A STUDY OF THE EFFECTS OF DEXCLAMOL AS THE NEUROLEPTIC COMPONENT IN NEUROLEPTANAESTHESIA

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SUMMARY

In a double-blind cross-over study in dogs, dexclamol was compared with droperidol as the neuroleptic component of a neuroleptanalgesic combination. Fentanyl was the narcotic analgesic. Neuroleptanaesthesia was induced with a mixture of the neuroleptic, the analgesic and nitrous oxide in oxygen. Dexclamol 200 µg/kg i.v. was as effective as droperidol at the same dose in inducing neurolepsy and in supplementing nitrous oxide anaesthesia. Changes in heart rate, respiratory rate and rectal temperature in the animals treated with dexclamol were not different from those observed in the animals treated with droperidol. A comparison of the adrenolytic properties of dexclamol and droperidol was made on the isolated rabbit aortic strip. Both compounds produced a parallel shift to the right of the noradrenaline cumulative dose–response curves, indicating competitive antagonism. The $pA_2$ values showed dexclamol to be approximately 15 times less potent than droperidol in inhibiting the noradrenaline-induced contraction of the rabbit aortic strip.

Dexclamol hydrochloride $\text{((+)-3S,4aS,13bS-2,3,4,4a,8,9,13b,14 - octahydro - 3 - isopropyl - 1H - benzo[6,7]cyclohepta[1,2,3, - de] - pyrido[2,1 - a]isoquinolin - 3-ol)}$ (Humber, Bruderlein and Voith, 1975) is a potent neuroleptic drug. When given to animals in very small doses it has been shown to antagonize the amphetamine-induced stereotyped behaviour in rats, and the apomorphine-induced emesis in dogs (Voith, K., unpublished observations). These tests have been reported to be highly characteristic and specific for neuroleptic drugs (Janssen, Niemegeers and Schellekens, 1965; Fog, 1972). When used alone, or in a suitable combination with a narcotic analgesic, dexclamol produced a profound potentiation of the anaesthetic effects of halothane in rats and therefore it has been proposed for neuroleptanaesthesia (Jaramillo, 1976). Neuroleptanaesthesia "... is a method in which a well chosen neuroleptic is combined with a well chosen analgesic in adequate proportions with the aim of obtaining a state of operative comfort for the patient as well as for the surgeon" (Boissier, 1968). The term was originally introduced by DeCastro and Mundeleer (1959).

The main advance in the application of neuroleptanaesthesia has come from its use as a supplement to light general anaesthesia (Holderness, Chase and Dripps, 1963; Foldes et al., 1966). The term neuroleptanaesthesia was proposed by Foldes and others (1966) to characterize the state of patients who receive fentanyl, droperidol and nitrous oxide, and who become analgetic, sedated and anaesthetized. It was further suggested that the term neuroleptanaesthesia be restricted to patients receiving neuroleptic and narcotic drugs who become analgetic, sedated and amnesic, but who are capable of obeying commands during surgery.

This paper summarizes the results of experiments performed in dogs in which dexclamol was compared with droperidol as the neuroleptic component of a neuroleptanalgesic preparation. A comparison was also made of the adrenolytic properties of the two compounds in vitro. Droperidol was used in this study as a reference standard. This drug is a butyrophenone derivative which has been reported to possess potent short-acting neuroleptic activity (Janssen et al., 1963). Droperidol in a fixed 50 : 1 mixture with fentanyl citrate (Innovar) has been used with nitrous oxide for neuroleptanaesthesia in man (Holderness, Chase and Dripps, 1963). The chemical formulae of dexclamol and droperidol are shown in figure 1.

Fig. 1. Structural formulae of dexclamol and droperidol.
METHODS

Dog studies

Sixteen beagle dogs (12 females, 4 males) weighing from 7.4 to 14.6 kg (average 11.4 kg) were studied. All received either dexclamol or droperidol on the first week of testing. Fifteen days later, the dogs which received dexclamol received droperidol and vice versa. An experimental protocol (table I) was designed to mimic the procedure followed in the clinic when a neuroleptanalgesic mixture is used in conjunction with light nitrous oxide in oxygen anaesthesia.

