RADIOPROTECTIVE EFFECT OF SOME PYRAZOLONE DERIVATIVES

A. V. Piskarev
and V. S. Nesterenko

UDC 615.849.1.015.25:547.775

Analgin, antipyrine, and aminopyrine, if administered to mice in large doses 3 h before irradiation (800 R), increased the survival rate and prolonged the life of the dying animals. In combination with cystamine, these compounds increased the chances of survival of the mice after the period of acute intestinal death following irradiation in a dose of 1050 R. In therapeutic doses the pyrazolone derivatives had a less marked radioprotective effect.

KEY WORDS: pyrazolone derivatives; acute radiation sickness.

Great importance is attached nowadays to hypoxia in the pathogenesis of radiation sickness [1]. Many radioprotective compounds are known to increase the resistance of animals to hypoxia [2, 5, 6]. Investigations have shown that pyrazolone derivatives – analgin, antipyrine, aminopyrine, and butadione – considerably increase resistance to hypoxia both of healthy mice and of irradiated mice at various periods of acute radiation sickness [3, 4, 7].

It was therefore decided to study the radioprotective properties of pyrazolone derivatives.

EXPERIMENTAL METHOD

Experiments were carried out on 600 noninbred albino mice of both sexes weighing 20-24 g. In the experiments of series I, to study the radioprotective effect of pyrazolone derivatives (analgin, antipyrine, aminopyrine, and butadione), the drugs were injected intraperitoneally in doses of 35% of LD_{50} 1, 2, 3, and 6 h before whole-body γ-ray irradiation in a dose of 800 R, dose rate 30 R/sec. In the experiments of series II the radioprotective properties of the pyrazolone derivatives were studied in combination with cystamine in animals irradiated in a dose inducing the intestinal form of acute radiation sickness (1050 R). The animals in this series of experiments received one of the test compounds 3 h before irradiation, and an intraperitoneal injection of cystamine* (150 mg/kg) 15 min before irradiation. In each group not less than 10 mice were tested at the same time. In the experiments of series III the protective properties of the pyrazolone derivatives were studied in therapeutic doses 3 h before irradiation of the mice in a dose of 800 R.

The radioprotective action of the preparations was assessed from the survival rate of the animals on the 30th day after irradiation and from changes in the mean life span of the dying animals.

EXPERIMENTAL RESULTS

Analgin (1000 mg/kg), antipyrine (400 mg/kg), and aminopyrine (100 mg/kg), if injected 3 h before irradiation, had a radioprotective action: the survival rate of the animals was increased to 30-45% (from 12.5% in the control); the mean life span of the dying animals also was increased (Table 1). Butadione had no radioprotective effect. The radioprotective effect of pyrazolone derivatives when injected 3 h before ir-

*2-aminoethanethiol.

Department of Radiation Pathophysiology, Research Institute of Medical Radiology, Academy of Medical Sciences of the USSR, Obninsk. (Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Zakusov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 80, No. 7, pp 58-60, July, 1975. Original article submitted October 21, 1974.

TABLE 1. Radioprotective Action of Some Pyrazolone Derivatives When Injected 3 h before Irradiation in a Dose of 800 R

Compounds studied, doses	Number of mice	Number dying	Number surviving	Survival rate, %	Mean life span of dying animals (in days)
Biological control	20	—	20	100	—
Irradiated control	80	70	10	12,5	12,6±1,5
Analgin (1000 mg/kg)	40	22	18	45,0	19,0±1,2
Antipyrine (400 mg/kg)	40	26	14	35,0	17,2±1,4
Aminopyrine (100 mg/kg)	40	28	12	30,0	17,0±1,5
Butadione (400 mg/kg)	20	18	2	10,0	12,8±1,1
Cystamine (150 mg/kg 3 h before irradiation)	20	16	4	20,0	12,2±1,8
Cystamine (150 mg/kg 15 min before irradiation)	20	—	20	100,0	—

TABLE 2. Radioprotective Action of Combined Administration of Pyrazolone Derivatives and Cystamine in Mice Irradiated in a Dose of 1050 R

Compounds studied, doses	Number of mice	Number dying	Number surviving	Survival rate, %	Mean life span of dying animals (in days)
Biological control	20	—	20	100	—
Irradiated control	40	40	—	—	4,5±0,5
Cystamine (150 mg/kg 15 min before irradiation)	40	40	—	—	11,6±2,2
Analgin (1000 mg/kg) + cystamine (150 mg/kg)	40	34	6	15	13,4±2,8
Antipyrine (400 mg/kg) + cystamine (150 mg/kg)	40	36	4	10	12,4±2,2
Aminopyrine (100 mg/kg) + crystamine (150 mg/kg)	40	36	4	10	14,4±2,5

radiation was higher than that of cystamine given at the same times. When the preparations were given 1, 2, and 6 h before irradiation, their radioprotective effect was less.

The experiments of series II showed that the combined administration of pyrazolone derivatives and cystamine greatly alleviated the course of acute radiation sickness; 80-95% of the animals of the experimental groups survived the period of "intestinal death" (7th day after irradiation), compared with 100% mortality at the same period among the irradiated mice of the control group; 10-15% of animals survived until the 30th day after irradiation. The mean life span of the dying animals in the experimental groups was three times greater than that of the control irradiated mice (Table 2). The combined action of pyrazolone derivatives and cystamine exceeded the radioprotective effect of cystamine alone, administration of which (150 mg/kg) 15 min before irradiation of the mice, did not increase the survival rate of the animals, but increased the mean life span of the dying mice by only 2.5 times compared with the control irradiated animals.

In the experiments with antipyrine (50 mg/kg), analgin (50 mg/kg), and aminopyrine (25 mg/kg), the survival rate of the animals by the 30th day averaged 25%, compared with 10% in the control group. It must be emphasized that butadione, in a therapeutic dose (0.16 mg/kg), aggravated the course of acute radiation sickness (all the mice died on the 14th day after irradiation).

LITERATURE CITED

1. G. A. Vasil'ev, Med. Radiol., No. 1, 41 (1959).
2. E. Ya. Kaplan and V. V. Ogleznev, in: Problems in Space Biology [in Russian], Vol. 7, Moscow (1968), p. 235.
3. A. V. Piskarev, Abstracts of Proceedings of a Scientific Conference of Junior Research Workers and Specialists [in Russian], Obninsk (1972), p. 85.
4. A. V. Piskarev, V. S. Nesterenko, and S. I. Suminov, Farmakol. i Toksikol., No. 1, 48 (1973).
5. Yu. F. Udalov, Vopr. Pitaniya, No. 5, 22 (1956).
6. J. Doull and K. DuBois, Proc. Soc. Exp. Biol. (New York), 84, 367 (1953).
7. W. Flacke and V. Mülke, Arch. exp. Path. Pharmak., 218, 95 (1953).