Scand J Rehab Med 1: 43–53, 1969

CHLORMETHIAZOLE, AMOBARBITAL, LIDOCAINE AND PLT 101 IN SPASTICITY AND RIGIDITY: A STUDY OF CLINICAL AND EMG-REGISTRABLE EFFECTS ON INTRAVENOUS INJECTION[1]

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ABSTRACT. The occurrence of reducing effects upon spasticity and rigidity was studied in 33 patients, in each of whom was tested one or more of the following preparations: Chlormethiazole, Lidocaine, Amobarbital and PLT 101 (a preparation related to Chlormethiazole) in intravenous injection.

It could be evinced here that Chlormethiazole, given in a quantity sufficient to induce perceptible drowsiness, had a significantly better reducing effect on rigidity than Lidocaine given in standard dosage. Comparison with Amobarbital, also given in a dosage to bring about incipient drowsiness, showed that Chlormethiazole had possibly the better effect on rigidity ($p = 0.06$). In spasticity, no difference appeared between the effects of Chlormethiazole, Amobarbital and PLT 101.

An objectification of changes in the threshold for the elicitation of stretching reflex was performed. A significant increase could be shown here in spastic patients following injection of Chlormethiazole. In non-spastic patients no change in threshold values could be demonstrated.

Parallel with reduction of involuntary activity, improvement in voluntary movement capacity resulted.

In a preliminary communication (1966) Petersén and Leissner showed that Chlormethiazole in intravenous injection had a reducing effect both in spasticity and in rigidity in man.

This present paper gives a more detailed description of the effects of Chlormethiazole in a larger material of patients with spasticity and rigidity. For comparison we have studied also the effect of a barbiturate, selecting for this purpose Amobarbital.

It had previously been shown (1, 10, 21) that barbiturates have an appreciable inhibitory effect upon the patellar reflex, and that in higher dosages a reduction of the amplitude of this reflex by about one half can be obtained. To obtain pronounced effect upon the spinal internuncial neuron are needed dosages of such magnitude as to produce also an appreciable depression of the reticular system (2, 12) as well as of the cerebral cortex (6). The sedative effect has thus been marked, for which reason very little use has been made clinically of barbiturates in these indications.

We have also studied the effects of Lidocaine, which in contrast with the above in dosages used here has little effect upon the reticular system and afferent inflows and only a slight influence upon the mono- and polysynaptic reflexes while however it induces a very considerable reduction of the cortical facilitating effect upon the spinal motor neurone (3).

Finally we decided to test a new Chlormethiazole derivative, code name PLT 101, the effect of which on spasticity and rigidity is unknown.

METHOD

Clinical testing

The patient was placed in a half sitting position, which was made as comfortable as possible. The arms were rested on arm-supports with about 90° flexion of the elbow joints. Under the knees were placed a hard rollable cushion to create an angle of about 90° between the thigh and the lower leg.

It was made certain that the bladder had recently been emptied or, in cases needing catheterization, that the catheter functioned properly. At an early stage a needle of the Olofsson type was introduced intravenously into one forearm. This needle was kept open with small quantities of heparin. On the other arm was placed a blood pressure cuff.

[1] Chlormethiazole, Lidocaine and PLT 101 from Astra Pharmaceutical Co., Sweden.