Table I. Protocol for studying the effects in dogs of dexclamol or droperidol, fentanyl and nitrous oxide in oxygen

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Drug treatment or procedure</th>
<th>Dose</th>
<th>Route of administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>-30</td>
<td>Diphenhydramine</td>
<td>5 mg/kg i.m.</td>
<td>i.m.</td>
</tr>
<tr>
<td>-15</td>
<td>Pethidine</td>
<td>5 mg/kg i.m.</td>
<td>i.m.</td>
</tr>
<tr>
<td>-14</td>
<td>Atropine</td>
<td>50 μg/kg i.m.</td>
<td>i.m.</td>
</tr>
<tr>
<td>-5</td>
<td>Observations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-4</td>
<td>Insert i.v. catheter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>Dexclamol or droperidol</td>
<td>200 μg/kg i.v.</td>
<td>i.v.</td>
</tr>
<tr>
<td>9</td>
<td>Observations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Fentanyl</td>
<td>5 μg/kg i.v.</td>
<td>i.v.</td>
</tr>
<tr>
<td>12</td>
<td>Fentanyl</td>
<td>2 μg/kg i.v.</td>
<td>i.v.</td>
</tr>
<tr>
<td>13</td>
<td>Nitrous oxide in oxygen</td>
<td>4:1 mask</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Fentanyl</td>
<td>2 μg/kg i.v.</td>
<td>i.v.</td>
</tr>
<tr>
<td>20</td>
<td>Lignocaine—intubation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Nitrous oxide in oxygen</td>
<td>3:1 trachea spray</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>Skin incision</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>Observations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>Fentanyl*</td>
<td>2 μg/kg i.v.</td>
<td>i.v.</td>
</tr>
<tr>
<td>31</td>
<td>Nitrous oxide in oxygen</td>
<td>2:1 Observations</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>Observations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>44</td>
<td>Observations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>Fentanyl*</td>
<td>2 μg/kg i.v.</td>
<td>i.v.</td>
</tr>
<tr>
<td>50</td>
<td>Observations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>59</td>
<td>Observations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>Fentanyl*</td>
<td>2 μg/kg i.v.</td>
<td>i.v.</td>
</tr>
<tr>
<td>65</td>
<td>Observations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70</td>
<td>Skin incision</td>
<td></td>
<td></td>
</tr>
<tr>
<td>74</td>
<td>Observations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>75</td>
<td>Fentanyl*</td>
<td>2 μg/kg i.v.</td>
<td>i.v.</td>
</tr>
<tr>
<td>80</td>
<td>Observations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>90</td>
<td>Nitrous oxide withdrawn—extubation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* When required.

The premedication was diphenhydramine 5 mg/kg i.m., administered 30 min before the neuroleptic and pethidine 5 mg/kg and atropine 50 μg/kg given i.m. 15 min after diphenhydramine. The neuroleptic (either dexclamol or droperidol) was injected slowly into the tubing of a 0.9% saline infusion into the cephalic vein. Fentanyl was given into the infusion: 5 μg/kg 10 min after the neuroleptic and 2 μg/kg every 15 min thereafter with additional 2-μg/kg dosages when required. Nitrous oxide 80% in oxygen was administered 13 min after the neuroleptic with the aid of a face mask. Seven minutes later (20 min after the neuroleptic) the trachea was intubated. To reduce the incidence of laryngeal spasm, the epiglottis and larynx were sprayed twice with lignocaine (10 mg/spray, Astra Endotracheal Aerosol). Nitrous oxide 75% in oxygen was then continued with a reduction in the nitrous oxide concentration to 66% 10 min later. The procedure was continued for a total of 90 min. Nitrous oxide administration was then discontinued and the tracheal tube was removed.

Heart rate, respiratory frequency and rectal temperature were recorded at intervals throughout the experiment. The animals were subjected to two skin incisions in the abdominal region at 25 and 70 min after the administration of the neuroleptic. The response of the animal to these incisions and to the subsequent suturing was recorded.

Immediately after the experimental procedure the animal was placed on the floor and the degree of satisfactory neuroleptanaesthesia was scored on a 0–5 scale by each of the experimenters (usually three) as follows:

0 = No effect
1 = Neuroleptic activity (apparent sedation; indifference)
2 = Score 1 plus loss of righting reflex after initial administration of nitrous oxide
3 = Score 2 plus possible for investigator to intubate the trachea and make first skin incision
4 = Score 3 plus possible for investigator to complete protocol; animal appeared to be in light anaesthesia just before narcotic was given
5 = Score 4 plus animal under stable, deep neuroleptanaesthesia.

