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Biological monitoring of Italian soldiers deployed in Iraq. Results of the SIGNUM project

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ABSTRACT

Background: Leukemia/lymphoma cases reported in 2001 among United Nation soldiers or peacekeepers deployed to the Balkans aroused alert on the exposure to depleted uranium. Recent epidemiological studies carried out in different European countries among peacekeepers who served in the Balkans failed to demonstrate a higher than expected risk of all cancers but, mostly due to their limitations in size and follow up time, leave open the debate on health risk of depleted uranium. The aim of SIGNUM (Study of the Genotoxic Impact in Military Units) was to identify potential genotoxic risk associated with the exposure to depleted uranium or other pollutants in the Italian Army military personnel deployed in Iraq.
Methods: Blood and urine samples were collected before and after the deployment from 981 Italian soldiers operating in Iraq in 2004–2005. As, Cd, Mo, Ni, Pb, U, V, W, and Zr were determined in urine and serum. DNA-adducts, 8-hydroxy-2′-deoxyguanine and micronuclei frequency were evaluated in blood lymphocytes. Three different genetic polymorphisms, *GSTM1*, *XRCC1*, *OGG1* were analyzed.
Results: Significant *T*0–*T*1 reduction in the total concentration of uranium, increases for Cd, Mo, Ni, Zr, and decreases for As, Pb, W, and V in urine and plasma were observed. Increases in oxidative alterations and in micronuclei frequency, included in the range of values of non-occupationally exposed populations, were observed at the end of the period of employment.
Conclusions: Our results did not detect any toxicologically relevant variation of DNA-damage biomarkers related to the deployment in the operational theater.

Introduction

Alarming reports appeared starting from 2001 in the international press, referring leukemia/lymphoma cases among United Nation (UN) soldiers or peacekeepers deployed to the Balkans from different European countries (Lamb, 2000; BBC News, 2001; CNN, 2001)

Moreover the development of multisymptomatic chronic medical conditions was reported in peacekeeping forces as well as residents of Kosovo and Bosnia–Herzegovina (BH) and called "Balkan Syndrome" (Duraković, 2001) in analogy with the "Gulf War Syndrome" observed in veterans of the Gulf War in 1991 (Fukuda et al., 1998; Wolfe et al., 2002; Steele et al., 2012; Smith et al., 2013). Depleted uranium (DU), used as an armor-penetrating ammunition in international conflicts (Army Environmental Policy Institute, 1995) was investigated as a common threat that links concerns about leukemia and other adverse health effects.

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A large body of data has been generated on the possible association between the environmental and occupational exposure to DU and the risk of cancer or adverse health effects in humans.

Epidemiological studies on cancer risk in occupationally exposed populations, including uranium miners, millers, and other processors worldwide were reviewed by the US National Academy of Sciences with the conclusion that for both lymphatic and bone cancer there is inadequate or insufficient evidence to determine the association with uranium exposure (US Public Health Service, 1999; McDiarmid, 2001).

A number of studies were also available on cancer risk of exposure to DU from ammunition deployed during the Gulf War. The cancer incidence among UK Gulf veterans up to 11 years after the end of the war showed no increased overall or site-specific cancer incidence as compared with service personnel not deployed in the Gulf War (US Public Health Service, 1999). Other evidence comes from a small surveillance study of 60 US Gulf war veterans who were victims of friendly fire with DU. None of them, including 15 subjects with retained fragments of DU in soft tissue and excreting high uranium concentrations in their urine, developed leukemia, bone cancer or lung cancer (McDiarmid et al., 2000). A review on the state of scientific knowledge on health hazard, including epidemiological studies and considering the typical levels of exposure to DU on the battlefield over a wide range of scenarios, concluded that the excess risk of cancer (mainly represented by lung cancer and leukemia), except in extreme circumstances, is likely to be very small and undetectable above the general risk of cancer during a normal lifetime (The Royal Society, 2001). Alternative causes have been suggested to explain the leukemia/lymphoma cases among UN soldiers or peacekeepers deployed in the Balkans, including smoke from burning oil wells or different chemical releases after bombing (The Royal Society, 2001; McDiarmid, 2001).

The Committee of the Chiefs of Military Medical Services in NATO (COMEDS) reconmmended NATO countries to plan studies on cancer risk among Balkan veterans (COMEDS, 2001).

