IODINE PROPHYLAXIS AND NUCLEAR ACCIDENTS

ZDENKO FRANIĆ

Institute for Medical Research and Occupational Health, Zagreb, Croatia

Due to high volatility and environmental mobility, radioactive isotopes of iodine pose a serious risk in the acute phases of a nuclear accident. The critical organ for iodine is the thyroid. A number of studies dealing with thyroid protection from exposure to radioiodine have shown that radioiodine uptake by the thyroid can be effectively blocked by administration of stable iodine, usually in the form of potassium iodide (KI) pills. However, unless perfectly timed, this protective action may be counterproductive. The International Atomic Energy Agency recommends potassium iodide prophylaxis in cases when an avertable thyroid dose by protective action exceeds 100 mGy. This paper reviews experiences and practices with potassium iodide in the thyroid protection. This kind of information should serve as the basis for discussion and decision making on KI prophylactic programmes in nuclear emergency situations in Croatia. If Croatia adopts such programme, it will still have to develop the most effective way of KI stockpiling and distribution or predistribution.

Key words:
^{131}I, blocking efficiency, emergency preparedness, potassium iodide, thyroid

Iodine is a highly volatile element, which makes it very mobile in the environment. It is unevenly distributed in nature, as it is present in the litosphere approximately 5 times as much as in the ocean waters. Of at least 25 iodine isotopes with mass numbers ranging from 117 to 141, all except ^{127}I are radioactive (1, 2). From the point of view of environmental contamination, and resulting doses to man, the most important isotopes of iodine are ^{131}I and ^{129}I. They are the only radioactive isotopes of iodine produced by fission with half-lives longer than one day. ^{131}I is a beta emitter

with half-life of 8.06 days and maximum beta energy of 0.81 MeV. It emits gamma rays of 0.36 and 0.64 MeV and some other energies. ^{129}I has a very long half-life (1.57×10^7 years). It is also a beta emitter with maximum energy of 0.15 MeV and accompanying gamma ray of 0.09 MeV in 8% of its disintegrations. Like any other fission products, the two radionuclides are released into the environment through spontaneous fission of natural uranium. The main source of ^{131}I and ^{129}I, however, are nuclear explosions, releases from nuclear reactors, and nuclear fuel waste reprocessing plants. In the Pressurized Water Reactor (PWR) type of nuclear power plants, the equilibrium activity of ^{131}I is established after a few weeks of irradiation of uranium fuel in a nuclear reactor at a value of 3×10^{15} Bq per MW(e) (1). This value slightly increases with the burn-up of nuclear fuel reaching the end of the fuel cyclus as a result of a larger fission yield of plutonium, which also contributes to the build-up of ^{131}I activity concentrations. The activity of ^{129}I produced in a nuclear reactor is much lower than that of ^{131}I, as the inventory of ^{129}I after three years of fuel irradiation is 1.5×10^8 Bq per MW(e). In case of a severe accident in a PWR nuclear power plant, the conservative assessment is that 95% of noble gasses (Xe and Kr) contained in the core, 25–35% of iodine and caesium, and up to 10% of other activation and fission products, including ^{90}Sr, would be released into the environment. In the acute phase of a major nuclear accident, the plume (cloud-like formation) of radioactive material that might be released in the environment primarily consists of the radioactive isotopes of iodine, especially ^{131}I and noble gases due to their high volatility.

EMERGENCY PREPAREDNESS

Iodine enters the metabolism of living organisms and selectively targets the thyroid gland. According to a simple, three-compartment model adopted by the International Commission on Radiological Protection (ICRP), 30% of iodine entering the body transfer compartment is translocated to the thyroid, while the remainder is directly excreted (3). Iodine in the thyroid is believed to have a biological half-life of 120 days, which is, luckily, about 15 times the radiological half-life of ^{131}I. The biological half-life of iodine in all other organs is 12 days (3). However, the effective half-life of iodine in a thyroid (time for the thyroid to obtain one-half of its maximum burden during chronic exposure) was estimated to be 7.6 days (4). Therefore, in case of a severe nuclear accident, it is essential to protect general population from the exposure to the plume. The principal types of exposure are:

a) whole body external exposure to gamma radiation from the plume and from deposited material; and

b) inhalation exposure to a passing radioactive plume. The duration of exposure could range from half an hour to several days.