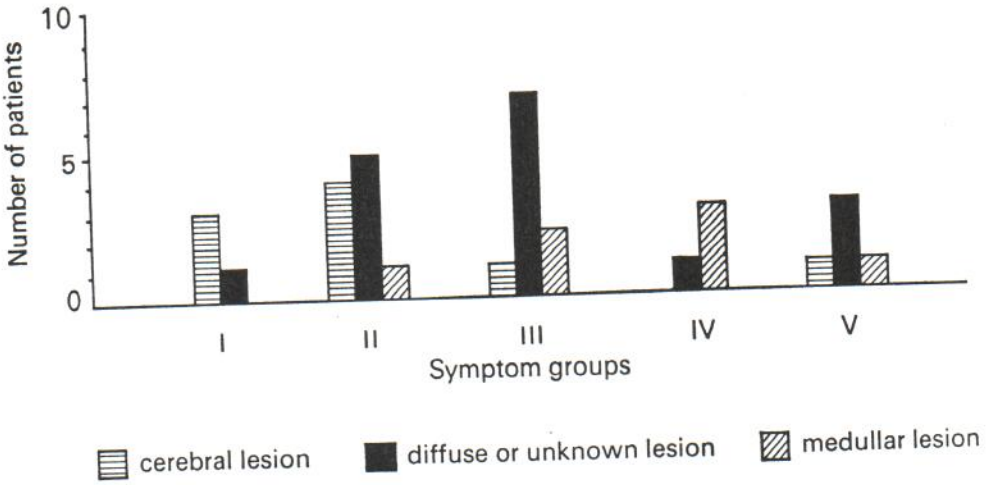

Fig. 1. Localisation of injury in patients with only rigidity (Group I), with only spasticity (Group V), with both but rigidity dominating (Group II), with both but spasticity dominating (Group IV) and both equal (Group III).

Clinical determination was made of the resistance to slow, passive stretching of the extensor and flexor muscle groups in the upper arms, forearms, thighs and lower legs respectively (4). Results were recorded on a scale from 0 to 3, 0 representing complete absence of such resistance and 3 representing a degree of resistance which needed a great deal of strength and time to overcome. Next, the stretch reflexes for biceps, triceps, quadriceps and the calf musculature were graded 0 to 3 in the usual way, 3 designating an inexhaustible clonus. Finally any evidence of spontaneous spasm was noted.

EMG registration

Skin electrodes were placed on the affected, or the most affected extremities, covering both flexor and extensor groups and disposed longitudinally right over the bulges of the muscles. Connection was made with a Disa electromyograph for film registration and thence with an oscillograph (Elema-Schönander mingograph 42). Film speed was 50 mm/sec and paper speed 5 mm/sec for slow courses, or, alternatively, 50 mm/sec for more rapid courses. Registration took place while the patient was at rest and during slow passive stretching of the musculature, commencement and completion of movements being marked. The position arrived at was held constant for 5 to 20 sec. Provided there were no contractures the stretching movement completed an angular change of 90°. Registrations were made in cases with clonus, subclonus and positive Babinski induced by the drawing of a knitting needle along the lateral edge of the foot. Registered finally was the patient's capacity for active movement during the rapidest possible movements without loading.

Objective reflex tests were performed with a reflex hammer, with an accelerometer built in at the head and coupled to the mingograph, on which the activities of the respective muscles were registered simultaneously. The accelerometer was calibrated with a 2 mm free fall. The hammer weighing 100 g, the kinetic energy at the moment of retardation was 20 gcm (100 g × 0.2 cm) (20).

The tests described were repeated immediately following injection of the respective drugs.

The intravenous injections of the different preparations were in each case made with simultaneous control of blood pressure, pulse and degree of awakeness. In the event of side effects, these were noted. The Chlormethiazole was given in a 0.8% solution at an injection rate of 3–5 ml/min to a total quantity of about 5 mg/kg body weight. The Lidocaine was injected in a 1% solution to a total quantity of 15–20 ml, i.e. 2–3 mg/kg body weight, at an injection rate of 3–4 ml/min, the PLT 101 was injected in a 2% solution to a total of about 4 mg/kg body weight at an injection rate of about 2 ml/min, and, finally, the Amobarbital was given in a 10% solution to a total quantity of about 4 mg kg body weight, at an injection rate of $^1/_2$ ml/min.

While injection proceeded the patient was kept in continuous conversation to permit observation of changes in degree of awakeness and possible euphoria. Provided no untoward side effects intervened, the injection continued until a very slight drowsiness came on, perceptible by both patient and observer. At the standard dosage of Lidocaine, 2–3 mg kg body weight, degree of awakeness did not appear to undergo any appreciable change.

It should be observed here that the durations of the Chlormethiazole and PLT 101 injections were longer than that of the Amobarbital. This circumstance may give rise to differences between time effect curves. No detailed studies have, however, been made from such comparisons on account of the difficulty of grading drowsiness. The estimations of rigidity and spasticity after injections were performed in a regular order as was the EMG registration and objective reflex testing. Clinical estimation, EMG registration and objective reflex testing required on the average 20–30 min following completion of injections. Cessation of these stimuli to the attention created another opportunity for observing drowsiness. At this stage, drowsiness, if any, was generally less marked than immediately on termination of the injection without noteworthy differences between preparations as to this effect.