Follow-up studies were started among military and civil personnel involved in UN missions in the Balkan in different countries in Europe, Sweden, Denmark, the Netherlands, and Norway (Gustavsson et al., 2004; Storm et al., 2006; Bogers et al., 2013; Strand et al., 2014).

An expert Committee was commissioned by the Italian Ministry of Defence to investigate on the high incidence of leukemia and lymphomas among the Italian soldiers who were involved in peacekeeping operations in Bosnia and Kosovo where depleted uranium was used. The Committee concluded that an excess of Hodgkin's lymphoma occurred among this cohort of soldiers (12 observed vs 5.08 expected cases among 43,058 subjects over the years 1996–2001; SIR 2.36) while the incidence for other cancers were lower than expected (Mandelli et al., 2002). No evidence of contamination by depleted uranium was observed among veterans suggesting different possible causes for cancer incidence.

A voluntary clinical follow up during 5 years after returning from the Balkans among active-duty and retired Italian soldiers formerly deployed in Bosnia and Kosovo and a cancer surveillance activity covering all the army personnel, started in January 2001.

The SIGNUM project (Study of the Genotoxic Impact in Military Units) was promoted by the Italian Ministry of Defense to integrate the epidemiological studies and the clinical follow up in order to investigate the potential carcinogenic/genotoxic risk associated with the peacekeeping operations in army personnel. The opportunity to realize a large size biomonitoring study in military personnel was offered by the peacekeeping operation Antica Babilonia involving 3000 soldiers in Iraq.

The Balkans and Iraq are major examples of theater where DU was extensively used.

A number of reports described increases of cancer incidence, mainly breast cancer, lung cancer, leukemia and lymphoma, and birth defects supporting mutation-related health effects in civil populations in southern Iraq attributed to the exposure to DU. (Shelleh, 2012; Busby et al., 2010). Further studies suggested the induction of chromosomal instability (Miller et al., 2010) and over expression of oncogenes in DU exposed subjects (Al-Dujaily et al., 2008). Increases of chromosomal damage in exposed populations and in veterans in Balkans as well as in the Gulf war were also described (Schröder et al., 2003; Krunić et al., 2005).

However data on DU exposure in the studied populations are limited. Moreover military personnel and partially local populations in the areas of operative theaters are exposed to multiple factors such as explosives and ammunitions, solvents, particulate matters, combustion products from burning pits, exhausts from hydrobarbon combustion. In Iraq dust and sand storm characteristics of the region increase the ambient particulate matter (Engelbrecht et al., 2009; Falvo et al., 2015). In addition other factors specific to military service such as physical and psychological stress, mandatory vaccinations, could modulate the effects of the exposure

The aim of SIGNUM project was to identify potential long term risk associated with the complex exposure during the deployment in operational theaters using a battery of biomarkers by means of sampling military units personnel before and after the deployment areas. The study focused on the possible biological effects of depleted uranium purported to be present in the operative theater. Accordingly, we evaluated exposure by analyzing internal doses of xenolements as well as molecular doses of genotoxic compounds (DNA adducts for bulky genotoxic compounds including PAH and nitropyrenes). These biomarkers are much more informative than environmental monitoring reflecting the host-environment interaction.

The project involved a biomonitoring study, including biomarkers of exposure and early effects, in a cohort of 981 military units deployed in 2004–2005 in Iraq.

Material and methods

Study population

The study population is represented by personnel belonging to the Italian military contingent operating in Iraq in the context of the operation Ancient Babylon. The study was approved by the ethical committee of the Health Section of the Italian Ministry of Defense. All the participants were informed on the aims and the methods of the study and gave a written consent. A detailed questionnaire was used to collect information on demographic characteristics, height and weight, diet, tobacco and alcohol consumption, physical activity, medical history, drug consumptions, radiographies, vaccinations and to reconstruct their activities during the deployment.

Sample collection

Blood and urine collection was carried out by a team of military health personnel in two steps: (a) before the deployment (*T*0) in the locations of belonging and (b) at the end of the deployment period (*T*1) in the operative theater at the last day of the mission. The samples were sent to the laboratories for analysis. For cytogenetic tests, delivery of the *T*0 samples was ensured within 24 h, whereas the *T*1 blood samples were cultured and processed by trained military personnel in an ad hoc laboratory established at the operative theater, than sent to the laboratories involved in the analyses.