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Drinking water nitrate and prevalence of methemoglobinemia among infants and children aged 1–7 years in Moroccan areas

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Abstract

Context: Nitrate is ubiquitous in environmental media (air, water and soil) and other sources (some medicines, inorganic fertilizers and household's chemicals). It is a hemoglobin-oxidizing agent that can cause methemoglobinemia. The effect of nitrate on infants is well known but less is known about nitrate-induced methemoglobinemia in young children.

Method: Two cross-sectional studies were carried out in Salé, Morocco to determine the prevalence of methemoglobinemia among 411 infants and children aged 1–7 years in two adjacent areas that were similar in terms of the air quality, available vegetables and medicines but different in terms of the drinking water quality (nitrate-contaminated well water versus municipal water).

Results: In the exposed area, nitrate concentration was measured in 78 wells and ranged from 15.39 to 246.90 mg/l as NO_3^-. Nitrate levels were higher than 50 mg/l in 69.2% of the surveyed wells, and 64.2% of the participants were drinking nitrate contaminated well waters.

The prevalence of methemoglobinemia among study children was 36.2% in the exposed area, and 27.4% in the non-exposed area. Study children drinking well water with a nitrate concentration >50 mg/l were significantly more likely to have methemoglobinemia than those drinking well water with a nitrate concentration <50 mg/l ($p = 0.001$ at 95% CI = [1.22–2.64]) or than those drinking municipal water ($p<0.01$ at 95% CI = [1.16–2.21]). In the exposed area, the mean methemoglobin (MetHb) level increased with age ($R^2 = 0.79$, $p = 0.04$), whereas in the unexposed area, the mean MetHb level remained relatively stable in the first 6 years of life ($R^2 = 0.21$, $p = 0.44$). Mean MetHb was normal when the nitrate concentration in water was below 50 mg/l as NO_3^-, and reached an abnormal level, when the nitrate concentration in water ranged between 50 and 90 mg/l as NO_3^-. This last level was statistically similar to mean MetHb at nitrate level above 90 mg/l as NO_3^- (up to 246.9 mg/l as NO_3^-). No association

Abbreviations: Ci, confidence interval; Hb, hemoglobin; MetHb, methemoglobin; mg/l, milligrams per litre; No_3^-, ion nitrate; *p*, *p*-value; R^2, correlation coefficient; SD, standard deviation; WHO-EMRO, World Health Organization-eastern Mediterranean regional office.

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was observed between methemoglobinemia prevalence and gender. This is the first study about methemoglobinemia conducted in Morocco.

Keywords: Nitrate; Drinking water; Methemoglobinemia; Infants and children; Morocco

Introduction

Nitrate in groundwater is a major problem in Morocco. A study (Maroc. DGH, 1998) about nitrate levels in Moroccan ground waters (550 analyzed water samples across the whole country), carried out in 1995–1996, showed that 32% of the levels detected were higher than 50 mg/l of nitrate (NO_3^-), the acceptable value according to the Moroccan standards for drinking water quality in public water systems, and a heath-based guideline value of the World Health Organization (WHO, 1993). Private water systems (wells and springs) in Morocco are not required to meet this standard.

High intake of nitrate and its subsequent reduction to nitrite (ATSDR, 1991) leads to the formation of methemoglobin (MetHb) (Haddad and Winchester, 1990; Mansouri and Lurie, 1993). This derivative of hemoglobin (Hb) cannot bind oxygen because the iron component has been oxidized from the ferrous (Fe^{++}) state in the Hb to the ferric (Fe^{+++}) state. Signs and symptoms, including cyanosis, headache, fatigue, dizziness, syncope, seizures, coma and death (Goldfrank et al., 1998; Jaffe, 1981) depend on the MetHb level. The normal MetHb level in humans should not exceed 2% of the total Hb (Frejaville et al., 1971), and cyanosis is observed in patients with MetHb concentrations $\geqslant 1.5$ g/dl (Finch, 1948; Goldfrank et al., 1998; Mansouri and Lurie, 1993). Below this level, methemoglobinemia is generally not a noticeable disease. When accompanied with cyanosis, it is frequently misdiagnosed as heart or pulmonary disease (Wintrobe et al., 1981), which may be one reason it is under-reported in Morocco and elsewhere. To date, there have been no reported cases of methemoglobinemia associated with drinking water intake in Morocco.

The effect of nitrate in drinking water on infants is well known (Comly, 1945; Knobeloch et al., 2000; Shearer et al., 1972). Infants younger than 6 months are particularly sensitive to nitrate-induced methemoglobinemia because of many reasons: (1) they have a low capacity to reduce MetHb back to normal Hb (WHO, 1998); (2) they consume more water relative to their body weight than adults (US EPA, 1991), and thus have a higher relative exposure to nitrate when drinking formula or other drinks made with contaminated water; (3) a large proportion of Hb in infants is in the form of fetal Hb, which is more readily oxidized to MetHb than adult Hb (WHO, 1998); (4) the gastric environment in infants is more alkaline than in adults, providing optimal conditions for growth of bacteria that promote MetHb formation (WHO, 1996); and (5) gastroenteritis with vomiting and diarrhea, which is more common in infants than adults, enhances conditions for MetHb formation (ECETOC, 1988; Wright et al., 1999).

Less is known about nitrate-induced methemoglobinemia in young children. Some studies (Diskalenko, 1968; Kapanadze, 1961; Petukhov and Ivanov, 1970; Subbotin, 1961; Gupta et al., 1999) have revealed an association between this medical condition and nitrate-contaminated water among children whereas a study undertaken in the USA (Craun et al., 1981) has shown no such association. An experiment (Keohane and Metcalf, 1960) done on blood cells showed that the increased sensitivity to nitrate persists until about the time of puberty and is not solely a property of fetal Hb.

The present work was undertaken to examine the prevalence and risk factors for methemoglobinemia among infants and young children in Morocco.

Materials and methods

Methemoglobinemia may be acquired due to exposure to nitrate in drinking water (Haddad and Winchester, 1990; Mansouri and Lurie, 1993; Wright et al., 1999), some vegetables (Haddad and Winchester, 1990; Mansouri and Lurie, 1993; Wright et al., 1999), foods where nitrite is used as food preservative (Askew et al., 1994; Finan et al., 1998), some medications (Ash-Bernal et al., 2004; Haddad and Winchester, 1990; Jaffe, 1981) or to some household chemicals (Haddad and Winchester, 1990; Mansouri and Lurie, 1993; Wright et al., 1999). Methemoglobinemia can also be hereditary due to NADH–methaemoglobin reductase deficiency, or the presence of Hb M (Haddad and Winchester, 1990; Mansouri and Lurie, 1993; Wright et al., 1999).

Two adjacent study areas were chosen in the Hssaine Commune, Salé, Morocco. The exposed area (the term "exposed" refers to exposure to nitrate in drinking water) is a semi-rural area that consists of four small regions, and whose population (total population = 8670 people) (Maroc. HCP. CLAD, 2006) uses well water for their daily needs (drinking water, irrigation, cooking and washing). Electrification is available, which encourages installation of electric water pumps. Some households have their own wells and others use