Each patient was subsequently, between free intervals of a few days, examined with regard to any of the other preparations in the series. As far as possible all examinations were performed in identical conditions, for instance as to time of day. Order of sequences as between preparations was varied constantly to avoid as far as possible any systematic sources of error such as due to patient's individual attunement to the examination circumstances.

Processing of statistical material

The statistical evaluation of the results obtained was performed with the aid of sign test at 5% level. In one instance (change of threshold value for quadricep reflex in connection with Amobarbital injection) Student's *t*-test was used, similarly at 5% level.

MATERIAL

Some 89 tests were performed, 32 with Chlormethiazole, 19 with Amobarbital, 19 with Lidocaine and 19 with PLT 101, on 33 patients: 25 men and 8 women aged between 18 and 74, average age 47. Of these patients 9 had a purely cerebral lesion, in 4 Parkinson's disease and in 5 tumour, trauma or vascular lesion. Seven patients had a purely medullary injury caused by tumour or trauma. Nine patients had multiple sclerosis with spinal as well as cerebral symptoms. The remaining 8 were without definite clinical diagnosis, even though in several there were suggestions of MS.

Patients were grouped respectively according to degree of rigidity and/or spasticity and to the relations between the two conditions. In 4 cases there was very marked rigidity without spasticity (Group I). In 10 cases rigidity symptoms were distinctly dominant over spasticity (Group II). In 10 cases the rigidity and the spasticity were classified as equal (Group III). In 4 cases the spasticity symptoms exceeded those of rigidity (Group IV). Finally, in 5 cases there was very marked spasticity without appreciable signs of rigidity (Group V).

The grouping of patients according to symptoms was performed together with the localization of the injuries. Groups I and II represented mainly patients with cerebral lesions, 7 patients compared with 1 patient with medullary injury, the purely medullary lesions appearing mainly in patients which the spasticity dominated (Groups IV and V) (see Fig. 1).

RESULTS ON THE BASIS OF NEUROLOGICAL EXAMINATION

Effects upon rigidity (see Fig. 2)

Chlormethiazole was tested in 27 cases of rigidity. In all cases a reducing effect was obtained. In 6 patients this was so marked that only extremely slight rigidity, if any at all, could be established after injection at the clinical estimation.

Lidocaine was tested in 15 cases where rigidity occurred. At 9 examinations a reducing effect had been obtained, and in no case had a more marked effect been brought about. In the course of one of the examinations the injection had to be broken off after a small inflow because of a lowering of the blood pressure. In the remaining 5 cases no effect whatever appeared.

Amobarbital was tested in 16 cases where rigidity was present. In 13 of these a reducing effect was noted. In no case was the rigidity completely terminated. Neither in any case could a marked reduction in the rigidity be attained. In 3 cases, no change of status followed injection.

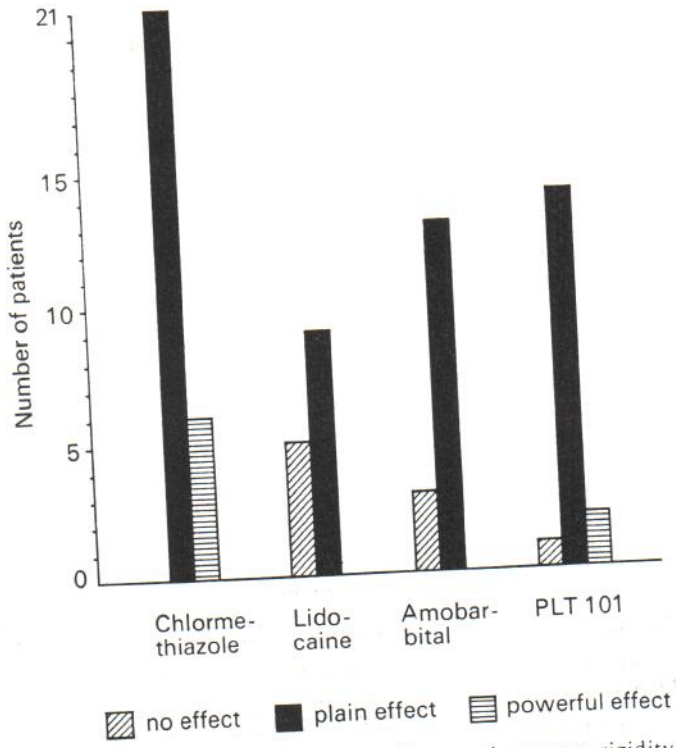

Fig. 2. Effects of the preparations in question upon rigidity.