The study was conducted in a double-blind fashion: none of the experimenters knew in advance whether the animal was receiving dexclamol or droperidol.

All drugs were dissolved in isotonic saline. Dosages are expressed in terms of the salt. Nitrous oxide and oxygen were administered using an anaesthesia machine (Fraser Sweatman, Model 800001).

The scoring values and the variations in heart rate, respiration and temperature at specific time intervals were analysed by Student's t test. For group comparison, the area under the curve for each animal (-5 to +65 min) was calculated. The areas were then averaged and compared by a paired t test. The
number of incisions performed and the number of animals reacting to such procedures were compared statistically by the Chi-square test applied to a $2 \times 2$ contingency table. Data on the time of intubation, extubation and the righting reflex were analysed by both the paired $t$ test and the Chi-square test. The statistical comparison of the amounts of fentanyl used was performed by a paired $t$ test.

In vitro studies

Male, albino New Zealand rabbits weighing 2–3 kg were used. The animals were sacrificed and the thoracic aorta was removed. Helically cut aortic strips were prepared according to the method of Furchgott (1960).

Four strips (4–5 cm in length) were suspended in separate muscle baths filled with 15 ml of Krebs solution, bubbled with 95% oxygen and 5% carbon dioxide and kept at 37.5 °C. A resting tension of 2 g was applied and a 2-h incubation period was allowed. The bath fluid was changed and the tension was readjusted every 30 min during incubation.

Increases in tension after administration of the drug were recorded isometrically on a Grass Model 7 polygraph using a Grass FT-03 force displacement transducer. Cumulative dose–response curves were obtained by a stepwise increase in concentration of the agonist. After a full dose–response curve was obtained, the preparation was allowed to rest for 1 h with changes in the bath fluid every 20 min. At the end of 1 h the antagonist was introduced into the bath. The dose–response curve was repeated 30 min after introduction of the antagonist. The agonist used was noradrenaline. Dexclamol and droperidol were dissolved in double deionized water and the pH was adjusted to 7.4 with NaOH 0.1 mol/litre. All drug concentrations were calculated in terms of total bath volume. Analysis of variance was carried out according to the method of Finney (1964). $pA_2$ values were calculated by the method described by Arunlakskana and Schild (1959).

The drugs used in this study were: droperidol (Inapsine), dexclamol HCl, noradrenaline bitartrate, diphenhydramine HCl (Benadryl), meperidine HCl (Demerol), atropine sulphate and fentanyl citrate (Sublimaze).

**RESULTS**

**Dog studies**

*Degree of satisfactory neuroleptanaesthesia.* No difference was noted between dexclamol and droperidol (table II). The mean score for all the dogs which received dexclamol was 3.3 (SEM ± 0.2). The degree of neuroleptanaesthesia produced in part by dexclamol or droperidol was dependent upon the particular dog used. For example, when one dog was given either dexclamol or droperidol, the scoring rates were 5.0 and 4.5, respectively, whereas when another dog was given the same drugs under identical conditions, scoring rates of 1.0 were recorded.

*Heart rate.* Figure 2 shows the heart rate changes observed during the initial 80-min period in which the animals were subjected to the procedure. After a short initial increase in heart rate a progressive reduction was observed, reaching a plateau 1 h later. The reduction in heart rate was 30% approximately of the initial value for dexclamol and 20% for

**TABLE II. Intubation, extubation and anaesthesia times in dogs under neuroleptanaesthesia**

<table>
<thead>
<tr>
<th></th>
<th>Intubation time (min)</th>
<th>Extubation time (min)</th>
<th>Anaesthesia time (min)</th>
<th>Mean score neuroleptanaesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexclamol</td>
<td>20.57 ± 0.86</td>
<td>77.0 ± 5.7</td>
<td>78.0 ± 5.8</td>
<td>3.2 ± 0.17</td>
</tr>
<tr>
<td>Droperidol</td>
<td>20.21 ± 1.22</td>
<td>78.6 ± 4.6</td>
<td>79.5 ± 4.8</td>
<td>3.3 ± 0.15</td>
</tr>
</tbody>
</table>

![Fig. 2. Changes in heart rate of dogs (n = 16) subjected to light nitrous oxide anaesthesia. Anaesthesia induced with 200 μg/kg of either dexclamol or droperidol i.v.](image-url)
droperidol. No statistically significant differences were found, in the effects on heart rate, between dexclamol and droperidol.