Shelter and/or evacuation are likely to be the principal immediate protection from exposure to the plume. It is desirable that the area around the facility on which the accident happened initially be evacuated beyond the perimeter of about 3 to 10 kilometres, preferably in the general downwind direction. Iodine prophylaxis, that is, immediate administration of the thyroid blocking agent (usually potassium iodide),

should be considered as the next step. One of the central issues in the emergency planning is to determine whether and at what projected thyroid radiation dose should stable iodine be given to the population (5).

In the process of establishing an international consensus on generic intervention levels (GILs) for urgent long-term protective measures, the International Atomic Energy Agency (IAEA) convened a number of technical meetings, which resulted in the Intervention Criteria in a Nuclear or Radiation Emergency (6). This safety guide represents the international consensus on values which subsequently became the basis for intervention guidance in the International Basic Safety Standards for Protection against Ionising Radiation and for the Safety of Radiation Sources (BSS) (7) jointly issued by the IAEA, Food and Agriculture Organization of the United Nations, International Labour Organization, Nuclear Energy Agency of the Organization for Economic Co-operation and Development, Pan American Health Organization, and World Health Organization. Table 1 shows the optimized generic intervention levels for urgent protective measures implemented in the BSS.

Table 1   *Recommended generic intervention levels for urgent protective measures*

Protective action	Generic intervention levels (dose avertable by protective action)*	Avertable dose period
Sheltering	10 mSv	2 days
Evacuation	50 mSv**	<1 week
Iodine prophylaxis	100 mGy	any

*Dose to be saved by protective action, that is, the difference between the dose to be expected with the protective action and the dose to be expected without it.
**In some countries a value of 100 mSv of avertable dose is considered to be more realistic for temporary evacuation. ICRP has recommended that evacuation would be justified for an avertable dose of 500 mSv (8, 9).

The values from the above table meet the following three basic principles:

1. serious deterministic health effects of ionising radiation should be avoided.

2. intervention should be justified in the sense that introduction of the protective measures should achieve more benefit than harm.

3. levels at which the intervention is introduced and at which it is later withdrawn should be optimized, so that the protective measure will produce maximum benefit.

The limit irradiation level above which iodine prophylaxis should be applied has been set to 100 mGy of avertable committed dose to a thyroid which was considered to be the optimal intervention level. The setting of GILs has taken into account price and cost of equipment and human labour in implementation of particular protective action, costs of insurance and reinsurance, and the consequences of social disruptions caused either by implementation or non-implementation of a particular protective action. The prophylaxis is implemented by administering or taking pills of potassium iodide (KI) which is a well known blocker of radioiodine uptake by thyroid gland (10–13). KI saturates the thyroid with stable iodine. Potassium iodide is an oral antithyroid agent used as an adjunct to other antithyroid agents in the treatment of hyperthyroidism, thyrotoxicosis. KI is also used preoperatively to induce thyroid involution. The drug has demonstrated high efficiency in treating cutaneous sporotricho-

sis. However, administration of KI as a protectant of the thyroid gland from exposure to radioactive isotopes of iodine raises the questions of appropriate timing, as well as of possible side effects (14–17).

CONTRAINDICATIONS TO POTASSIUM IODIDE

One may wish to note that literature speaks little about quantitative aspects of adverse reactions to potassium iodide. This is due to small study groups, selection bias, or limited follow-up (14). Recently, however, some data became available even *online*, that is, via Internet (18). Potassium iodide was officially approved by the American Food and Drug Administration (FDA) in 1939 (16). The FDA has evaluated the medical and radiological risk of administering KI for thyroid blocking under nuclear emergency conditions, and has approved the over-the-counter sale of the drug for this purpose.

The Mechanism of Action: Potassium iodide inhibits the thyroid hormone synthesis and release in the thyroid gland. Consequently, the thyroid gland vascularity is reduced, its tissue becomes firmer, the thyroid cell diminishes, the follicular colloid reaccumulates, and the bound iodine levels increase. As a post-irradiation protectant, KI blocks the uptake of radioactive iodine isotopes by the thyroid gland and minimises the risk of radiation-induced thyroid neoplasms. In treating sporotrichosis, KI enhances the tissue response to infection.

Pharmacokinetics: Potassium iodide is administered orally and is absorbed from the gastrointestinal tract as iodinated amino acids. It demonstrates significant extracellular distribution, with most of the drug accumulating in the thyroid gland. Potassium iodide distributes into breast milk and crosses the placenta in amounts sufficient to cause foetal harm. Therapeutic effects of KI are usually visible within 24 hours upon administration, with maximum efficiency occurring on days 10–15 of therapy. Potassium iodide is excreted renally.