PLT 101 was used in 18 cases in which rigidity was present. In 16 of these a reduction was noted. In no case was rigidity brought to an end. In one case the injection had to be stopped at an early stage because of reduction of blood pressure. In 1 patient, to whom the preparation had been administered in ordinary dosage, no change in the degree of rigidity could be observed.

Thus all preparations had effect upon rigidity. It is of interest therefore to establish whether any of the preparations had a better effect than the other. From Fig. 1 it appears that Chlormethiazole had more often effect than Lidocaine and Amobarbital. For practical reasons, however, it was impossible to test all preparations with all patients. The composition of the patient material being varied for the different preparations, the statistical processing of the above figures was regarded as yielding unreliable results. We therefore performed our comparisons in pairs, in order to note which of two preparations had the more marked effect upon a particular patient (see Fig. 3).

At a comparison based upon Chlormethiazole it was shown that this preparation was better than

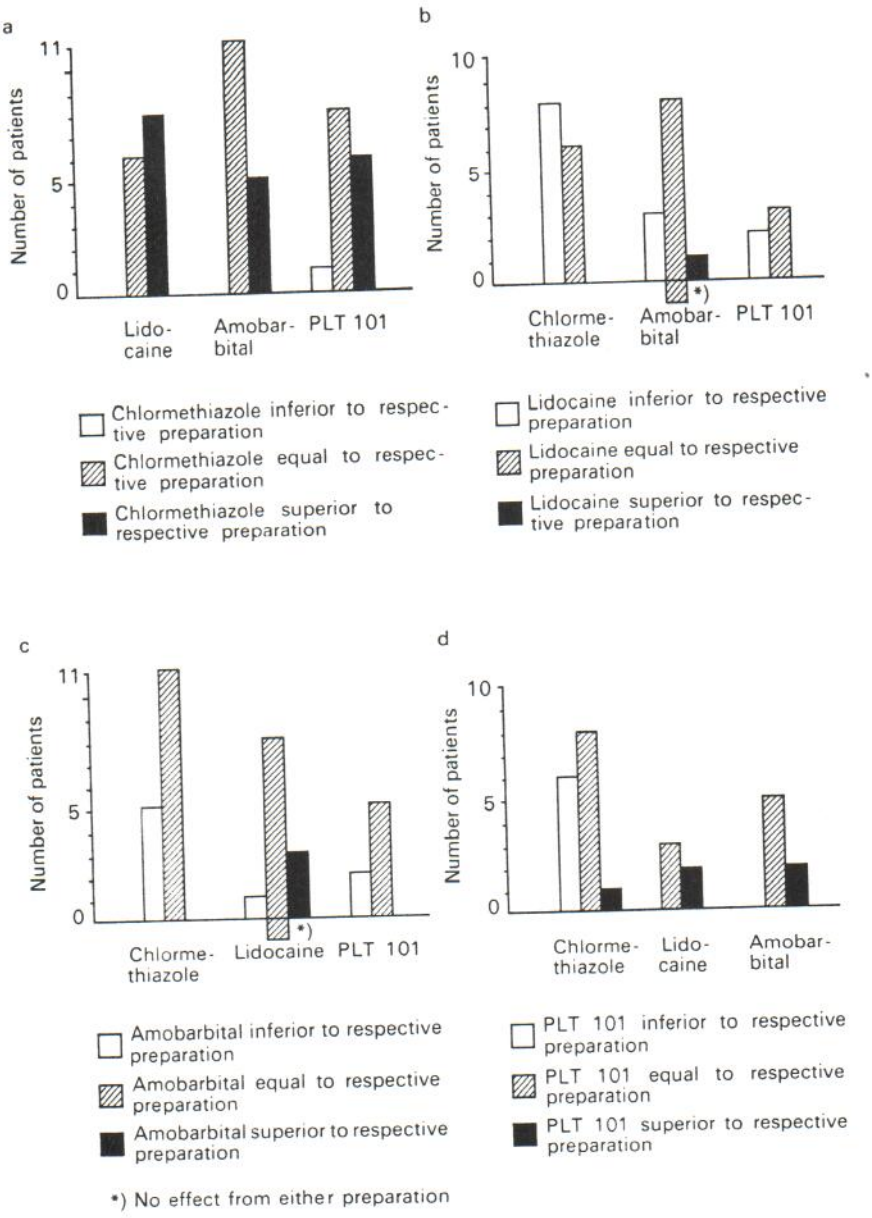

Fig. 3. Comparisons between preparations, in pairs upon the same patient, as to effect: (*a*) Chlormethiazole compared with other preparations; (*b*) Lidocaine compared with others; (*c*) Amobarbital compared with others; (*d*) PLT 101 compared with others.

others in 19 instances and equal to others in 25, and that in only one case it had proved inferior. In this latter case the comparison was with PLT 101.

