PREVENTION OF DEATH FROM AMETHOCAINE POISONING BY ARTIFICIAL RESPIRATION AND RESPIRATORY STIMULANTS

A. A. Zykov

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Many cases of poisoning by local anesthetics, often terminating in death, are described in the clinical literature. Most authors attribute death from poisoning by local anesthetics to paralysis of the respiratory center [6, 11, 12, 17]; the view has been expressed, on the other hand, that death takes place not only on account of severe depression of the respiratory center, but also of paralysis of the diaphragm and intercostal muscles [2] or as a result of asphyxia arising from spasm of the respiratory musculature [1].

Because of this notion that paralysis of the respiratory center is the main cause of death from poisoning by local anesthetics, some experimental workers have tried various analeptics in the treatment of this poisoning [3, 16, 18, etc.].

In the present investigation a study was made of the effect of artificial respiration and the new Soviet analeptics éthimizol (ethylnorantiphein) and corconium (subecholine) in the treatment of poisoning by amethocaine, one of the most toxic of local anesthetics.

EXPERIMENTAL METHOD

The experiments of series I were carried out on 20 rabbits. Amethocaine was injected intravenously into 10 control intact animals as a freshly prepared 0.5% aqueous solution in a dose of 4.28-5.96 mg/kg body weight. When these doses were injected into rabbits, respiratory arrest ensued. Tracheotomy was performed under ether anesthesia on 10 experimental animals, and 4 h later an intravenous injection of amethocain was given in a dose of 6.25-6.78 mg/kg (i.e., doses slightly larger than those given to the intact rabbits). After respiration ceased, artificial respiration was at once applied to the experimental rabbits by means of the special A-1937 (Kiev) apparatus. The volume of air pumped into the lungs was 40-50 ml and the number of respiratory movements 70-80 per min.

The experiments of series II were carried out on 240 sexually mature male albino mice: half of the animals were used as controls. These animals received a subcutaneous injection of amethocaine in the form of a freshly prepared 0.5% aqueous solution in doses causing death of 72-85% of the animals (45-50 μg/g body weight; spasms were observed in all the animals from these doses. Amethocaine was injected in the same doses into the experimental mice either 15 min after injection of corconium and éthimizol or simultaneously with corconium, or 5 min before injection of éthimizol. Corconium is a respiratory stimulant with reflex action [4, 5, 9, 10], and éthimizol has a central action [7, 8, 10]. These preparations were injected intraperitoneally in doses of 2 μg/g (corconium) and 10 μg/g (éthimizol).

RESULTS AND DISCUSSION

In series I chronic and tonic spasms developed in all the control rabbits during administration of amethocaine, respiration ceased, and the animals died very soon after. All the experimental rabbits receiving artificial respiration immediately after respiratory arrest survived. Spontaneous respiration was absent for 10-20 min, as was verified by periodically switching off the artificial respiration apparatus. Artificial respiration did not abolish the spasms. During the spasms the rabbits ground their teeth, salivated profusely and urinated.

The results of series II are given in the table, showing that corconium, when injected along with amethocaine, helps to preserve the life of the animals without influencing the development of spasm. The preliminary injection of corconium did not prevent death from amethocaine poisoning, and this may evidently be explained by the transient action of the preparation [4, 9]. The preliminary injection of éthimizol lowered the mortality from amethocaine poisoning by a statistically significant degree.

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Effect of Corconium and Éthimizol on Amethocaine Poisoning in Mice

Preparation	Dose (in μg/g)	Amethocaine (in μg/g)	Control	Expt.	P
Corconium (simultaneously with amethocaine)	2	50	36/50	22/50	<0,01
Corconium (preliminary injection)	2	50	30/40	21/40	>0,05
Éthimizol (preliminary injection)	10	50	30/40	10/40	<0,001
Éthimizol (subsequent injection)	10	50	17/20	17/20	—

Note. The number of animals in the experiment is given in the denominator; the number of animals dying in the numerator.

Administration of éthimizol 5 min after amethocaine had no effect on the outcome of amethocaine poisoning. Like corconium, injection of éthimizol did not prevent the onset of spasms.

The results obtained show that death from amethocaine poisoning can be prevented by artificial respiration; administration of respiratory stimulants prevents death of only some animals. These results are in agreement with reports of the beneficial effect of artificial respiration in poisoning by local anesthetics [1, 3, 13, 15, etc.].

The activity of analeptics in poisoning by local anesthetics has been investigated by other authors. Some investigators [16, 18], testing cardiazol, caffeine, coramine, and lobeline, observed survival of a higher proportion of animals than in the control series. Most investigators [3, 13, 14, etc.], however, report that respiratory stimulants are valueless in the treatment of poisoning by local anesthetics. Goodman and Gilman [14], Svec [13], and others consider that during the action of analeptics, as also of convulsant poisons, immediately after excitation, depression of the central nervous system develops, and its duration and depth are directly proportional to the degree of the preceding excitation; for this reason, analeptics may facilitate paralysis of the respiratory center.

In connection with these remarks, the beneficial effect of the new analeptics, demonstrated in the present experiment, is of particular interest. It can be accepted that these preparations cause less after-depression of the central nervous system than analeptics hitherto used. Corconium, in particular, with a quaternary nitrogen atom in its molecule, gives only a peripheral effect, for practically none of the drug enters the central nervous system.

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