Review Article

NUCLEAR AND RADIOLOGICAL AGENTS: CONTAMINATION AND DECONTAMINATION OF HUMAN BEINGS

Deepak Sharma[1], Sunil Kamboj[1]*, Suman Kamboj[1], Anroop B Nair[1] and Javed Ali[2]
[1]M. M. College of Pharmacy, M. M. University, Mullana, Ambala (HR), India.
[2]Department of Pharmacy, Jamia Hamdard University, New Delhi, India.
*Corresponding author's E-mail: sunilmmcp@gmail.com

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ABSTRACT

In the recent years there has been number of accidents which have been recorded worldwide with significant radioactive contamination. Radiation contamination can occur accidently or due to terrorists attack in the form of dirty bombs/non-conventional weapons. The release of radioactive materials with radiation has the potential of causing serious medical problems. Terrorist threats can results in internal and external radionuclide's contamination of large number of population. Radiation contamination of human beings can cause acute as well as chronic and late illness and well known health hazards such as Acute Radiation Syndrome (ARS) (sometimes known as radiation poisoning or radiation sickness). The increasing use of radionuclides in medical diagnosis also raises the possibility of accidental spills and contamination. Recent approaches to decontaminate human being from various harmful radiological agents in case of accidents or in case of any terrorist attacks are RSDL (Reactive skin decontamination lotions), mobilizing agents, chelation therapy in case of internal contamination through i.v, RSDecon lotion formulations. Surface decontamination techniques by using soap and detergents

Keywords: Acute radiation syndrome, Dirty bomb, Ionizing radiations, Radionuclides decontamination.

INTRODUCTION

There are number of incidents which occurred and caused hazards such as the accidents in Chernobyl, USSR in 1986 and in Goiania, Brazil in 1987[1]. Terrorist attacks on U.S in 2001 and 'anthrax spores via mail' have stressed the importance of knowing how to manage the radioactive contamination of persons and there decontamination. Such management requires knowledge of the chemistry and metabolism of various radionuclides in humans and methods to increase their elimination from the body[2]. In the event of radiological contamination, rapid treatment can be lifesaving. The radioactive contamination depends on the two main factors one is time of exposure and second is distance of person from contaminated area. Proper and rapid decontamination can help in controlling mortality and further spread of contamination. The possibility of radiological contamination is always present because of the wide use of radioactive materials in various fields such as medicines, research, nuclear plants and industry[2-4].

Other than the accidents the exposure to radionuclide can be done intentionally as a terrorist's attack as a weapons of mass destruction. Terrorist incidents could involve a radiological dispersion device (RDD) or called 'Dirty bomb'[4,5]. The possibility of radioactive substances used by terrorist is increased. Nuclear and radiological weapons pose a significant terrorist threat. In the past, terrorists have attacked discrete locations with explosive materials that are not inherently toxic. Recent terrorist threats such as attack on U.S in 2001 and use of anthrax spores via mail raised the fear that terrorists can use dirty bombs like weapons. An example of recently happened accident in Mayapuri, Delhi, also raised the alarm for the possibility of radionuclide contamination and terrorist's threats[6]. In April 2010, the locality of Mayapuri has been affected by a serious radiological accident due to exposure of cobalt 60 and caused causes serious injuries to the workers and locality of Mayapuri and lead to deaths. The lack of knowledge of radiations made the case much severe and resulted in high radiation exposure and contamination.

Terrorists can spread contamination by using various devices or bombs such as dirty bomb or radiodispersal devices. A dirty bomb or Radiodispersal device (RDD) is simply a device designed to spread radioactive contamination by ejecting it into a target area. Such a weapon can contain radioactive materials in liquid or particulate forms. It involves adding a radionuclide to an existing bomb to create an RDD that can contaminate both victims and the surrounding area. These devices would cause contamination through conventional blast and also would complicate medical treatments within the contaminated area.

It is important that the first responder and medical management team should be familiar with the nuclear and radiological agents, so that they can detect, protect and cure the contaminated persons as soon as possible and save their life. The main objective of this article is to highlight various radiations and their contamination to the human beings by means of internal and external routes. It also includes basic strategies for the prevention of radiation contamination, their harmful effects and recent approaches to decontaminate human being from various harmful radiological agents in case of accidents or

in case of any terrorist attacks. Such events increased the focus on the development of protection, different decontamination methods and safe effective products.