Lidocaine in comparison with other preparations proved its advantage in one instance, and that was against Amobarbital. In all 34 comparisons, this preparation proved equal in 20 cases and inferior in 13.

Compared with other preparations, Amobarbital gave the better results in 3 cases, each in comparison with Lidocaine. In 25 instances results proved equal (in one of these cases, however, neither the Amobarbital nor the object of comparison, which was Lidocaine, showing any effect at all on rigidity). Amobarbital proved inferior to other preparations 8 times out of a total of 36 comparisons.

PLT 101 proved better than other preparations 5 times, equal 16 times, and inferior 6 times. Only when compared with Chlormethiazole did PLT 101 prove inferior to the other preparation. Compared with Lidocaine and Amobarbital, PLT 101 proved better 4 times and equal 8 times.

Statistical processing with the use of the sign test yielded the result that Chlormethiazole was significantly superior to Lidocaine ($p = 0.008$). Chlormethiazole showed moreover a tendency to produce better results when compared with Amobarbital ($p = 0.06$). No advantage for Chlormethiazole over PLT 101 could, however, be proved ($p = 0.13$).

Effects upon spasticity

Chlormethiazole, on testing, showed an appreciable reducing effect upon spasticity in 10 cases,

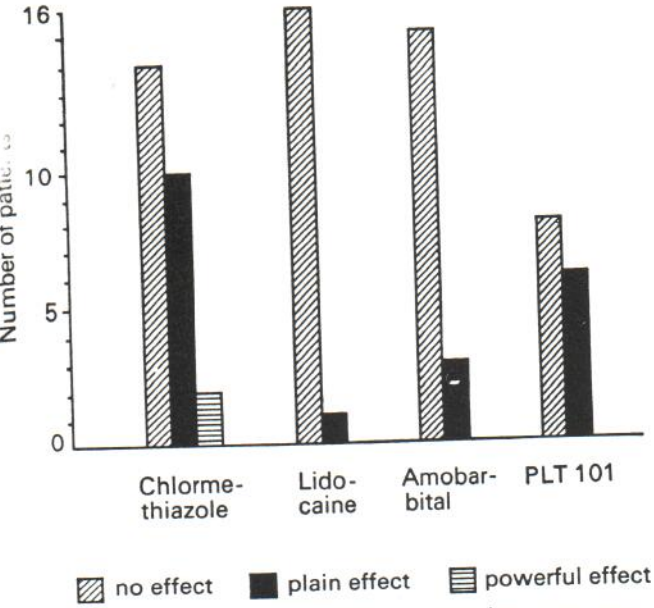

Fig. 4. Effects of the preparations in question upon spasticity.

marked such effect in 2 cases and no demonstrable effect in 14 cases. In 2 cases it was impossible to estimate effect because of the concurrence of massive rigidity.

Lidocaine, in one instance, had a reducing effect, but in 16 cases proved entirely without effect.

