and incisor hypo-mineralization in the fluoridated community, and 17.5% in the non-fluoridated community.[11] A higher prevalence of developmental defects including hypo-mineralization in the non-fluoridated community could be the effect of both fluoride and/or non-fluoride factors. Fluoride exposure could be because of the "Halo effect", which is fluoride consumption in a non-fluoridated community from other sources such as foods and beverages manufactured using fluoridated water. Consumption of fluoridated toothpaste or fluoride supplements could also increase levels of systemic fluoride. Non-fluoride reasons could include physical injuries, systemic illnesses (for example, some neurological or endocrine disorders) or certain medications taken during childhood during the formative stage of tooth development, which can also result in such oral manifestations.[12]

Infant formula with fluoridated water and fluorosis

One systematic review from Australia,[8] two primary studies (Australia, the U.S.),[27,31] and two grey literature reports,[40,41] assessed the effect of fluoridated water used to reconstitute infant formula on dental fluorosis.

Higher fluoride intakes from reconstituted powdered formulas and other water-added beverages at the age of 3-9 months increased the risk of mild fluorosis.[27,31] Each 0.1 mg/L increase in fluoride level in the water that is mixed with infant formula was associated with a 5% increase in enamel fluorosis of any level.[8] The authors concluded that infant formula mixed with fluoridated water is potentially associated with an increased risk of developing enamel fluorosis.[8]

According to an expert panel convened in 2011 by the American Dental Association (ADA), dentists can continue to advise parents and/or caregivers to reconstitute infant formulas with optimally fluoridated water while being cognizant of the potential risks of enamel fluorosis development.[40] According to the CDC, if a child is consuming only infant formula mixed with fluoridated water, the chances of developing faint white markings of very mild or mild dental fluorosis on teeth may be increased.[41] The CDC advises the use of bottled water (low-fluoridated) sometimes instead of tap water (optimally fluoridated) to mix infant formula; it is important to note, "these bottled waters are labeled as de-ionized, purified, demineralized, or distilled, and without any fluoride added after purification treatment." [41] The Ontario Dental Association (ODA), citing both the ADA and the CDC, also states that if a "child is exclusively consuming infant formula reconstituted with fluoridated water, there may be an increased chance for mild enamel fluorosis, but enamel fluorosis does not affect the health of the child or the health of the child's teeth." [45]

Bone Health including skeletal fluorosis, bone mineral density, and fractures

Four primary studies, two from the US;[30,32] and one each from Canada[9] and Ireland,[19] and two grey literature reports[38,39] assessed the impact of water fluoridation on physical and structural properties of bone. One additional study conducted in Sweden[33] assessed the impact of fluoride in drinking water on hip fractures. We did not identify any studies released since the 2010 Health Canada fluoride document to comment on the association with skeletal fluorosis.

The Canadian study compared the fluoride content and structural or mechanical properties of bone between adults from Toronto (fluoridated community) and Montreal (never fluoridated), and found a weak relationship among fluoride exposure, accumulated fluoride, and the physical characteristics (density and compressive mechanical property) of bone.[9] The fluoride content of bone of Toronto residents was significantly higher ($p < 0.001$) than residents of Montreal; however, the range for the Toronto specimens fully included the range of the Montreal ones. Although, the mean density of cancellous cores of Toronto specimens (0.90 ± 0.04 g/cm^3) was significantly greater than Montreal (0.75 ± 0.05 g/cm^3), the density of cancellous cores in the study did not correlate closely with the fluoride content. Interestingly, a prospective US cohort study observed children from birth to adolescence, and performed gender-stratified analysis for 11-year-olds and found no associations between average daily fluoride intake and bone outcomes for girls (Spearman association between daily fluoride intake and DXA bone measures were $r = -0.01$ to 0.24), but found a non-significant positive association for boys (Spearman correlation of $r=0.04$ to 0.24).[32] In addition, when observing the same cohort at 15 years of age, the same study found fluoride exposures do not have significant effects on bone mineral measures.[30] The authors noted the need for additional research to better understand the potential gender and age-specific effects of fluoride intake on bone development.[32]