IONIZING RADIATIONS

Ionizing radiation is a form of energy which is often disruptive in biological systems and can cause mutations and cancer. These types of radiations generally occur in radioactive decay and waste, examples of ionizing radiations are Alpha particles, Beta particles, Gamma particles, neutrons and X-rays[1,2,7]. The alpha particles consist of fast moving helium nucleus and stopped by a sheet of paper. They are high energetic but show low penetration. The beta particles consists of an energetic electron, it is less ionizing than alpha radiations but more than gamma. The electrons can be stopped with a few centimetres of metal but they can penetrate a few centimetre of tissue, which causes burn on the skin called "Beta burn". Beta emitting materials also cause significant internal hazards. X-rays and gamma rays, which are highly energetic photons, penetrate deeply which are difficult to stop and their damage depends on their energy. Radioactivity can measured in different units, Roentgen (r), defined as the amount of ionizing radiation which produces 2.08x10 ion pairs in $1cm^3$ of air. RAD (Radiation absorbed dose) is the amount of radiation that puts 10 J of energy in 1kg of absorbing materials[8].

DETECTION OF RADIATION

Radiation can't be smell, see or taste, so for their detection various detectors are used. There are several radiation detectors[8,9]. The Proportional counters are the most common device for detecting alpha radiation in the laboratory[10]. Scintillation counters are currently used for determining radioactivity contamination, but they are less sensitive than proportional counters. Instruments for measuring either type of radiation are similar, but the Geiger- Mueller (GM) counter is the most common detection device. Unfortunately, high radiation level can saturate GM counters and give false or even zero readings. Ionization chambers can measure higher dose rates. Both are sensitive to extremes of heat and humidity, and both may fail in a corrosive chemical environment. Shielding the probe of the detection device will provide a relatively pure reading of the gamma component, and the difference between the shielded and unshielded readings provides the beta (and often soft gamma) component. Examples of available radiation detectors are pocket dosimeter, watch dosimeter and telerad[11].

EFFECTS OF IONIZING RADIATIONS

Contaminated persons could suffer acute symptoms of radiations injury and could develop cancer or genetic damage[12,13]. The effects of radiological contamination dispersed by an explosion are difficult to predict and depend on diverse factors like environmental conditions (temperature, relative humidity, wind conditions, precipitation), chemical and physical form of the radioisotope (particle size etc.), type and amount of explosives, local environment etc. Ionizing radiations causes physical damage to cells and DNA. The radiations may affect the cells in direct or indirect way[14]. The radiations may directly cause cell death or cause severe damage leading to malfunction. The radiation can also damage a cell indirectly by creation of unstable and toxic hyper oxide molecules which in turn can damage sensitive molecules. The higher dose of radiation can cause acute radiation syndrome (sometimes known as radiation toxicity or radiation sickness). The early clinical responses associated with the radiation contamination include: nausea, vomiting, headache, fever, fatigue, tachycardia, weakness, abdominal pain and arrhythmia. Table 1 gives summary of acute radiation syndromes.

CONTAMINATION

Contamination is the presence of unwanted constituent which occurs when people ingest, inhale or are injured by radiological materials. It is of different types depending upon the routes of contamination.

Types of contamination are:[1,2,14]

1. External contamination: It occurs when radionuclide dust comes into contact with person's skin, hair and clothing.
2. Internal contamination: It occurs when radioactive materials entered into the person body through different routes.

The primary routes of entry for radionuclides into the body are inhalation, ingestion, and absorption through skin and wound.

Radionuclides that gain entry into the body remain for varied periods of time and cause irradiation until they eliminated from the body. Alpha and low-energy beta emitters are not hazardous as external sources of radiation, but if they got entered into the body they cause more hazards. Inhaled radioactive gases show different amounts of absorption into blood depending upon their nature, some of them are deposited into different organs and some may be excreted in urine and stool[15].

DECONTAMINATION/DECORPORATION

Decontamination is the process of removal of contaminated materials or cleansing the human body to remove contamination of radioactive substances and infectious materials[1,16,17]. The two main objectives of decontamination are to make the individual free from the contaminants and to reduce the concentration of the contaminant to a level that is safe for survival. The second objective is to make area safe for survival. Early detection of the contaminants helps in early response for decontamination and decrease the potency of hazards. The treatment for decontamination should begin within hour of exposure. In case of external contamination, decontamination can involve removal of a contaminant from the skin. Usually such decontamination must be

done quickly, since the contaminant may be absorbed through the skin where it can cause internal damage. The appropriate treatment regimen is based on the time of exposure after the nuclear event. Treatment is determined by the particular radioisotopes. In a complete nuclear detonation, over 400 radionuclides are released. However, only about 40 radionuclides are potentially hazardous to humans[12]. The most significant radioisotopes from unspent nuclear fuel are tritium, plutonium, and uranium[16].

