

Possible Implications of Nitrate Contaminated Water to Human Health- A Review

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Abstract

Water is one of the fundamental resources for maintaining the life on earth and therefore preserving the availability and quality of this resource is extremely important. Due to anthropogenic activities like intensive use of agrochemicals mainly nitrogenous fertilizers, discharge of municipal and domestic sewage, septic systems, road and buildings processes, it could be chemically, physically, or microbiologically contaminated. Each of which is linked to various sources and health related problems and consequences. Long-term exposure to high nitrate drinking water may increase human health risks which may lead to chronic poisoning, linked to methaemoglobinemia. Nitrate contamination in groundwater and surface water is extensively explored problem at global level. Water containing high concentration of nitrate is unfit for human consumption and can contribute to eutrophication if discharging to fresh water sources. The objective of this review paper is to study the possible implications of nitrate present in different water sources to human health.

Key words: Nitrate contamination, water sources, methaemoglobinemia, human health

1. Introduction

Out of the fundamental resources like air, soil and water, water is an important resource as sustainable social and economic growth of mankind is largely dependent on it. However, securing water quality to satisfy the needs of humans and ecosystems is one of the primary challenging issues of the 21st century (Amangabara and Ejenma, 2012). About 70% of Earth's surface is covered by water of which 97.5% is salty and 2.5% is fresh water and Less than 1% of this

2.5% amount of freshwater is accessible (Mishra and Dubey 2015). Ground water accounts for about 98% of global freshwater on Earth (Lui *et al.* 2011) which is used by approximately 2.5 billion people worldwide for their daily needs (Margat, 2008, Margat and van der Gun, 2013). Assessment of water quality is necessity in order to provide quality drinking water intended for human consumption and for other usual domestic purposes (Jain *et al.* 2009).

Consumption of contaminated deteriorating water quality affects livelihoods at risk (Leelavathi *et al.* 2016). Nitrate contamination is one of the most widespread groundwater problems worldwide (Almasri, 2007; Gupta *et al.*, 2008). Water containing high concentration of nitrate is unfit for human consumption and can contribute to eutrophication if discharging to fresh water sources due to excess nutrients (Vitousek *et al.*, 1997; WHO, 1999; Mason, 2002). Primary factors responsible for nitrate in groundwater include fertilizers, septic systems, and manure storage or spreading operations. Inverse relationships between nitrate concentration and aquifer depth have been reported in previous studies (Spalding and Exner 1993; Ray and Schock 1996; Ako *et al.* 2011). The contaminants coming from these various sources can be transported to surface waters by surface runoff and groundwater discharge. Several studies indicate that rural land uses, especially agricultural practices, can cause nitrate contamination of underlying groundwater. In addition, regions experiencing significant population growth may be substantially contributing to the groundwater nitrate contamination (Ako *et al.* 2011).

The World Health Organization has set the limit values for nitrate and nitrite in drinking water to 50 and 3 mg/l, respectively. These values are based on epidemiological evidence for methemoglobinemia

(WHO, 2007). Nitrate levels at or above this level have been known to cause a potentially fatal health disorder in infants under six months of age called Methaemoglobinemia or "blue-baby" syndrome (reduction in the oxygen carrying capacity of blood) (Fan and Steinberg, 1996; WHO, 1999; WHO, 2004; Horing and Chapman, 2004). Therefore, the nitrate pollution is a severe environmental problem that should be of high concern.

2. Source of contamination

Nitrate contamination is a common water problem throughout the world (Burden, 1982; Spalding and Exner, 1993; Beeson and Cook, 2004). During the past two centuries, the man made activities has substantially altered the global nitrogen cycle thereby increasing both the availability and the mobility of nitrogen (Vitousek *et al.*, 1997; Carpenter *et al.*, 1998; Galloway and Cowling, 2002). Nitrate (NO_3^-) is very soluble in water and is negatively charged and thus has a high mobility and potential for loss from the unsaturated zone by leaching and can remain in groundwater for decades (Manassaram *et al.*, 2006). Nitrate in ground water has a variety of sources classified as point source (from a single, identifiable source) and non-point source (from many diffuse sources). Point source includes livestock farms, sewage disposal systems, including septic tanks, slurry lagoons and non-point source includes fertilized cropland, land runoff or naturally occurring sources of nitrogen such as precipitation, atmospheric deposition, drainage, seepage, or hydrological modification (Manassaram *et al.*, 2006; Yang *et al.*, 2007; Gupta *et al.*, 2008). Alternative sources such as sewer breakthrough and animal waste can also cause a significant increase of nitrate concentrations (Hudak and Blanchard 1997).