A study in Ireland found no significant relationship between the proportion of households with a fluoridated water supply and bone health (index of bone stiffness calculated as a measure of bone mineral density).[19] The Ireland Health Services report also found no association between fluoridation of drinking water at the recommended levels and risk of bone fracture.[38] According to the report from Public Health England, "there was no evidence of a difference in the rate of hip fractures between fluoridated and non-fluoridated areas."[39] In the Swedish study, Nasman et al., found no association between chronic fluoride exposure from drinking water and the occurrence of hip fracture.[33]

Cancers including osteosarcoma

Five primary studies, two from England,[21,25] two from the US[28,34] and one in Ireland,[17] as well as two grey literature reports[39,42] assessed the effect of water fluoridation on bone cancers.

Findings from the primary studies were consistent with the 2010 Health Canada fluoride document. None of the recent studies found a relationship between fluoridation and incidence rates of osteosarcoma at any age.[17,21,25,28,34] Furthermore, Public Health England stated there was no evidence that osteosarcoma rates differed between fluoridated and non-fluoridated communities.[39] Also, Public

Health England stated there was no evidence for an association of fluoridated water consumption with bladder cancer and all cancers, in general. The EUSCHER report also concludes, "epidemiological studies do not indicate a clear link between fluoride in drinking water, and osteosarcoma and cancer in general".[42]

Reproductive/developmental effects

No peer-reviewed articles assessing the reproductive or developmental effects of fluoride in water were identified. Two grey literature reports discussed reproductive and developmental effects.[39,42]

The Public Health England report stated there was no evidence of a difference in the rate of Down's syndrome between fluoridated and non-fluoridated communities.[39] The EUSCHER concludes that fluoride at concentrations in drinking water permitted in the EU did not influence the reproductive capacity of males or females.[42]

Neurobehavioral effects

Two primary studies, one in New Zealand[29] and another in the US,[18] as well as one grey literature report[42] assessed the neurobehavioral effects of fluoridated water.

The recent New Zealand prospective cohort study detected no clear differences in IQs between the fluoride-exposed (mean (SD): 100.0 (15.1)) and non-exposed group (mean (SD): 99.8 (14.5)), suggesting that community fluoridated water is not neurotoxic. [29]

The US ecological study assessed the relationship between water fluoridation and Attention Deficit Hyperactivity Disorder (ADHD) among 4-17 year olds using administrative data.[18] The authors concluded that states with a greater proportion of people receiving fluoridated water from public water supplies had higher proportions of parents reporting medically-diagnosed ADHD among their children, which warrants future studies to explore this relationship further.[18] This study was critiqued by other researchers for methodological limitations including measurement error and no consideration for other potential explanatory variables (such as pre-term birth or exposure to tobacco, alcohol, arsenic or lead) apart from SES.[43] The results are advised to be interpreted with great caution due to high risk of ecological fallacy (water fluoridation measured at state level) and confounding bias.[43]
The EUSCHR report concluded that based on available human studies, fluoride in drinking water at levels permitted in the EU does not impair children's neurodevelopment.[42]

Mutagenicity/genotoxicity

No studies assessing the impact of community-fluoridated water on mutagenicity/genotoxicity were identified. Future studies may be helpful to understand any potential relationship.

Hypothyroidism

One study, conducted in England, assessed the association of fluoridated water and hypothyroidism. [20]

This study found that clinical practices located in fully-fluoridated areas are nearly twice as likely to

report high hypothyroidism prevalence in comparison to non-fluoridated areas.[20] This study was highly critiqued by scientists; Newton et al stated that the authors did not establish a clear prior hypothesis for the association, misrepresented the conclusions of the existing literature, did not adequately control for potential confounding variables, and categorised variables with arbitrary cut-offs that deviated from normal practice.[44]

Current literature does not provide enough evidence to assess the relationship between the consumption of fluoridated water and hypothyroidism. Future studies with greater methodological rigour will be helpful in this regard.

