EFFECT OF A COMBINATION OF TRIMEPERIDINE AND TRANQUILIZERS ON THE ANALGESTIC EFFECT OF LOCAL ANESTHETICS

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The local anesthetics in wide use at the present time, despite their many advantages, do not always reliably prevent pain. Because of the ability of the central cholinolytics and tranquilizers to potentiate the action of analgesics, it is of both theoretical and practical interest to examine the effect of certain central cholinolytics and tranquilizers on the effect of local anesthetics using an adequate method of stimulation.

EXPERIMENTAL

The pain sensitivity of 16 male rabbits weighing 2-3 kg was studied by stimulating the pulp of a tooth [1, 2] for 3 sec with rectangular pulses of electric current with a duration of 1 msec and frequency of 20 cps at intervals of 10 min, before and after administration of the anesthetic alone or the anesthetic together with a mixture of trimeperidine and tranquilizers.

The minimal threshold of pain sensitivity was determined by the licking reaction and the maximal threshold by the beginning of a reaction of violent biting and withdrawal of the head. The mucous membrane of the transitional fold was infiltrated with 0.6 ml of 4% procaine solution in the region of the superior incisors and the palate near the incisive foramen. The substances used in the investigation were trimeperidine (2.5 mg/kg), metamysil, haloperidol (0.5-1 mg/kg each), and chlorpromazine (0.5 mg/kg). The substances were injected into the marginal vein of the rabbit's ear 5 min after the injection of procaine. Altogether 72 experiments were carried out.

EXPERIMENTAL RESULTS

Procaine raised the minimal threshold of nociceptive sensitivity on the average from 1.8 to 2.9 V, i.e., by 61% and the maximal threshold from 7.4 to 7.8 V, i.e., by 5%. Metamysil and haloperidol in doses of 1 mg/kg and chlorpromazine in a dose of 0.5 mg/kg did not alter the local anesthetic effect of procaine. When trimeperidine was given in a dose of 2.5 mg/kg, in conjunction with metamysil, haloperidol, and chlorpromazine in the doses indicated above, in every case marked potentiation and prolongation of the procaine action was observed. In supplementary experiments to study the analgesic effect of trimeperidine and tranquilizers, a mixture of these substances alone was found to increase the maximal and minimal thresholds of nociceptive sensitivity. However, in conjunction with procaine, these indices increased to a higher degree, so that a summation effect took place.

The mean values (of not less than 6-10 observations in each case) of the minimal and maximal thresholds of nociceptive sensitivity are given in Figs. 1 and 2. The results showing the changes in the maximal pain threshold for administration of combinations of trimeperidine with tranquilizers were obviously underestimated, because it was impossible to stimulate the pulp with a voltage greater than 15 V because of the fear of injuring the pulp, and in this case a relative characteristic was used (the time required to lower the threshold to the appearance of a reaction in response to stimulation by a current of 15 V or less). When the action of procaine was assessed from the increase in the maximal and minimal thresholds of nociceptive sensitivity against the background of the mixtures, of all the combinations of trimeperidine with one of the substances named, that which produced the best anesthetic effect was a mixture of metamysil in a dose of 1 mg/kg and trimeperidine, when the minimal pain threshold was increased by 367%

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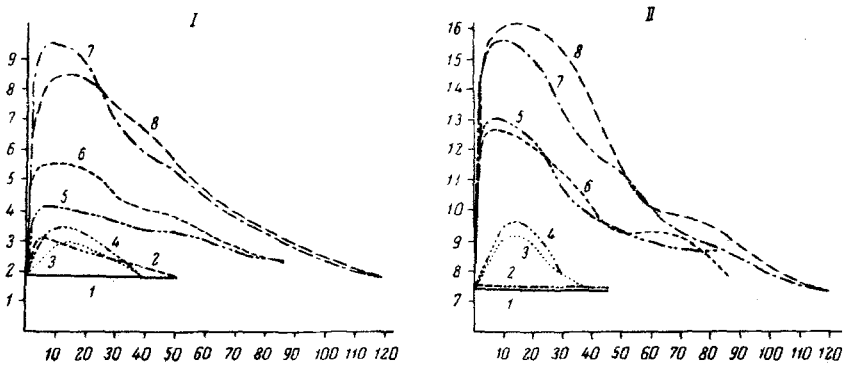