Contamination of nitrate was also determined by the depths of well and borehole (Kross *et al.* (1993). Such a distribution clearly indicates that nitrate species in most of the considered groundwaters are of superficial origin (anthropogenic).

High concentration of nitrate can result in many environmental and ecological problems, such as blooms of toxic algae, eutrophication of lakes and reservoirs and extinction of species in the river ecosystem (Gautam and Iqbal, 2010, Li *et al.*, 2013). In addition, long-term exposure to high nitrate drinking water may increase human health risks (Carpenter *et al.*, 1998, Li *et al.*, 2014), which may lead to chronic poisoning, linked to Methaemoglobinemia (Itoh *et al.*, 2011, Yang *et al.*,

2012, Liu *et al.*, 2013). To prevent these deleterious effects of nitrate on human health, drinking water quality criteria have been established: the USA federal maximum contaminant level is 10 mg $\text{NO}_3\text{-N/l}$ (US Environmental Protection Agency, 1986; Nash, 1993; Scott and Crunkilton, 2000).

3. Nitrogen cycle

The nitrogen cycle is one of the most important nutrient cycles in terrestrial ecosystems. Nitrates and nitrites are chemical compounds that are produced naturally in the nitrogen cycle. Nitrogen cycling involves four major steps: nitrogen fixation, ammonification, nitrification and denitrification. Use of large amounts of nitrogenous fertilizers to agricultural fields influences these processes, especially nitrification and denitrification, and results in increased production of N_2O (Akiyama *et al.*, 2006) and pollution of ground water by leaching of nitrate from agricultural fields. In the nitrogen cycle, nitrogen from different sources such as atmosphere, animal and human wastes, decaying vegetation, and nitrate containing fertilizers are initially converted to ammonia by saprophytic soil-dwelling bacterial action in a process known as ammonification. Ammonia is subsequently converted to nitrite by soil-dwelling, nitrogen-fixing bacteria in a process known as nitrification. Nitrites may be further oxidized by soil-dwelling nitrifying bacteria and enter groundwater as nitrates. Denitrification is central to the nitrogen cycle and involves the reduction of nitrate via a chain of microbial reduction reactions to nitrogen gas (Knowles, 1982). The organisms capable of denitrification tend to be ubiquitous in surface water, soil and groundwater (Beauchamp *et al.*, 1989).

The reaction mechanism for different processes of nitrogen cycle is as:

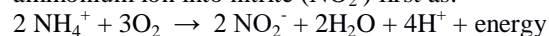
The utilization of molecular nitrogen (N_2) by particular bacteria such as *rhizobium*, cyanobacteria is called nitrogen fixation.

Reduction of $\text{N}_2 \rightarrow \text{NH}_3$ (ammonia)

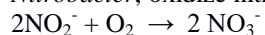
Ammonia produced by this process is further converted to proteins, nucleic acids (DNA), and other nitrogen-containing organic molecules

$\text{NH}_3 \rightarrow$ nitrogenous organic molecules: proteins, nucleic acids and so forth

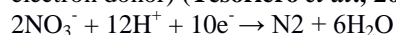
Nitrification is two step microbial processes in which NH_4^+ is oxidized to NO_3^- . Nitrosifiers, such as the bacterium *Nitrosomonas*, convert ammonium ion into nitrite (NO_2^-) first as:



Later, nitrifying bacteria, such as the bacterium *Nitrobacter*, oxidize nitrite into nitrate as:



And finally conversion of nitrate (NO_3^-) into gaseous nitrogen compounds such as N_2O , NO , and N_2 by different bacteria in soils is called denitrification, or nitrate reduction. The nitrate reduction reaction can be written as a half equation that illustrates the role of electron (e^-) transfer in the process (non-specific to the electron donor) (Tesoriero *et al.*, 2000):

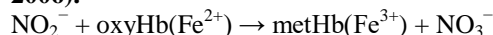


4. Nitrate and health issues

The exposure to nitrate by humans is dependent on an individual's intake of vegetables and the local concentration of nitrate in drinking water as well as the total amount of NO produced in the body. Nitrate ingested from the diet is rapidly absorbed in the small intestine, mixes with the endogenous nitrate from oxidation of NO and is readily distributed throughout the body (Walker, 1996). About 25% of an oral nitrate load is concentrated and excreted by salivary glands (Spiegelhalder *et al.*, 1976), so that salivary nitrate concentration is approximately 10 times higher than plasma nitrate. Approximately 20% of salivary nitrate is reduced to nitrite in the mouth by facultative anaerobic bacteria which are found on the surface of the tongue (Bjorne *et al.*, 2004; Doel *et al.*, 2005; Lundberg *et al.*, 2004) resulting in about a 5% reduction of total ingested nitrate to nitrite. As a result, nitrate ingestion is the main source of nitrite exposure.