Kidney Stones/Urolithiasis

One grey literature report assessed the impact of optimally fluoridated water on kidney stones.[39] No peer-reviewed studies were identified.

According to the Public Health England report, there was strong evidence that the rate of kidney stones was lower in fluoridated communities than in non-fluoridated areas following adjustment for age, gender, deprivation and ethnicity.[39] Future studies may be helpful to further understand any potential association.

Discussion and Conclusion

This report is a summary of the evidence published since the 2010 Health Canada fluoride document to May 10, 2017 about the adverse health effects of optimally controlled fluoridated water, including the effects when mixed with infant formula.

Overall, the existing literature suggests that at an optimal concentration of water fluoridation, the only adverse health consequence observed is a mild form of dental fluorosis. As the timing and dosage of fluoride exposure is critical in attributing the severity of dental fluorosis, the results of such studies further emphasize that early exposure to other forms of fluoride, including fluoride toothpaste, should be monitored to reduce cumulative fluoride exposure. For example, fluorosis was observed in some non-fluoridated communities as well.

Always mixing infant formula with fluoridated water has been recognized to increase the potential for mild dental fluorosis. Both Canadian and American organizations including ODA, ADA, and the CDC recommend occasional use of low-fluoridated bottled water as an alternative instead of always using optimally fluoridated tap water.[45]

Attaining an optimal concentration of fluoride in community drinking water is considered crucial in establishing a trade-off between dental caries and dental fluorosis. A 2011 study by Frazão et al. analyzed the fluoride concentration in drinking water, taking into account the balance between the benefits and risks to health.[46] The authors concluded that fluoride levels should be between 0.6 and 0.9 mg/L in order to prevent dental caries, and that concentration > 0.9 mg/L presents a risk to the dentition among children under the age of 8 years.[46] The authors also concluded that, to reduce the proportion of children and adolescents with fluorosis levels of aesthetic significance, the water fluoridation levels should be in the range of 0.5 to 0.7 mg/L.

The 2010 Health Canada fluoride document states that there is no evidence to support a link between exposure to fluoride in drinking water at or below 1.5 mg/L and any adverse health effects such as any types of cancer, developmental defects, neurobehavioral effects, or genotoxicity.[7] The studies conducted and the organizational reports published after the 2010 Health Canada fluoride document and until May 10, 2017 corroborate these findings.

Considering that the studies included in this report assessed the impact of optimally fluoridated water and most of them were from countries that have similar demographic and socio-political environments, their findings can be generalized to the Canadian context. Health Canada recommends water fluoridation at 0.7 mg/L, which is much lower than the maximum acceptable concentration of 1.5mg/L; therefore, the likelihood of any adverse health consequences at this concentration is low.

Limitations

This report is based on a review of recent studies conducted across a range of jurisdictions. Not all

findings may be directly comparable to the Ontario context because of variations in exposures to other forms of fluoride, general oral health behaviours or access to the healthcare system, for example. In addition, our search focused on studies reported in the English language, which means some relevant literature could have been missed.

Implications for Practice

The fluoridation of community drinking water has been considered a safe and cost effective population-based approach to reduce dental decay. The current literature (to May 2017) has identified the mild form of dental fluorosis, which is not of health concern, as the only inadvertent effect of consuming drinking water fluoridated at optimal levels.

There is a dose-response relationship between fluoride exposure and health effects. Therefore, as a practice consideration, fluoridating water at an optimal concentration, where a suitable trade-off is achieved (benefits are maximized and adverse effects are minimized), is important.

The age of fluoride exposure is also an important consideration. Exposure during the first three to four years of life, during the formative stage of tooth development, is associated with increased fluorosis risk. As such, if a child is solely consuming infant formula, mixing it with low-fluoridated water on an occasional basis can reduce the risk of mild fluorosis. In addition, the consumption of fluoridated toothpastes and mouth rinses needs to be monitored.

The studies included in this report are those that were published until May 10, 2017. Evidence updates may be provided as new relevant evidence emerges.