Amobarbital, in 3 instances, had a reducing effect, but in 15 cases proved without effect. PLT 101 had a reducing effect in 6 cases and no effect in 8. In 3 cases estimation of result was made impossible by massive rigidity (see Fig. 4).

Comparisons in pairs as between different preparation were made as to effect on the same patient. In these, Chlormethiazole as compared with PLT 101 was shown to have the better effect in 3 cases, the opposite obtaining in 4. Any comparative ranking between them was thus impossible. Chlormethiazole in 6 cases proved better than Amobarbital, in 3 cases less effective: this difference was not statistically significant. The reducing effect upon spasticity of Lidocaine proved in the course of this study very slight. Its inferiority to Chlormethiazole proved statistically significant according to sign test.

Of the 23 Chlormethiazole-treated patients in whom spasticity and rigidity concurred, Chlormethiazole in 14 cases was shown to have effect upon rigidity but not upon spasticity. In none of the patients had it any effect upon spasticity without at the same time inducing a reduction in rigidity. According to sign test, the effect on rigidity was significant better than that on spasticity.

In the corresponding group of 13 patients which was treated with Lidocaine, a reduction in rigidity was shown in 7 cases, but not in spasticity, while in 1 case spasticity was reduced but not rigidity. Of the patients examined with Amobarbital, 8 showed effects upon rigidity without any reduction of spasticity, while in no case was there any reduction in spasticity without a reduction at the same time in rigidity. The corresponding figures for PLT 101 were 7 and 0 respectively. In both these latter preparations the effects on rigidity are significantly better than those on spasticity.

Effects on spontaneous spasms

Eight patients had spontaneous flexion and/or adduction spasms, or were subject to them in

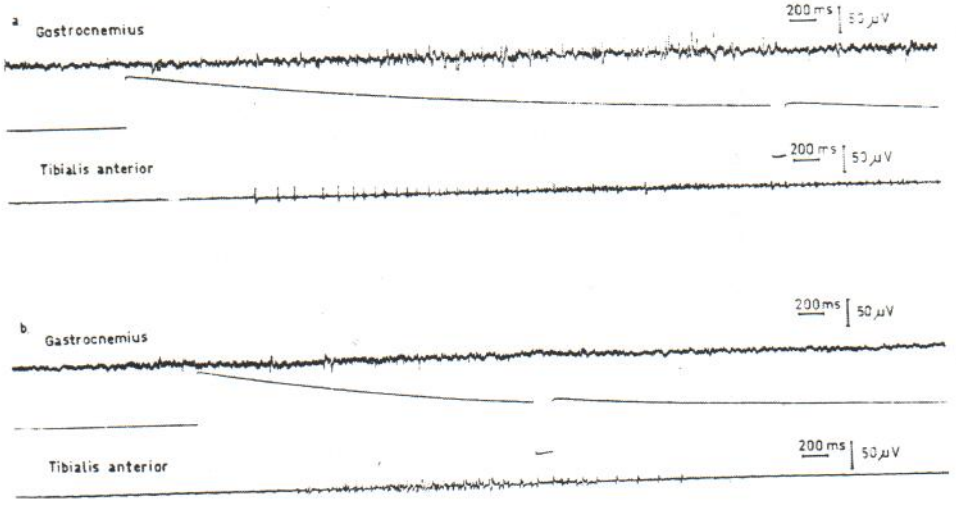

Fig. 5. Activity in the gastrocnemius muscle, with skin electrode applied, during slow passive stretching of the muscle from maximum downward to maximum upward stretching of the anklejoint (*a*) before, and (*b*) after injection of 60 ml Chlormethiazole. An appreciable increase in activity attained before the injection was not repeated following the injection. Stretching movement was marked on the line below EMG registration from the gastrocnemius.