Respiratory frequency. Because of marked variability, no significant trend was noticed. Six out of the 10 animals receiving dexclamol exhibited a gradual decrease in rate up to approximately the 35–44-min period of the experiment. Ten out of 11 animals receiving droperidol showed the same tendency.

Rectal temperature. Figure 3 shows the changes in rectal temperature. There was a progressive reduction in most animals at the second reading after the administration of the neuroleptic agent (either dexclamol or droperidol). At the end of the recording period the rectal temperatures of both groups of animals were approximately 2 °C less than those observed at the beginning of the experiment. There was no statistically significant difference between the two drug groups.

![Image](image.png)

**Fig. 3.** Changes in rectal temperature of dogs (n = 16) subjected to light nitrous oxide anaesthesia. Anaesthesia induced with 200 µg/kg of either dexclamol or droperidol i.v.

Intubation and extubation times—duration of anaesthesia. Because of the relatively large degree of variation in sensitivity of the animals to the neuroleptic and anaesthetic, or both, it was not always possible to perform endotracheal intubation at the stipulated time. Whether intubation was advanced or delayed appeared to depend mainly upon the reaction of the animals to the drugs administered. Thus, the intubation times reflect the degree of difficulty encountered in the process of the tracheal intubation. The intubation times for dexclamol varied from 16 to 26 min and those of droperidol from 17 to 32 min. The average intubation times (20.6 min for dexclamol and 20.2 min for droperidol) were very close to the times stipulated in the protocol.

In some of the dogs removal of the tube occurred when the level of neuroleptanaesthesia was insufficient for the animals to tolerate the tracheal tube in spite of the local anaesthetic provided just before intubation. In those cases anaesthesia was discontinued and the animals were allowed to recover. The extubation times and the number of animals with which the entire procedure could be completed are indications of the depth of anaesthesia achieved in the animals. Table II shows the intubation and extubation times and the times at which the righting reflex was regained after discontinuing anaesthesia. No significant difference between the drug groups was found in the intubation, extubation or anaesthesia times. Table III shows the number of animals in which intubation was successful. Again, there was no significant difference between the groups. The number of animals receiving dexclamol and who were continued to the 90-min period (extubation) was similar to that for droperidol. The time required for these animals to regain the righting reflex (recovery time) following the discontinuance of the anaesthesia is presented in table III also.

Reaction to skin incisions. Table IV shows the number of animals subjected to incisions and their reactions. A positive reaction to the incision was

<table>
<thead>
<tr>
<th>Neurleptic drug</th>
<th>No. of animals intubated</th>
<th>No. of animals completing protocol</th>
<th>Recovery time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexclamol</td>
<td>14/16*</td>
<td>9/16*</td>
<td>1.6 ± 0.6</td>
</tr>
<tr>
<td>Droperidol</td>
<td>15/16*</td>
<td>8/16*</td>
<td>1.4 ± 0.5*</td>
</tr>
</tbody>
</table>

* $\chi^2 = 0.03$; n.s.  
* $t = 0.25$  
* $t = 0.29$  
* n.s.

<table>
<thead>
<tr>
<th>Neuroleptic drug</th>
<th>Incision</th>
<th>Total incisions</th>
<th>Total experiments</th>
<th>Reaction to incision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexclamol</td>
<td>First</td>
<td>13/16</td>
<td>3/13</td>
<td>5/9</td>
</tr>
<tr>
<td></td>
<td>Second</td>
<td>9/16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Droperidol</td>
<td>First</td>
<td>13/16*</td>
<td>1/13†</td>
<td>6/9†</td>
</tr>
<tr>
<td></td>
<td>Second</td>
<td>9/16*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* $\chi^2 = 0.01$; n.s.  
† $t = 0.29$; n.s.
recorded when the animal moved its legs, body or had a distinct change in respiratory frequency immediately following the incision or during suturing. When the degree of neuroleptanaesthesia was obviously unsatisfactory, no incision was made. On average, the first incision was made at 27 min and the second at 70 min. This was irrespective of drug group. There was no significant difference between the groups in respect of the number of incisions.