Pregnancy: Potassium iodide crosses the placenta in amounts sufficient to cause foetal goiter and/or hypothyroidism. Although its prolonged use during pregnancy is not advised, potassium iodide was used in short terms (10 days) in the treatment of labor-induced thyrotoxic crisis and in treatment prior to thyroidectomy in pregnant women. As potassium iodide is excreted into the breast milk, rash or thyroid suppression can occur in the nursing infant. However, the American Academy of Pediatrics does not consider breast-feeding as contraindication.

Patients with sulphite hypersensitivity and/or asthma should use potassium iodide with caution because some formulations of this drug contain sodium bisulphite. Asthmatic patients are more sensitive to it than the nonasthmatic patients. Potassium iodide is contraindicated for patients with acute bronchitis.

Cautious administration or application of potassium iodide should also be true for patients with renal dysfunction. The impaired renal filtering of electrolytes may lead to an increase in serum potassium. Potassium iodide can also exacerbate hyperkalemia or myotonia congenita (Thomsen's disease). Those patients should be monitored for serum potassium and signs or symptoms of potassium toxicity. Further-

more, extreme caution is advisable in the following conditions: acute dehydration, heat cramps, adrenal insufficiency, and cardiac disease. Caution is advisable to patients with acne vulgari, as halogens in general can produce an acneiform rash or aggravate existing acne.

Extreme caution is advised to patients with tuberculosis, because potassium iodide may cause pulmonary irritation and increased secretion. In fact, patients with tuberculosis should avoid potassium iodide treatment if at all possible.

It is well known that chronic ingestion of iodine or iodine-generating compounds in amounts surpassing daily requirements for hormone biosynthesis ten or more times may lead to iodide goiter in certain subjects (11). This is why patients with iodine hypersensitivity should use potassium iodide with extreme caution. The risk group includes patients with hypocomplementemic vasculitis, goiter, or autoimmune thyroid disease.

There have been reports that the administration of stable iodine in the prophylactic treatment of endemic goiter is associated with an increased incidence of papillary carcinoma (19), although it was not possible to quantify any stable iodine carcinogenic potential, especially after the additional effect of radiation exposure (6). Nevertheless, this potential warns against selecting intervention levels of only a few mGy. After all, this is one of the reasons why the recommended generic intervention level for iodine prophylaxis has been established at 100 mGy (Table 1).

Intrathyroidal and extrathyroidal side effects that occurred after administering a single dose of KI were discussed in detail by *Nauman and Wolf* (14) in a study on effects of iodine prophylaxis in Poland after the Chernobyl accident. There were no serious adverse reactions in the population of approximately 18 million people who were given KI, except for two adults with known iodide sensitivity. The severe reactions to KI of the two individuals serve as a warning that such patients must be identified and educated about their sensitivity and excluded from the prophylactic programmes.

EFFICIENCY OF POTASSIUM IODIDE AND DOSAGE

The efficiency of KI in protecting the thyroid gland, that is, in blocking the uptake of radioiodine, strongly depends on the time of intake relative to the start of exposure to radioactive iodine. Based on the study performed by *Il'in and co-workers* (10), the findings of which have been adopted by the United States Nuclear Regulatory Commission (NRC) (20), the best results are obtained if KI is taken 1–2 hours before or immediately after the start of exposure. Taking the recommended dose of KI just before or at the time of exposure can block over 90% of the radioactive iodine uptake by the thyroid (Figure 1). When taken approximately 3–4 hours after the start of the acute exposure, KI is able to block about 50% of the uptake. Once radioactive iodine has concentrated in the thyroid, KI starts to block its excretion. The KI dosage recommended by the FDA is 130 mg/day (which contains 100 mg of stable iodine) for adults and children above one year and 65 mg/day for children below one year of age (20). The duration of protection is, like the extent of protection, dose-related. That is,
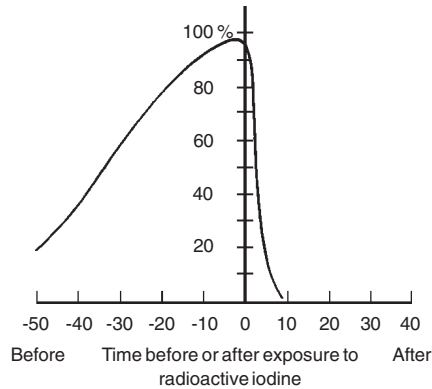
Figure 1 *Percentage of thyroid blocking by 130 mg of potassium iodide as a function of time in hours.*

even a large single dose will not protect for much longer than approximately 36 hours (14). Therefore, KI should be administered for at least three consecutive days after the acute exposure to prevent accumulation of radioiodine excreted from other body compartments in the thyroid gland.