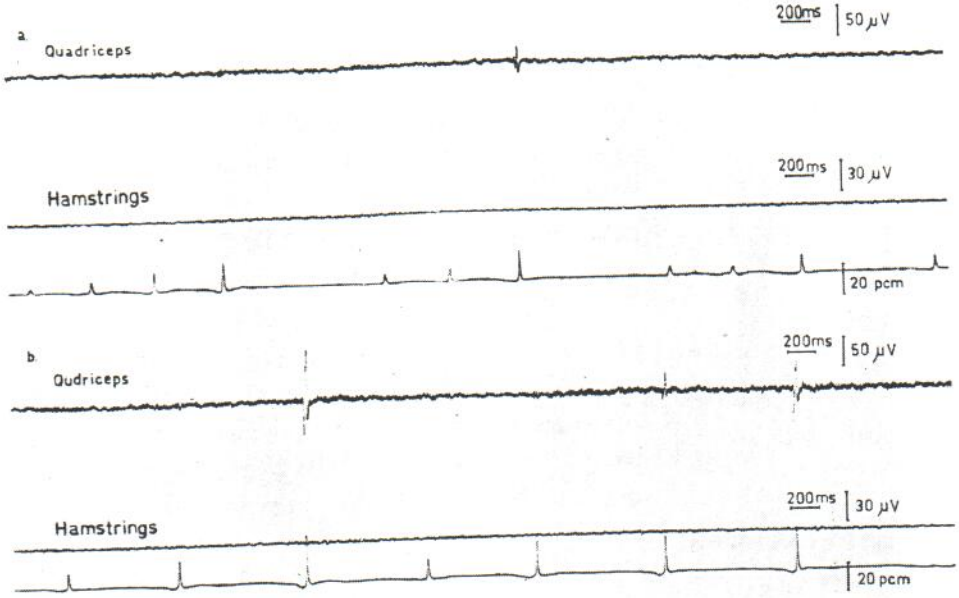

Fig. 6. Activity in the quadriceps, with skin electrode applied during elicitation of stretch reflex by reflex hammer strokes at a constant point on the patellar tendon. Linear registration was made of retardation in the strokes on the lower line (*a*) before, and (*b*) after injection of 60 ml Chlormethiazole. The minimum force of impact needed to obtain a perceptible reflex was, before injection, 20 gcm, and after injection 25 gcm. Position of the skin electrode was not altered, nor was the striking point on the patellar tendon.

response to very slight stimulation. Seven of these patients were given Chlormethiazole, in 6 cases with favourable effect. In 2 of these cases the effect was very pronounced, and remained for as much as 6 hours after injection. In the remaining cases it lasted 2–4 hours. Five patients were given PLT 101, resulting in 2 cases in remarkable improvement. Three patients received Lidocaine, in 1 instance with possible reducing effect. One patient was administered a high dose of Amobarbital, here also with a certain reducing effect.

Results of EMG registration

During testing of resistance to slow passive stretching of a muscle group, patients with rigidity displayed an appreciably increased amount of EMG registrable activity in the stretched muscle. In some patients this increase remained for a few seconds after cessation of the stretching movement (see Fig. 5).

The EMG registrations obtained thus objectified the appearance or absence of rigidity. The testing conditions, however, did not permit quantitative determination of the degree of rigidity with the aid of EMG registration, it having been impossible to perform the passive stretching movement with demonstrable constancy of speed or force. Estimations concerning the presence or absence of rigidity with the aid of EMG registration in no case showed any appreciable departure from the clinical picture.

The threshold value of the stretching reflex according to the method applied varied in spastic patients between 4 and 22 gcm. Normal values have not yet been published but should range according to our own experience between 30 and 80 gcm. Conjoined with the injection of preparations in spastic patients, it has frequently been possible to note a raising, even sometimes a doubling, of this level (see Fig. 6).

In 11 patients with spasticity receiving Chlormethiazole injections the threshold value before injection averaged 15 gcm, and after injection 20 gcm. In 10 of the 11 patients there appeared a raising of the threshold value of between 2 and 18 gcm, while in 1 patient it fell by 2 gcm. Statistical testing with sign test proved that this increase in the threshold value was significant.

In 10 spastic patients receiving Lidocaine injections the value before injection averaged 12.5 gcm, and after injection 12.7 gcm. In 4 patients there appeared a slight raising of the threshold value and in 4 patients a fall in the threshold value. Differences lay between 2 and 5 gcm. Thus, with Lidocaine injectiion, no change in the threshold value could be established.