4.1. Methaemoglobinemia

Nitrate itself is not toxic to humans. It becomes a problem only when it is converted to nitrite in the human body, resulting in Methaemoglobinemia or "Blue Baby Syndrome" which cannot bind oxygen (NAS, 1977, Majumdar, 2003, Manassaram *et al.*, 2006).



Due to the formation of methaemoglobin the oxygen delivery to tissue is impaired (Knobelock *et al.*, 2000; Speijers & Van den Brandt, 2003). Blue baby syndrome or Methaemoglobinemia occurs if this oxidation process overwhelms the protective reduction capacity of the cells (Jaffe, 1981, safe drinking water act of 1974). Nitrate is converted to nitrite (under anaerobic conditions in the gut), and nitrite acts as the oxidizing agent to form methaemoglobin in the red blood cells (Manassaram *et al.*, 2006). Thus, nitrate reduces the total oxygen carrying capacity of the blood

(Sandstedt, 1990; Amdur *et al.*, 1991; Wolfe and Patz, 2002). As different parts of the body get deprived of oxygen, clinical symptoms of oxygen starvation start to appear, the main being cyanosis which appear when concentrations of methaemoglobin (metHb) are 15–20% of the total haemoglobin. The clinical symptoms of hypoxia, such as fatigue and dyspnoea occur at concentrations greater than 30% of the total haemoglobin. The lips or even the skin start to become blue hence the common name, the blue baby syndrome. Methaemoglobin concentrations greater than 50% can quickly lead to coma and death (Knobelock *et al.*, 2000). In addition to drinking water, which contributes an estimated < 3–21% of the average adult intake of nitrate, other sources include vegetables, meat, and meat products preserved with sodium nitrite (Jaffe, 1981, Wogan, 1995). Nitrite is also a substrate in the formation of N-nitroso compounds from nitrosatable drugs (Brender *et al.*, 2004).

4.2. Reproductive and developmental toxicity

Several epidemiologic studies have attempted to evaluate the reproductive and developmental effects of nitrate. Nitrate, nitrite, and N-nitroso compounds may traverse the placenta and affect the fetus in utero (Fan *et al.*, 1987, Bruning-Fann and Kaneene, 1993). Earlier studies have reported that at extremely high levels of exposure, nitrate (NO_3^-) and nitrite (NO_2^-) produced adverse reproductive effects on test animals like rats and mice (Fan *et al.*, 1987). Gestational studies with nitrate (NO_3^-) and nitrite (NO_2^-) showed no significant differences in fertility, birth weight, litter size and sex ratio in these test animals. However, exposure of rats to nitrite (NO_2^-) in drinking water during gestation appeared to affect pup growth and hematological status (Roth *et al.*, 1987, Roth and Smith, 1988) while no maternal toxicity was observed. Pant and Srivastava (2002) have reported effects of nitrate exposure on semen quality in male mice at 900 ppm. On aquatic animals the main toxic action of nitrate is due to the conversion of oxygen-carrying pigments (e.g., haemoglobin, hemocyanin) to forms that are incapable of carrying oxygen (e.g., methemoglobin) (Grabda *et al.*, 1974; Conrad, 1990; Jensen, 1996; Scott and Crunkilton, 2000; Cheng and Chen, 2002). Results from animal studies of both nitrite and nitrate exposure via drinking water have shown effects on male rat testosterone production and testicular size and for nitrate these effects have been seen at concentrations close to the allowed limit in drinking water (Panesar and Chan, 2000). Earlier

studies have reported increase toxic effect to tadpoles with increasing concentrations and exposure times of nitrate (Baker and Waights, 1994; Hecnar, 1995; Xu and Oldham, 1997; Marco *et al.*, 1999; Schuytema and Nebeker, 1999a). The tolerance of amphibians to nitrogen fertilizers may however increase with increasing body size (Schuytema and Nebeker, 1999b) and environmental adaptation (Johansson *et al.*, 2001). Nitrogen fertilizers, such as ammonium nitrate (NH₄NO₃), potassium nitrate (KNO₃) and sodium nitrate (NaNO₃), may be contributing (with pesticides) to the decline of amphibian populations in agricultural areas (Wederkinch, 1988; Berger, 1989; Hecnar, 1995; Oldham *et al.*, 1997; Birge *et al.*, 2000).