MECHANISM OF DECORPORATION

Different mechanisms are employed for decorporation of radionuclides and to minimize the adverse effects cause by the radionuclides[19,21]. In case if the radionuclide is present in the gastrointestinal tract then decorporation can be done by increasing clearance speed or by increasing transist time, which increase the excretion rather than absorption. In this case laxatives are effective as decorporation agents. Certain chelating agents are stable and water soluble complexes with specific radionuclides, which can be excreted easily and safely without absorption. In case if the radionuclides enter the blood, the radionuclide is blocked by administration of non radioactive potassium iodide to block radioiodide incorporation into thyroid hormone and subsequent storage in the thyroid gland[22,23,27]. Other mechanism is to change the chemical state to the less toxic form. The diuretics can be used to increase urinary excretion by forced diuresis.

EXTERNAL DECONTAMINATION

Skin is generally impermeable to various radionuclides but wounds and burns may become a route of entry[29]. Decontamination of skin or external body is performed to remove contaminants which are adhered to the external surface of the body and which may enter to the body by means of permeation through skin and wounds[30]. If a decontamination process is to be efficient, it must be started as soon as possible after a confirmed or suspected contamination. The primary objective of external decontamination of persons is to remove the highest possible degree the radioactive contaminant from the body parts. The process requires removing the contaminants not just from the skin surface, but also from the clothing and protective equipments[24,26]. The decontamination of skin involves different methods. The most frequently used method is a simple washing with warm water and soap using face cloths, brushes etc. Apart from soap, the decontaminating agents include washing pastes, shampoos and various decontamination solutions[20,24,29]. To decontaminate radioactive material from eye or nose irrigate them with 0.9% saline solution, or if it is not available irrigate with tap water but care must be taken that the contaminated water doesn't get swallowed[32,33]. Care should be taken that solution for decontamination must be non irritant to skin and other organs.

There are many researchers who performed different research in this field. Sharov et al. and associates proposed a formula for a thermoplastic hydrophilic gel-base skin decontamination agent supplemented with EDTA and triethanolamine. It is applied after warming up to 323 k. The agents were efficient in removing the radioactive substances deposited in deeper layers of skin therefore recommended as generally applicable suitable skin decontamination agents.

Merrick and co-worker compared the effectiveness of four agents applied to decontamination of the skin contaminated with radioactive drugs tagged with ^{99}mTc, ^{123}I and ^{51}Cr. An abrasive-containing paste appeared to exhibit the highest decontamination efficiency, and may therefore be recommended as a universally applicable decontaminant for all kinds of skin contamination.

INTERNAL DECONTAMINATION

Internal radioactive contamination can arise from accidents involving nuclear reactors, industrial sources or medical sources. Internal contamination occurs by four main routes: inhalation, ingestion, wound contamination and percutaneous absorption[2,26,30]. The percutaneous route is not much effective in internal contamination because skin is impermeable to number of radionuclides. As long as these radioactive contaminants remain in the body, they may cause significant health risks. The risks are long term and depend upon the type, nature and concentration of the radioactive material. It also depends upon the health conditions of the exposed person. The uptake and retention of a radionuclide are influenced by its route of entry, chemistry, solubility, metabolism, and particle size. The health risks involve development of cancer of the lung, liver, thyroid, stomach, and bone. The size of the radioactive particles determines if it will deposit in the lungs[32-35]. The mean clearance times of the human digestive tract are as: stomach 1 hr, small intestine 4 hrs, upper large intestine 13-20 hrs and lower large intestine 24 hrs, resulting in a total mean emptying time of 42 hrs. The long transit time of large intestine gives much contact time to the nonabsorable radionuclides, which causes high risk of damage. This can only be prevented by shortening of intestinal transits time and which can be done by administering purgatives and emetics[33].