Total dose of fentanyl. Fentanyl was administered at certain prescribed times and doses and not as a continuous i.v. infusion. The data are presented here in μg/kg/min in order to account for the differences in anaesthesia time between one dog and another. There was good agreement between the amount of fentanyl required for a particular animal under dexclamol-nitrous oxide anaesthesia (0.272 ± SEM 0.02 μg/kg/min) and the amount required for the same animal under droperidol-nitrous oxide anaesthesia (0.293 ± 0.03 μg/kg/min). The difference between the means was not significant.

In vitro studies

Dexclamol at the $1 \times 10^{-6}$ and $1 \times 10^{-5}$ mol/litre concentrations reduced the noradrenaline-induced contraction of the rabbit aortic strip. These two concentrations produced a parallel shift of the noradrenaline dose–response curve to the right, indicating competitive antagonism. The calculated dose ratios with 95% confidence limits were 5.14 (3.46–7.85) and 45.54 (32.34–65.66) for the $1 \times 10^{-6}$ and $1 \times 10^{-5}$ mol/litre concentrations of dexclamol, respectively.

Droperidol at $1 \times 10^{-6}$ and $1 \times 10^{-5}$ mol/litre also caused a parallel shift of the noradrenaline dose–response curve to the right. The calculated dose ratios with 95% confidence limits for $1 \times 10^{-6}$ and $1 \times 10^{-5}$ mol/litre droperidol were 36.94 (25.22–55.44) and 225.4 (141.4–403.2), respectively.

All the dose–response curves for “before” and “after” drug administration were found to be valid, linear and parallel through analysis of variance (Furchgott, 1960).

The $pA_2$ for dexclamol and droperidol were 6.58 (6.34–6.84) and 7.90 (7.78–8.00), respectively (fig. 4).

**DISCUSSION**

Our experiments have shown that the scores for the dogs treated with dexclamol and for those treated with droperidol were identical, indicating that there was a comparable degree of neuroleptanaesthesia in both groups. Most of the animals received a score of 2 or more, signifying that under the influence of the neuroleptic drugs the dogs lost their righting reflex following the administration of nitrous oxide. Since nitrous oxide is a relatively weak anaesthetic agent, animals not pretreated with a neuroleptic would not be expected to lose their righting reflex at the concentrations used in this study. This was especially true during maintenance anaesthesia, when the inspired nitrous oxide concentration was 66%. Bert (1878) reported that in order to achieve anaesthesia in dogs and humans at normal atmospheric pressure, it is necessary to inhale pure nitrous oxide. More recently, Steffey and others (1974) reported that nitrous oxide does not provide significant anaesthesia at concentrations in the range 25–75%.

The necessity of assisting ventilation manually involved tracheal intubation in our animals. This operation has been described as constituting a good test of analgesia (Desvaux and Leroy, 1966) and of the indifference of the subject (Huguenard, 1968), especially when myoneural blocking drugs have not been used. Intubation was usually performed without difficulty in all of our animals subjected to dexclamol or droperidol. It should be noted that the two animals in which intubation could not be performed under dexclamol were the same animals in which intubation under droperidol was not possible or was delayed.

Another indication of the degree of analgesia and level of general anaesthesia achieved in our experiments is given by the number of incisions to which the animals were subjected and by their reaction to them. Under either dexclamol or droperidol, 13 out of 16 animals had at least an apparent satisfactory level of analgesia or neuroleptanaesthesia, or both, at the time of the first incision, and only a few animals (three
receiving dexclamol and one receiving droperidol) showed an undesirable reaction to the incisions. With time, the level of analgesia and anesthesia lessened. In both groups only nine animals could be subjected to the second incision and more animals showed a positive reaction to the second incision. This is probably a result of the relatively low concentration of nitrous oxide (66%) delivered during the last 60 min of anesthesia. This may explain also the relatively short period of recovery (1.4–1.6 min) in all of the animals after discontinuation of the nitrous oxide.

The need for analgesia varied markedly from animal to animal. It is of interest also that the highest doses of fentanyl were administered to those animals in which a good level of neuroleptanalgesia could not be achieved and which, therefore, received the lowest score when the quality of anesthesia was graded.