Appendix A: Background from the 2010 Health Canada fluoride document

Developmental defect of teeth including dental fluorosis, enamel opacities, and hypo-mineralization

Dental Fluorosis

According to the literature synthesized in the 2010 Health Canada fluoride document, the "moderate level" of dental fluorosis (as per the Dean's index) is the end-point of concern and the prevalence of "very mild" and "mild" dental fluorosis is of no concern.[7] However, the 2010 Health Canada fluoride document also considers "mild" fluorosis or worse as dental fluorosis of aesthetic concern.

The risk for and severity of fluorosis is related to various aspects including the timing, dose and duration of fluoride intake (irrespective of the source).[7] The period for susceptibility to dental fluorosis is during the first three to four years of life. Prolonged periods of fluoride exposure during the formative stage of tooth development is associated with increased fluorosis risk; however, if higher exposure is limited to the first year of life and the following years have low exposure it may not be as much of a concern. A suitable trade-off between dental caries and dental fluorosis appears to occur around 0.7 mg/L. At this level, both caries experience and fluorosis severity appear to be lower than that seen at 1.0 mg/L.

In regards to the prevalence of mild or worse forms of fluorosis, the Canadian Health Measures Survey (2007 to 2009) from the 2010 Health Canada fluoride document, shows 12.0% dental fluorosis classified as Very Mild, 4.4% as Mild, and only 0.3% had Moderate or Severe fluorosis among children 6-11 years old.[7] As of 2008, 45.1% of Canadians had access to fluoridated water (usually at the level of 0.7 mg/L).

Infant formula with fluoridated water and fluorosis

Powdered infant formula reconstituted with fluoridated drinking water has a higher fluoride concentration than ready-to-use infant formulas. Among 7-12 month olds, if they are breastfed then the daily fluoride intake from food and beverages can be 0.017- 0.021 mg/kg-bw/day in a fluoridated community and 0.011- 0.012 mg/kg-bw/day in a non-fluoridated community.[7] For non-breastfed infants, the intake can be 0.024 - 0.026 mg/kg-bw/day in a fluoridated community, and 0.013 -0.014 mg/kg-bw/day in a non-fluoridated community.[7] Infant formulas with higher levels of fluoride can lead to an increased risk of mild dental fluorosis.

Bone Health including skeletal fluorosis, bone mineral density, and fractures

Skeletal fluorosis is an excessive accumulation of fluoride in bone resulting in increased bone density and outgrowths.[7] Studies in the 2010 Health Canada fluoride document did not show any correlation of water fluoridation and skeletal fluorosis at concentrations of 1.2 and 3.3–6.2 mg/L for 10 years or more.

Regarding fractures, studies showed exposure to fluoride concentrations at 1.0-1.5 mg/L was occasionally associated with a positive effect on bone mineral density; however, it did not significantly increase the risk of fractures.[7] Also, there was inconsistent evidence for an association between water fluoridation and increased risk of hip fracture, primarily because the incidence of hip fractures in several studies was too small to enable definitive conclusions about the risk of such fractures.[7]

Cancers including osteosarcoma

Reviews in the 2010 Health Canada fluoride document suggested no clear association between water fluoridation and overall cancer incidence including osteosarcoma.[7] Some major challenges were recognized in assessing fluoride exposure as a risk factor for osteosarcoma. Firstly, the incidence of osteosarcoma is so low that not many studies are able to capture the new cases in a study population; secondly, it is difficult to estimate precisely the fluoride intake because of multiple sources of fluoride exposure; and lastly, the method of measuring fluoride in bones of studies participants' is too invasive.[7]

Reproductive/developmental effects

Only a few studies in the 2010 Health Canada fluoride document assessed the link between fluoridated drinking water and reproductive or developmental effects. No associations were found between fluoride intake and spontaneous abortions, congenital cardiac disease, or stillbirths.[7] Infants exposed to fluoridated water supplies in utero were not at increased risk for sudden infant death syndrome (SIDS).[7] In addition, there was inconclusive evidence of an association between water fluoride level and Down's syndrome.[7]