IODINE PROPHYLAXIS IN POLAND AFTER THE CHERNOBYL ACCIDENT

The largest epidemiological study on the effects of KI prophylaxis ever performed was the one in Poland after the Chernobyl accident. The accident at the Chernobyl nuclear power plant in Ukraine took place on April 26, 1986. Two explosions that occurred, the steam explosion followed by the explosion of hydrogen, expelled fission products, as well as some material from fuel elements to the exterior. Because of the ignited graphite moderator, the release was prolonged and elevated. Consequently, volatile radioactive material was accumulated in a cloud reaching the height up to seven km. It was estimated that 1.3×10^{18} Bq of ^{131}I (i.e., 20% of the ^{131}I core inventory) has been released (21). The increased air radioactivity was first detected in Poland on April 27. The spectra showed that 80% of the total radioactivity were iodine isotopes (14). On April 29 at noon, the Polish Minister of Health ordered the centralized pharmacy to prepar KI solutions for distribution in 11 most affected provinces. The KI doses were prepared according to the following protocol:

    a) 15 mg for newborns,
    b) 50 mg for children five years or under,
    c) 70 mg for all others,

d) Because the cancer risk for adults was believed to be low, and some side-effects might be anticipated, iodine prophylaxis was not recommended to adults.

e) Iodine prophylaxis was recommended to lactating women, but was not mandatory.

Stable iodine was given as a single dose of KI solution to 10.5 million children and seven million adults. Children showed no serious side effects, whereas only two adults (with previous history of iodine sensitivity) had severe respiratory distresses. However, side effects of KI other than those related to the thyroid were more frequent than expected. Vomiting was the most common, followed by a few cases of diarrhea, whereas both children and adults complained of gastric disturbances. It remained unclear to what extent all these could be related to the administered iodide. The control values for the side-effects, which could have been obtained from the population not receiving KI, are not available. This is why one can hardly be as certain as to associate the side effects with KI treatment rather than with panic. The Polish experience showed that rapid response to widespread nuclear accidents is as much a social issue as a medical or scientific one, and that it requires rapid organization of large numbers of people and facilities.

IODINE PROPHYLAXIS PRACTICE IN THE USA

In the USA, which counts the most operating nuclear power plants, the issue of stockpiling KI pills for prophylaxis of general public in the event of a nuclear reactor accident is still open, although it is generally accepted that KI is an effective thyroid-blocking agent. The cost of KI is not prohibitive since a 130 mg tablet costs US $ 0.07. Therefore, supplying with KI pills to all residents within the 8 km perimeter (i.e., within the emergency planning zone) of one of the United States' 107 operating nuclear reactors would cost about US $ 200,000 (this figure should be added to distribution and disposal cost). Furthermore, the safety of the drug is not disputed. However, there is a major dilemma whether having KI at hand would make some residents trust their fate to a pill rather than to evacuation. Namely, many federal states, as well as the nuclear industry, believe that evacuation should be given priority in a nuclear emergency. Potassium iodide would »create a false sense of security as well as 'ambiguity' through choice« (22). It has been left to states or local governments to decide which course to take (23).

The high incidence of thyroid cancer in Belarus and Ukraine in children exposed to radiation following the Chernobyl nuclear plant acciolent in 1986 (24) has caused many physicians and public health officials in the USA and other countries to reconsider the urgency of making KI readily available to the public. Consequently, supporters of stockpiling contend that it would be negligent of the nuclear industry and of state and federal governments not to endorse what they call »a simple and cheap insurance policy«. For example, the American Thyroid Association, through its Public Health Committee, has strongly recommended the stockpiling of KI for prophylaxis in the event of a nuclear reactor accident (25).