Hansen *et al.*, 2009 examined how *in utero* exposure to nitrate would affect male rat fetuses. In addition, endocrine disrupting activity of nitrate and nitrite were studied in two *in vitro* assays, the H295R assay and T-screen and found no consistent indications that nitrate induces anti-androgenic effects in male fetuses or that prenatal nitrate exposure affected the thyroid axis. The indications for endocrine disrupting effects of nitrate and nitrite and especially their ability to interfere with androgen production in males raise a concern for effects during male sexual development. The prenatal period has been shown to be the most sensitive period for effects of numerous endocrine disrupting chemicals, including certain anti-androgenic phthalates. These phthalates have been shown to decrease the anogenital distance (AGD) and impair steroidogenesis in fetal and neonatal male rats at critical periods of sexual development leading to malformations in the male reproductive system and reduced sperm count later in life (Barlow *et al.*, 2004; Borch *et al.*, 2006; Carruthers and Foster, 2005; Ema *et al.*, 2000, 2003; Gray *et al.*, 2000; Parks *et al.*, 2000). Other adverse reproductive effects, such as mummified fetuses; lesions on the cervix, uterus, and placenta; and maternal death were also reported by earlier experimental studies reviewed by Fan *et al.* (1987).

4.3. Carcinogenic effect

Nitrate has been implicated in bladder, ovarian, stomach and liver cancers (Tsezou *et al.*, 1996; Mueller *et al.*, 2001; Weyer *et al.*, 2001). According to the findings of Gulis *et al.* (2002) on cancer, there was a positive association between nitrate level and incidence of non-hodgkin lymphoma and colon cancer, with an excess risk among women. In addition, ingested nitrates have a potential role in developing

cancers of the digestive tract through their contribution to the formation of nitrosamines, which are among the most potent of the known carcinogens in mammals (Harte *et al.*, 1991; Nash, 1993). In contrast, many epidemiological researches indicated that nitrate intake did not link to cancer. They had, however, produced contradictory effects (Archer 2002). Long term consumption of water at the concentration of 5.5 mg/l also would not increase the incidence of bladder cancer (Ward *et al.* 2003).

4.4. Thyroid

Ingestion of nitrate at high doses can competitively inhibit iodine uptake and induce hypertrophy of the thyroid gland (De Groef *et al.* 2006). Some epidemiological studies in children showed that the goitre develops easily in areas where the contamination of drinking water by nitrates exceeds the permissible daily limit of 50 mg/l fixed by the WHO (1998) (Gatseva *et al.*, 1998; Vladeva *et al.*, 2000). However, dietary nitrate, the predominant source of intake, was associated with increased prevalence of hypothyroidism but not hyperthyroidism. Effects on thyroid hormones and increased weight of the thyroid gland have been observed in adult female rats after nitrate exposure of 50 mg/l (Esciocak *et al.*, 2005). Zaki *et al.* (2004) exposed male rats to nitrate in the drinking water and reported a dose-dependent increase in weight of the thyroid gland as well as decreased levels of triiodothyronine (T3) at nitrate concentrations of 150 and 500 mg/l and a decrease in thyroxine (T4) at 500 mg/l. Furthermore, increased thyroid volume has been reported in humans living in areas with high concentrations of nitrate in their drinking water. However, other possible thyroid disruptors than nitrate were not measured in the drinking water in these studies (Tajta kova *et al.*, 2006; van Maanen *et al.*, 1994).

Other health effects associated with high concentration of nitrate in drinking water as per earlier studies are type 1 childhood diabetes (T1D), blood pressure, and acute respiratory tract infections in children (Ward *et al.* 2005).

5. Conclusion

Ground water and surface water contamination by nitrate is a widespread problem in our world. Agricultural drainage, leachate from waste pile, and pollution from human and animal waste, are responsible for a vast increase of nitrate concentrations

in different water source. Populations with the highest exposure to nitrate from their drinking water are those living in agricultural regions. By affecting the drinking water quality it can cause public health problems, and environmental degradation of ecosystems. Nitrate concentrations in global water supplies are likely to increase in the future due to population growth, increases in nitrogen fertilizer use, and increasing intensity and concentration of animal agriculture. Adverse effects of nitrate contaminated water can be minimized by proper water management and good governance to mitigate the risks for nitrate contamination. However, in order to better manage nitrate contamination in groundwater systems, researchers, water resources specialists and policy makers do need information on the scope, distribution and severity of groundwater nitrate contamination. In other words, it would be better to facilitate early diagnosis of possible changes and widen their inspiration for selecting effective measures for interventions.

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