Neurobehavioral effects

A number of studies from China in the 2010 Health Canada fluoride document measured the impact of fluoride on children's intelligence quotient (IQ).[7] The significance of these studies is uncertain and concern has been raised about their validity and generalizability, due to lack of methodological rigour and the dose of fluoride exposure (i.e., fluoride concentration of 4.12 mg/L) in those studies.[7]

Mutagenicity/genotoxicity

A study from China in the 2010 Health Canada fluoride document investigated the genotoxic risks of long-term ingestion of drinking water containing fluoride (0.2, 1.0, or 4.8 mg/L) in humans.[7] Results showed numerically small but significant differences; subjects with low fluoride in the water (0.2 mg/L) had higher sister chromatid exchange (SCE) frequencies than those with optimal (1.0 mg/L) or higher (4.8 mg/L) fluoride exposures. Reasons for the reduced SCE frequency in subjects with optimal higher

fluoride exposure were unclear; however, authors concluded that long-term exposure to fluoride in the drinking water, even at an elevated level, does not have genotoxic effects in humans.[7]

Hypothyroidism

As per the 2010 Health Canada fluoride document, fluoride may adversely affect endocrine glands such as the thyroid.[7] The effects of fluoride on thyroid function might depend on the intake of iodine, as there is an association of thyroid dysfunction with low iodine intake; however, in Canada, this is unlikely to occur because iodized salt is mandatory.

Kidney Stones/Urolithiasis

There were no studies in the 2010 Health Canada fluoride document that assessed the impact of optimally fluoridated water on the formation of kidney stones. Only studies from fluoride endemic areas (3.5 to 4.9 mg/L) found the prevalence of kidney stones was 4.6 times higher when compared to non-endemic areas.[7]

References

References

1. Reece-Stremtan S, Marinelli KA. ABM clinical protocol #21: guidelines for breastfeeding and substance use or substance use disorder, revised 2015. Breastfeed Med [Internet]. 2015 01 Apr;10(3):135-41. Available from: https://doi.org/10.1089/bfm.2015.9992

3. Seay A, Freysteinson WM, McFarlane J. Positive parenting [conference abstract]. Nursing forum;

4. Exclusive Breastfeeding: Provides the Best Possible Beginnings for Lifelong Health [Internet]. Toronto, ON: Provincial Council for Maternal and Child Health; cited 2017 Oct 13]. Available from: http://www.pcmch.on.ca/wp-content/uploads/2015/07/PCMCH_BreastFeeding_Placemat_2012.pdf

5. OPHA Breastfeeding Promotion Workgroup Members. Creating a Breastfeeding Friendly Workplace. Toronto, ON: Ontario Public Health Association; 2008. Available from: http://opha.on.ca/OPHA/media/Resources/Resource%20Documents/BreastfeedingFriendlyWorkplace-Sep08.pdf?ext=.pdf

6. Ontario Public Health Association, OPHA Breastfeeding Promotion Network. Informed decision-making & infant feeding position paper. Toronto, ON: Ontario Public Health Association; 2014. Available from: http://www.opha.on.ca/getmedia/9f1864f4-66e1-4a4e-8064-a547bdd45a59/Informed-Decision-Making-Infant-Feeding-OPHA-Position-Paper.pdf.aspx

7. Wellington-Dufferin Guelph Public Health,. Introduction to Adverse Childhood Experiences. In press

8. Amann M, Romer LM, Subudhi AW, Pegelow DF, Dempsey JA. PMC2075206; Severity of arterial hypoxaemia affects the relative contributions of peripheral muscle fatigue to exercise performance in healthy humans. J Physiol (Lond). 2007;581:389-403.

9. Martinez D, Saccone PA, Liu F, Slifstein M, Orlowska D, Grassetti A, et al. Deficits in dopamine D(2) receptors and presynaptic dopamine in heroin dependence: commonalities and differences with other types of addiction. Biol Psychiatry. 2012;71:192-8.