Fig. 1. Increase in minimal (I) and maximal (II) thresholds of nociceptive sensitivity under the influence of procaine, various tranquilizers, and procaine against the background of tranquilizers (mean results of 6-10 observations in each case). Abscissa: time (in min); ordinate: voltage (in V). 1) Normal conditions; 2) administration of trimeperidine (2.5 mg/kg); 3) procaine (mean of 50 experiments); 4) procaine against the background of trimeperidine (2.5 mg/kg); 5) mixture No. 4 (trimeperidine 2.5 mg/kg, metamysil 1 mg/kg, haloperidol 1 mg/kg); 7) procaine against the background of trimeperidine (2.5 mg/kg) with metamysil (1 mg/kg); 8) procaine with mixture No. 4.

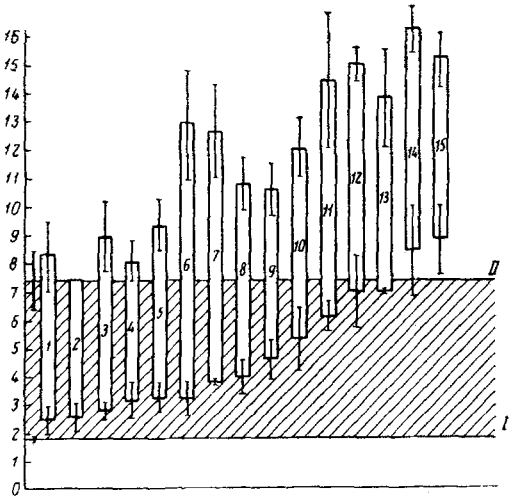

Fig. 2. Anelgesic effect 20 min after administration of analgesic mixtures alone, procaine, and procaine against the background of the mixtures. Ordinate: voltage (in V). I) Minimal; II) maximal thresholds of nociceptive sensitivity; the interval between the thresholds of stimulation in normal conditions is shaded; vertical lines: confidence limits. 1) Injection of trimeperidine (2.5 mg/kg) with chlorpromazine (0.5 mg/kg); 2) trimeperidine (2.5 mg/kg); 3) procaine; 4) trimeperidine (2.5 mg/kg) with haloperidol (1 mg/kg); 5) procaine against the background of trimeperidine (2.5 mg/kg); 6) mixture No. 3 (trimeperidine 2.5 mg/kg, metamysil 0.5 mg/kg, chloropromazine 0.5 mg/kg); 7) mixture No. 4 (trimeperidine 2.5 mg/kg, metamysil 1 mg/kg, haloperidol 1 mg/kg); 8) mixture No. 1 (trimeperidine 2.5 mg/kg, metamysil 0.5 mg/kg, haloperidol 0.5 mg/kg); 9) procaine against the background of trimeperidine (2.5 mg/kg) with haloperidol (1 mg/kg); 10) trimeperidine (2.5 mg/kg) with metamysil (1 mg/kg); 11) procaine against the background of trimeperidine (2.5 mg/kg) with chlorpromazine (0.5 mg/kg); 12) procaine against the background of mixture No. 3 (trimeperidine 2.5 mg/kg, metamysil 0.5 mg/kg, chlorpromazine 0.5 mg/kg); 13) procaine against the background of mixture No. 1 (trimeperidine 2.5 mg/kg, metamysil 0.5 mg/kg, haloperidol 0.5 mg/kg); 14) procaine against the background of mixture No. 4 (trimeperidine 2.5 mg/kg, metamysil 1 mg/kg, haloperidol 1 mg/kg); 15) procaine against the background of trimeperidine (2.5 mg/kg) with metamysil (1 mg/kg).

and the maximal by 89% (obviously underestimated) by comparison with the corresponding values during the action of procaine alone. Comparison of the thresholds of nociceptive sensitivity, after injection of procaine against the background of mixtures of trimeperidine and tranquilizers with their initial level, shows that this increase was 527% for the minimal and 213% for the maximal pain thresholds.

It may be concluded from these results that in order to obtain a reliable analgesic effect, the administration of a mixture of trimeperidine, metamysil, chlorpromazine, and haloperidol in addition to local anesthetics can be recommended, for it considerably potentiates the local anesthetic action of these substances.

LITERATURE CITED

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2. R. J. Montagne, Contribution à l'étude des analgésiques, Paris (1957).