In the summer of 1998, the Nuclear Regulatory Commission (NRC) decided that it would financially support those federal states which decide to stockpile KI pills. Previously, NRC recommended that potassium iodide be available mainly for emergency personnel, but not stored for general public. The US Department of Health and Human Services has been preparing guidance on the potassium iodide issue which will be considered by NRC and Federal Emergency Management Agency (26).

KI AND EMERGENCY PERSONNEL

In the acute phase of a nuclear accident, the information provided by emergency response mobile units is essential to estimate the dose of KI for general public (27, 28). Even in countries which are excellently covered with fixed telemetric monitoring stations, mobile units capable of transferring external dose-rate data and locality data in real time are useful for mapping radiation levels in locations not covered with fixed monitoring network (29). A primary function of a mobile unit team is to locate the plume and assess its magnitude. In order to minimize the risk of a mobile unit personnel exposed to radiation, it is necessary to survey as many locations as possible in as little time as possible. The maximum protection involves readily available respirators and KI pills. According to criteria established in several USA plants respirators are to be used at the radioactivity level of approximately 37 Bqm^{-3}, whereas criteria for administering KI pills vary between 0.1 Bqm^{-3} and 0.25 Bqm^{-3} (30). Principles for protection of workers of different categories potentially exposed to radiation in a nuclear emergency are given and discussed in full details elsewhere (6, 7).

CONCLUDING REMARKS

A number of studies have shown that radioiodine uptake by thyroid gland can be effectively blocked by administration of potassium iodide, provided that it occurs within a few hours before or after the exposure to iodine radioisotopes has started. Therefore, KI prophylactic programmes are an important part of nuclear emergency preparedness. This is particularly true for the highly populated areas which, for a number of reasons, cannot be effectively evacuated in a short time. One may wish to note that in 1989 the World Health Organization recommended preventive distribution of KI. By now, the recommendation has been widely implemented by France and Switzerland.

However, all individuals with iodide sensitivity have to be identified in order to prevent serious iodine-related side effects. That can be achieved through a public health care system.

In some countries it is recommended to stockpile KI in households. Stockpiling should not, however, occur before general public is well informed about the principles of emergency preparedness.

Like many other countries, the Republic of Croatia can accomplish that through national TV and radio network, teletext pages, and so on. It would also be useful to establish an »emergency preparedness information server« on the Internet. This can combine with real-time information about background radiation on several locations in Croatia which is already available (31). In adopting KI prophylactic programmes, competent Croatian authorities should be able to effectively resolve the issue of KI stockpiling and distribution or predistribution. Such solutions should then reflect in emergency plans giving detailed instructions on KI stockpiling and distribution procedures in nuclear emergencies.

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Sažetak

PROFILAKSA KALIJEVIM JODIDOM I NUKLEARNE NESREĆE

Zbog velike hlapljivosti, te stoga potencijalno vrlo brzog širenja kroz okoliš, u akutnoj fazi nesreće nekog nuklearnog postrojenja primarnu opasnost glede izlaganja radioaktivnom oblaku znače radioaktivni izotopi joda. Kritičan organ za jod je štitnjača. Brojna istraživanja o zaštiti štitnjače od kontaminacije radioaktivnim izotopima joda suglasna su da je učinkoviti način zaštite štitnjače unos stabilnog joda u organizam, obično u obliku tableta kalijeva jodida (KI). No, ta zaštitna mjera mora biti pravodobno provedena, inače ima suprotne učinke. Preporuka Međunarodne agencije za atomsku energiju jest da se profilaksi kalijevim jodidom pristupa ako se procijeni da bi doza koju štitnjača primi zbog izlaganja radioaktivnim izotopima joda mogla premašiti 100 mGy. U radu je dan pregled dosadašnjih spoznaja o učinkovitosti zaštite štitnjače kalijevim jodidom. Ove su pak informacije potrebne za iniciranje rasprave i donošenje odluke o programu KI profilakse u Hrvatskoj u slučaju kriznoga stanja glede nuklearne sigurnosti. Ako Hrvatska prihvati takav program, potrebno je razviti najučinkovitiji način uskladištenja, raspodjele ili preventivne raspodjele KI.

Ključne riječi:
[131]I, pripravnost u kriznim stanjima, štitnjača, unos stabilnog joda

Requests for reprints:

Zdenko Franić, Ph.D.
Institute for Medical Research and Occupational Health
Radiation Protection Unit
Ksaverska cesta 2, P.O. Box 291
HR–10001 Zagreb, Croatia
E–mail: *franic@imi.hr*