10. Miller P, McKenzie S, Lintzeris N, Martin A, Strang J. The community impact of RIOTT, a medically supervised injectable maintenance clinic in south London. Mental Health and Substance Use: Dual Diagnosis. 2010;3:248-59.

11. Oviedo-Joekes E, Guh D, Marsh DC, Brissette S, Nosyk B, Krausz M, et al. Characteristics and response to treatment among Aboriginal people receiving heroin-assisted treatment. Canadian Journal of Public Health. 2010;101:210-2.

12. Adamowicz P, Gieron J, Gil D, Lechowicz W, Skulska A, Tokarczyk B. The prevalence of new psychoactive substances in biological material - a three-year review of casework in Poland. Drug Testing & Analysis. 2016;8:63-70.

13. Dhalla IA, Persaud N, Juurlink DN. Facing up to the prescription opioid crisis. BMJ (Online). 2011;343:no pagination.

14. Bell J. Buprenorphine in the treatment of heroin addiction. Dusunen Adam. 2012;25:93-100.

15. Pilkinton MW, Robertson A, McCluskey DL. Drugged driving: increased traffic risks involving licit and illicit substances. J Drug Educ. 2013;43:183-201.

16. Begg DJ, Gulliver P. A longitudinal examination of the relationship between adolescent problem behaviors and traffic crash involvement during young adulthood. Traffic Injury Prevention. 2008;9:508-14.

17. Vogel M, Knopfli B, Schmid O, Prica M, Strasser J, Prieto L, et al. Treatment or "high": benzodiazepine use in patients on injectable heroin or oral opioids. Addict Behav. 2013;38:2477-84.

18. Bogstrand ST, Normann PT, Rossow I, Larsen M, Morland J, Ekeberg O. Prevalence of alcohol and other substances of abuse among injured patients in a Norwegian emergency department. Drug & Alcohol Dependence. 2011;117:132-8.

19. Zancanaro I, Limberger RP, Bohel PO, dos Santos MK, De Boni RB, Pechansky F, et al. Prescription and illicit psychoactive drugs in oral fluid--LC-MS/MS method development and analysis of samples from Brazilian drivers. Forensic Sci Int. 2012;223:208-16.

20. Hartman RL, Huestis MA. NIHMS488287 PMC3836260; Cannabis effects on driving skills. Clin Chem. 2013;59:478-92.

21. Brod E, Ogaard AF, Krogstad T, Haraldsen TK, Frossard E, Oberson A. PMC4867682; Drivers of Phosphorus Uptake by Barley Following Secondary Resource Application. Frontiers in Nutrition. 2016;3:12.

22. Kirschbaum KM, Musshoff F, Wilbert A, Rohrich J, Madea B. Direct ELISA kits as a sensitive and selective screening method for abstinence control in urine. Forensic Sci Int. 2011;207:66-9.

23. Thylstrup B, Schroder S, Hesse M. Psycho-education for substance use and antisocial personality disorder: A randomized trial. BMC Psychiatry. 2015;15:no pagination.

24. Cochems A, Harding P, Liddicoat L. Dextromethorphan in Wisconsin drivers. J Anal Toxicol. 2007;31:227-32.

25. Oviedo-Joekes E, Marsh DC, Guh D, Brissette S, Schechter MT. Potency ratio of hydromorphone and diacetylmorphine in substitution treatment for long-term opioid dependency. Journal of Opioid Management. 2011;7:371-6.

26. Popova S, Lange S, Rehm J. Twenty Percent of Breastfeeding Women in Canada Consume Alcohol. J Obstet Gynaecol Can. 2013;35(8):695-6.

27. Wenger LD, Lopez AM, Comfort M, Kral AH. The phenomenon of low-frequency heroin injection among street-based urban poor: drug user strategies and contexts of use. Int J Drug Policy. 2014;25:471-9.

28. Sidlo J. Psychoactive substance-related deaths in road traffic accidents in Slovakia between 2000 and 2007. Bratisl Lek Listy. 2009;110:468-71.

29. Abavare L, Abavare C. Wound botulism resulting from heroin abuse: can you recognize it? Journal of emergency nursing: JEN : official publication of the Emergency Department Nurses Association. 2012;38:301-3.