The goals of internal decontamination are to reduce absorption and to enhance elimination and excretion. Treatment is most effective if it is started as soon as possible after exposure. A number of isotopes which affect body parts after entering through various routes. (Table 2)

Table 1: Acute radiation syndromes

Syndrome	Dose	Prodromal Stage	Latent Stage	Manifest Illness Stage	Recovery
Bone Marrow	0.7 – 10 Gy (70 –1000 rads) (mild symptoms may occur as low as 0.3 Gy or 30 rads)	Anorexia, nausea and vomiting occur after exposure	Stem cells in bone marrow are dying, though patient may appear and feel well	Drop in all blood cell counts for several weeks. Primary cause of death is infection and haemorrhage	In most cases bone marrow cells will begin to repopulate the marrow. There should be full recovery for a large percentage of individuals from a few weeks up to two years after exposure
Gastrointestinal (GI)	10 - 100 Gy (1000 – 10,000 rads), Some symptoms may occur as low as 6 Gy or 600 rads)	Anorexia, severe nausea, vomiting, cramps and diarrhoea occur within a few hrs after exposure and lasts for 2 days	Stem cells in bone marrow and cells lining in GI tract are dying, though patient may appear and feel well	Anorexia, severe diarrhoea, fever, dehydration, electrolyte imbalance. Death is due to infection, dehydration and electrolyte imbalance	The LD_{100} is about 10 Gy (1000 rads)
Cardiovascular (CV)/ Central Nervous System (CNS)	> 50 Gy (5000 rads) (some symptoms may occur as low as 20 Gy or 2000 rads)	Extreme nervousness, confusion, severe nausea, vomiting, watery diarrhoea loss of consciousness, and burning sensations of the skin.	Patient may return to partial functionality	Return of watery diarrhoea, convulsions and coma begin 5 to 6 hrs after exposure. Death within 3 days of exposure	No recovery

Table 2: Treatment for some radioisotope[6,9,18,37]

Isotope	Route	Affected Area	Method of treatment	Decontamination	Dose
Iodine 131	Inhalation , ingestion, percutaneous, absorption (small amount)	Thyroid	Block uptake by thyroid	Saturated solution of potassium iodide	390 mg/day orally for 7 to 14 days
Cesium 137	Inhalation, ingestion	Whole body	Mobilization decreases gastrointestinal uptake	Prussian blue (Ferric Ferrocyanide)	1g in 100-200 ml of water orally three times daily for several days
Plutonium 239	Inhalation, absorption, wound incorporation	Bone liver lung	Chelation increases excretion of the isotope	DTPA	1g/day for 5 days
Tritium	Inhalation ingestion, percutaneous absorption	Whole body	Dilution increases excretion of the isotope	Water diuresis	3 to 4ltr/days for 2 weeks
Technetium	Inhalation, ingestion	Thyroid	Displacement with iodine	Saturated solution of potassium iodide	390 mg/day orally for 7 to 14 days

Table 3: Some examples of oral decorporating drugs

S.No	Drugs	Mechanism
1	Calcium	It is used as decorporating drug, it interfere with the absorption of different radioactive materials such as strontium, radium and barium. Calcium can compete with radioactive materials in bone deposition.
2	Ammonium chloride	It is given orally for decorporation of strontium from body. This is more effective when combined with intravenous calcium gluconate. It shows some side effects vomiting, nausea, and gastric irritation. It should be avoided in case of patients suffering from liver disease.
3	Potassium phosphate	It is useful in blocking uptake of radioactive phosphate, but it is contradicted in renal insufficiency, hyperphosphatemia and infected phosphate stones
4	Propylthiouracil	It is given to decrease the retention of radioiodine in thyroid. It is available in tablet form.
5	Sodium alginate	It is given in powder form. It binds with strontium and prevents its absorption in gastrointestinal tract. Adult dose is 10 gm powder.

GASTROITESTINAL TRACT AS A ROUTE OF ELIMINATION

Gastric absorption can be reduced by stomach lavage[37-39], emetics, purgatives, laxatives, ion exchangers[39]. Stomach lavage is effective only if it is performed immediately after contamination and ingested dose is high. The most commonly used emetic agents are apomorphine (5-10 mg, subcutaneous) and ipecac (1-2 g in capsule or 15 ml in syrup), which should be given concomitantly with 200-300 ml of water. However, use of emetics and purgatives is not always feasible. But these methods show limitation as these cannot be administered to a person with poor health state. In case if person is unconscious then emetics are contradicted and purgatives should not be used in individuals with abdominal pain. Certain nonabsorbable binding resins are capable in preventing the uptake of various radioactive materials in the gut. For example, Prussian blue, it is a nonabsorbable pigmented resin has been used orally to enhance the faecal excretion of cesium and thallium by means of ion exchange process[40]. Other example is sodium polystyrene sulfonate it is approved in United States under the name of "Kayexalate". Some antacids are also shown the property of reducing the absorption of radioactive strontium if given immediately after the exposure; examples are aluminium containing antacids, aluminium hydroxide[40]. But none of them are approved as decorporating agents in United States because their potency has not been established.