In summary, dexclamol would appear to be as effective as droperidol in inducing neurolepsy and in supplementing nitrous oxide anesthesia. However, significant differences were found in the way these substances interfere with the adrenergic system. Droperidol was found to be approximately 15 times more potent than dexclamol in blocking the effects of noradrenaline on the isolated rabbit aortic strip.

Because of its α-adrenergic blocking action, droperidol is known to cause arterial hypotension (Holderness, Chase and Dripps, 1963; Israel, Janssen and Dobkin, 1965), variable changes in both systemic and pulmonary resistance (Macdonald et al., 1966) and a reduction in total peripheral resistance (Dixon, Holan and Steward, 1970; Ferrari et al., 1974). Therefore, dexclamol may be expected to cause less disturbance of the cardiovascular system.

ACKNOWLEDGEMENTS

The author wishes to acknowledge the valuable guidance of Dr F. F. Foldes in the preparation of the experimental protocol and in the initial experiments of this study. The author also acknowledges the co-operation of Mr K. Suffiad in the in vitro studies and the valuable technical assistance of Mr J.-C. Vigeant, Mr P. Rosenrot and Ms Helene Langis, in the dog studies.

REFERENCES


ETUDE SUR LES EFFETS DU DEXCLAMOL LORSQU'IL CONSTITUE L'ÉLÉMENT NEUROLEPTIQUE DANS LES NEUROLEPTANESTHESIES

RESUME
Lors d’une étude à double inconnue avec inversion des séries à la fin de la première période, effectuée sur des chiens, on a comparé le dexclamol et le droperidol en tant qu’élément neuroleptique d’une combinaison neuroleptanalgésique. Le fentanyl était l’élément narcotique analgésique. La neuroptanalgésie a été provoquée à l’aide d’un mélange de neuroleptique, d’analgésique et de protoxyde d’azote dans l’oxygène. Le dexclamol administré par voie intraveineuse à une dose de 200 µg/kg a été aussi efficace que le droperidol à la même dose pour provoquer la neurolepsie et en renforçant l’anesthésie par le protoxyde d’azote. Les changements observés en ce qui concerne les battements du cœur, le rythme respiratoire et la température rectale des animaux traités au dexclamol, n’ont pas été différents de ceux relevés sur les animaux traités au droperidol. La comparaison des propriétés adrenolytiques du dexclamol et du droperidol a été faite sur une bande aortique isolée de lapin. Les deux composés ont produit un glissement parallèle vers la droite des courbes de dose/réaction cumulées de la noradrénaline, ce qui indique qu’il existe un antagonisme compétitif. Les valeurs du $pA_2$ montrent que le dexclamol est environ 15 fois moins puissant que le droperidol pour modérer la concentration de la bande aortique de lapin lorsque cette contraction est provoquée par la noradrénaline.

UNE STUDIE DER WIRKUNGEN VON DEXCLAMOL ALS NEUROLEPTISCHE KOMPONENTE BEI NEUROLEPTISCHER NARKOSE

ZUSAMMENFASSUNG

UN ESTUDIO DE LOS EFEKTOS DEL DEXCLAMOL COMO COMPONENTE NEUROLEPTICO EN NEUROLEPTANESTESIA

SUMARIO
En un estudio intercruzado a doble ciego con perros, se comparó dexclamol con droperidol como componente neuroleptico de una combinación neuroleptanalgésica. Fentanil fue el narcótico analgésico. Se indujo la neuroleptanestesia con una mezcla del neuroleptico, el analgésico y óxido nitroso en oxígeno. Dexclamol 200 µg/kg endovenosamente fue tan eficaz como droperidol a igual dosis para la inducción de neurolepsia y en suplementar la anestesia con óxido nitroso (monóxido de nitrógeno). Los cambios en la frecuencia cardíaca, respiratoria, y temperatura rectal en los animales tratados con dexclamol no fueron diferentes de los observados en los tratados con droperidol. Se efectúó una comparación de las propiedades adrenolíticas de dexclamol y droperidol en la tira aórtica del conejo ("ordeño aórtico"). Ambos compuestos produjeron una desviación paralela hacia la dercha de las curvas dosis acumulativa-respuesta de la noradrenalina, indicando antagonismo competitivo. Los valores de $pA_2$ mostraron que el dexclamol es 15 veces menos potente, aproximadamente, que el droperidol en inhibir la contracción del ordeño aórtico del conejo, inducida por la noradrenalina.