CYTOGENETIC STUDIES IN MAMMALIAN SOMATIC CELLS EXPOSED TO RADIOFREQUENCY RADIATION: AN OVERVIEW

VIJAYALAXMI
University of Texas Health Science Center, San Antonio, TX 78229, USA.
vijay@uthscsa.edu

Introduction

In recent years there has been a steady increase in investigations assessing the genotoxic potential of radiofrequency radiation (RFR) exposure in mammalian cells, either alone or in combination with genotoxic agents. The potential adverse effects of RFR exposure on the genetic material (DNA) are very important. Damage in the DNA of somatic cells can lead to the development of cancer or cell death. Changes in the DNA of germ cells can lead to mutations that can be transmitted to subsequent generations. Hence, several researchers have used recently developed experimental techniques as well as classical cytogenetic methods to examine the extent of genetic damage following *in vitro* and *in vivo* exposure of prokaryotic and eukaryotic cells to RFR. The purpose of this review is to evaluate the genotoxicity studies published in scientific journals during the years 1990-2003 in which freshly collected and/or cultured mammalian somatic cells were exposed to RFR *in vivo* or *in vitro*. The end-points dealing exclusively with DNA single and double strand breaks, chromosomal aberrations, micronuclei and sister chromatid exchanges are considered in this review.

Results

Among the 53 reports published during 1990-2003, the conclusions from 31 investigations (58%) did not identify increased cytogenetic damage following RFR exposure *per se* while those from 12 studies (23%) indicated a genotoxic potential of RFR exposure. The observations presented in 10 other reports (19%) were inconclusive (Table 1). Among the limited number of 6 combination exposure studies investigating the epigenetic potential of RFR (i.e., RFR exposure *per se* is not genotoxic, but that such exposure could enhance the cytogenetic damage induced by other chemical and/or physical genotoxic agents), the data from 3 studies did not reveal epigenetic effects of RFR; the results from 1 report indicated such an effect while 2 other publications from the same researchers were inconclusive (Table 1).

Assessment of the published literature

The strength in the most of the reports which did not indicate significantly increased genotoxicity following *in vivo* and *in vitro* exposure of mammalian somatic cells to RFR comes from the following facts. (a) The studies were experimentally sound with adequate temperature controls and validated dosimetry. (b) The investigations were conducted by independent researchers in independent laboratories. (c) There were 'replication' investigations conducted under conditions duplicating the original study as well as 'confirmation' studies where conditions similar to those original investigations were used. (d) In general, the experimental protocols were described in detail so that the observations could be verified by independent researchers. (e) The data were not in conflict with the other established characteristics of RFR. (f) These studies also included larger sample size. In contrast, the reports which suggested the genotoxic potential of RFR had confounding factors, which were described and/or commented by the investigators themselves. The

interpretation of some of the data was hypothetical and not substantiated by experimental evidence. More importantly, the data were not confirmed by the same researchers in subsequent experiments. Also, multiple attempts by independent investigators could not confirm the original observations.

The absence of an increase in genotoxicity in mammalian somatic cells exposed to RFR, reported in the great majority of investigations, agrees with the large volume of published epidemiological and experimental findings which do not support the concept that *in vivo* and *in vitro* exposure to RFR is carcinogenic. Also, the limited cytogenetic data from the combination exposure studies described above did not point to a clear epigenetic potential of RFR (there are growing number of other *in vivo* and in vitro studies which indicate that non-thermal exposure to RFR does not have epigenetic activity). The genotoxic (and epigenetic) potential of RFR exposure should not be considered as 'established' unless a significant increase in genotoxicity in RFR-exposed cells is: (a) replicated by the same investigators, (b) replicated and/or confirmed by independent investigators in independent laboratories and (c) such data are published in peer-reviewed literature.

The preponderance of the scientific weight evidence thus far available in the literature shows that RFR exposure per se is not genotoxic in mammalian somatic cells.

Potential scources for the controversy

A careful survey of the information presented in individual publications reveal numerous variables that existed in the RFR exposure conditions and experimental protocols. This makes direct comparisons of the data obtained by the same investigators in different experiments and by independent researchers is almost impossible. The potential causes for the conflicting data can be grouped according to the suggestions and statements made by the investigators in the publications. (a) Most importantly, the increased genotoxicity observed in RFR-exposed cells could be related to RFR-associated with hyperthermia and may not be due to the RFR exposure per se. There is documented evidence that hyperthermia, >39^{o}C, has numerous effects in mammalian cells, including: (a) alterations in cell proliferation and viability, (b) induction of DNA strand breaks, sister chromatid exchanges and micronuclei and (c) inhibition of the repair of DNA damage. Historically, there has been a 10% incidence of sporadic and non-reproducible positive results in micronucleus test in *in vivo* investigations in rodents. (c) In *in vitro* investigations, changes in the osmolarity or pH of the medium during treatment/exposure and/or during the subsequent cell culture period have been shown to affect the incidence of chromosomal aberrations, micronuclei and sister chromatid exchanges: such subtle, non-apparent variations during experimentation could have led to erroneous conclusions. (d) Analysis of results obtained from multiple genotoxic end-points, without appropriate statistical procedures to consider the multiple observations tested, could have misidentified as a 'significant effect' one due to random chance occurrence.

Future research

The data from a well coordinated, multi-centered collaborative investigation with adequate statistical power will be needed to identify the factors contributing to the controversial observations about the genotoxic potential of RFR. Such studies probably will require RFR exposures to be conducted in a single laboratory with SAR levels in the range of 1 W/kg to 5 W/kg, with adequate temperature controls and validated dosimetry. Multiple genotoxicity end-points (e.g., chromosomal aberrations, micronuclei and sister chromatid exchanges) and multiple cell types of human origin (e.g., blood lymphocytes, skin fibroblasts and tumor cells)

should be examined. It may also be valuable to examine the response of cells with different genetic backgrounds (i.e., heterozygous and homozygous for human inherited syndromes, such as ataxia telangiectasia, whose cells exhibit 'hypersentive' response following exposure to chemical and/or physical genotoxic mutagens).

Reference

[1] Vijayalaxmi, and Obe G. (2004): Controversial cytogenetic observations in mammalian cells exposed to radiofrequency radiation. Radiation Research. 162, 481-496