The decorporation of radionuclides can be done by following different mechanisms, such as by using blocking agents, diluting agents, complexing agents and mobilizing agents[39,40].

1. Blocking and diluting agents

The blocking and diluting agents are used to reduce the uptake of radionuclides which are already present in the blood tissues. As the name signify blocking agents block the uptake of radionuclides into target tissue[27,40]. For example administering a blocking agent such as potassium iodide (KI) allows saturation of metabolic processes in the thyroid with stable and nonradioactive iodine thereby preventing the uptake of radioactive iodine[27]. Diluting agents as the name signifies they simply dilute the concentration of radionuclides in the body and decrease their absorption. As an example, water can be used to increase the excretion of tritium.

2. Mobilizing agents

Mobilizing agents are the compounds that enhance the natural turnover processes of radioactive contaminants and thereby accelerate their release from tissues. The treatment is most effective, if it is done immediately after the contamination, but they may also retain some effectiveness for up to 2 weeks after contamination. Examples of mobilizing agents are diuretics, propylthiouracil, expectorants, parathyroid extract and corticosteroids, ammonium chloride etc[36-38].

3. Chelating agents

Chelating agents or complexing agents are those substances which form complexes with certain metals to form a stable complex such as ethylenediaminetetraaceticacid (EDTA), diethylenetriamine pentacetate (DTPA)[37], nitrilotriaceticacid (NTA)[39]. These complexing agents form stable complex with certain radionuclides that form water soluble complexes which can be more rapidly eliminated from the body via excretion by the kidneys. Calcium and zinc salts of DTPA are approved as decorporating agent. DTPA forms water soluble, stable complexes with transuranium elements and increase their elimination from the body. Both Ca-DTPA and Zn-DTPA are safe for the treatment of plutonium, americium, or curium. Ca-DTPA is administered as a single intravenous injection or inhaled immediately possible after contamination, and repeated doses of Zn-DTPA administered intravenously which may be given daily as maintenance therapy, as necessary. Uranium contamination has been treated with oral sodium bicarbonate, regulated to maintain an alkaline urine pH, and accompanied by diuretics.

RECENT TRENDS IN RADIOLOGICAL AGENTS DECONTAMINATION

Various research industry and labs are regularly working on the development of new, safe and effective techniques and formulations for decontaminations. The various decontamination kits or solutions which have been developed are.

1. SHUDIKA decontamination kit has been developed by DRDO India[32,42,43]. The kit contains approved chemicals and meets the regulatory criteria. The decontamination kit is self usable, ease in handling and is used in a light weight portable box made up of polypropylene.

2. RSDecon lotion is a patented, broad spectrum topical skin decontamination product manufactured for the Healthcare Protective Products division of Bracco Diagnostics Inc[32]. RSDL is a self usable decontamination formulation which is used to remove or neutralise chemical warfare agents and various other toxins from skin.

3. Low-cost personal decontamination system (LPDS) is an easy to use wipe system. It consists a wipe or a sponge in which skin decontamination lotion is present to decontaminate radionuclides[32].

4. Oral decorporation formulations: Oral drug delivery is also used in decorporation of radionuclides, DRDO India has developed different oral drug delivery formulations which enhance the excretion of specific radionuclide materials[41-43]. On the bases of drug delivery technology and human modelling, a controlled release multidrug oral formulation has been developed by DRDO. These formulations are also alternative to the conventional Injectables. These oral decorporation formulations are capable of forming complexes with different mono, bi, and multivalent radioactive materials that have been

ingested or present in the blood. The main advantages of these formulations are their cost effectiveness, and non-invasive forms are given in Table 3.

CONCLUSION

There is always a risk of nuclear and radiological agents contamination by accidently or can be done intentionally by terrorist in the form of weapons of mass destruction (Dirty bomb). Radiological agents are hazardous to human beings, can cause acute radiation syndrome, radiation burns and genetic mutation. These effects depend on the factors: time of exposure of body, distance from the incident site and route of contamination. Decontamination can be done on the basis of route of contamination. There are various formulations and methods available for nuclear and radiological agents decontaminations but they are limited to certain radionuclides and are not fully effective in other case such as decontamination efficiency, cost effectiveness and safe. There is no single method/technique available which is effective in all conditions because of number of factors such as time of exposure, distance from the exposure, type of agent etc. So there is a requirement of development of such methods and formulation which achieve optimum level of decontamination and must be safe and cost effective.

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