30. Wille SM, Raes E, Lillsunde P, Gunnar T, Laloup M, Samyn N, et al. Relationship between oral fluid and blood concentrations of drugs of abuse in drivers suspected of driving under the influence of drugs. Ther Drug Monit. 2009;31:511-9.

31. Thombs DL, O'Mara R, Dodd VJ, Merves ML, Weiler RM, Goldberger BA, et al. Event-specific analyses of poly-drug abuse and concomitant risk behavior in a college bar district in Florida. Journal of American College Health. 2009;57:575-85.

32. Toth AR, Varga T, Molnar A, Hideg Z, Somogyi G. The role of licit and illicit drugs in traffic (Hungary 2000-2007). Leg Med. 2009;11 Suppl 1:S419-22.

33. Chen M, Chan KL. Effects of Parenting Programs on Child Maltreatment Prevention: A Meta-Analysis. Trauma Violence Abuse. 2016;17(1):88-104.

34. Blanken P, Hendriks VM, van Ree JM, van dB. Outcome of long-term heroin-assisted treatment offered to chronic, treatment-resistant heroin addicts in the Netherlands. Addiction. 2010;105:300-8.

35. Martin PR, Reid Finlayson AJ. Pharmacopsychosocial Treatment of opioid dependence: Harm reduction, palliation, or simply good medical practice? Dusunen Adam. 2012;25:1-7.

36. Padget SM, Bekemeier B, Berkowitz B. Collaborative partnerships at the state level: promoting systems changes in public health infrastructure. J Public Health Manag Pract. 2004;10(3):251-7.

37. Palinkas LA, Fuentes D, Finno M, Garcia AR, Holloway IW, Chamberlain P. Inter-organizational collaboration in the implementation of evidence-based practices among public agencies serving abused and neglected youth. Administration and Policy in Mental Health and Mental Health Services Research. 2014;41(1):74-85.

38. Neuhaus M, Eakin EG, Straker L, Owen N, Dunstan DW, Reid N, et al. Reducing occupational sedentary time: a systematic review and meta-analysis of evidence on activity-permissive workstations. Obes Rev. 2014;15(10):822-38.

39. Conn VS, Hafdahl AR, Cooper PS, Brown LM, Lusk SL. Meta-analysis of workplace physical activity interventions. Am J Prev Med. 2009;37(4):330-9.

40. van den Berg MH, Schoones JW, Vliet Vlieland TP. Internet-based physical activity interventions: a systematic review of the literature. J Med Internet Res. 2007;9(3):e26.

41. Hughes K, Bellis MA, Hardcastle KA, Sethi D, Butchart A, Mikton C, et al. The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. The Lancet Public Health. 2017;2(8):e356-66.

42. Hughes K, Bellis MA, Hardcastle KA, Sethi D, Butchart A, Mikton C, et al. The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. The Lancet Public Health. 2017;2(8):e356-66.

43. Violence: Early Childhood Home Visitation To Prevent - Child Maltreatment [Internet]. Atlanta, GA: The Community Guide; 2002 [updated February; cited October 13th, 2017]. Available from: https://www.thecommunityguide.org/findings/violence-early-childhood-home-visitation-prevent-child-maltreatment

44. Adolescent Health: Person-to-Person Interventions to Improve Caregivers' Parenting Skills [Internet]. Atlanta, GA: The Community Guide; 2007 [updated October; cited October 13th, 2017]. Available from: https://www.thecommunityguide.org/findings/adolescent-health-person-person-interventions-improve-caregivers-parenting-skills

45. Kim H. Immigration challenges and "multicultural" responses: The state, the dominant ethnic and immigrants in South Korea. Dissertation Abstracts International Section A: Humanities and Social Sciences. 2010;70:4467.

46. Bryanton J, Beck CT, Montelpare W. Postnatal parental education for optimizing infant general health and parent-infant relationships. Cochrane Database Syst Rev. 2013;(11):CD004068. doi(11):CD004068.

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