In 9 patients injected with Amobarbital, 1 patient showed an increase in the threshold value from 16 to 60 gcm. In the rest of these 9, the average value before injections was 11.5 gcm, after injection 15 gcm. Statistical testing showed no significant difference ($0.05 < p < 0.10$).

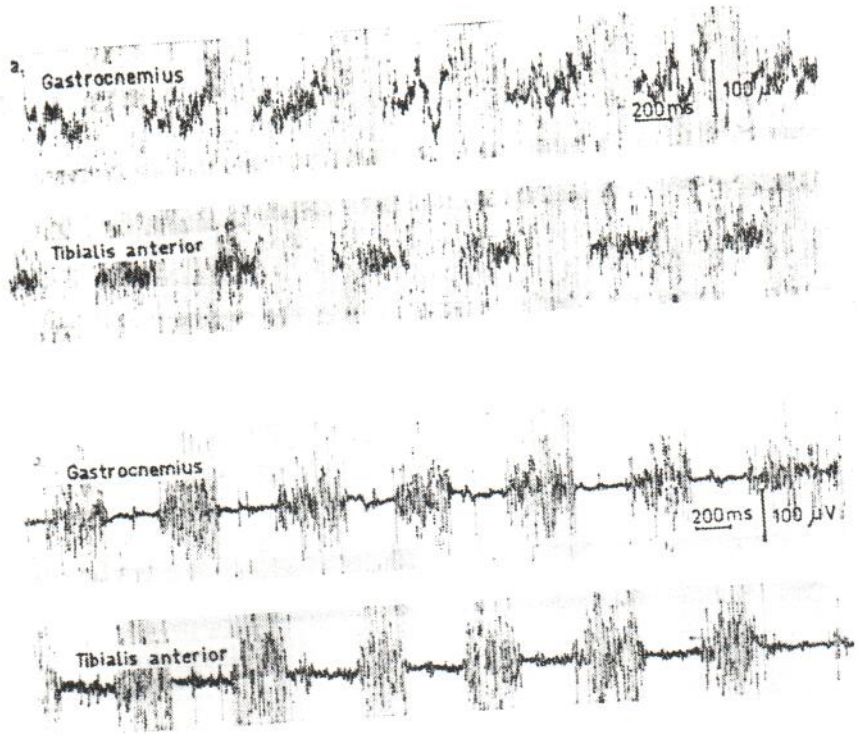

Fig. 7. Activity in the tibialis anterior and the gastrocnemius, registered with skin electrodes, during voluntary bending and stretching of the ankle-joint between extreme positions without loading, (*a*) before and (*b*) after injection of 60 ml Chlormethiazole. Before the injection a great deal of activity was noted in the antagonist muscles, this almost entirely disappearing after injection. Parallel with this, a good deal less activity was needed to bring about movement, which also was performed with appreciably greater speed after injection than before it.

Two patients with only rigidity displayed a threshold value of 40 gcm before injection. This level was thus substantially different from that displayed during examination by patients with spasticity. No appreciable change of level could be shown on injection of Chlormethiazole, Lidocaine or Amobarbital.

Patients' capacity for voluntary movements both before and after injection could well be displayed with the aid of EMG registration. In patients with rigidity as the dominating symptom a great increase in the activity also of the antagonist musculature could be noted at a voluntary movement. Following injection, especially of Chlormethiazole, there appeared a partial or complete cessation of activity in the antagonist musculature during the intended motion. It could be registered here how movements within a constant scope could be performed more rapidly after injection (see Fig. 7).

Spontaneous activity during examinations appeared partly in the form of more or less frequent involuntary spasms and partly in the form of a general increase in tone of the musculature. Flexion spasms and more continuous involuntary activity appeared frequently to have been reduced in extent on examination following the injection of preparations, especially Chlormethiazole (see Fig. 8). On account of the possibilities of spontaneous variations occurring (irritation of having to lie still for a long time, physic acclimatisation etc.), we made no attempt to record numerical values of such variations as came about.

We were not able to observe any change in the tremor accompanying the Parkinson syndrome, wether as to amount or as to frequency, following injection of any of the preparations.

Registration of muscular activity in the tibialis and gastrocnemius muscles in connection with painful stimulation of the lateral edge of the foot shows no important changes in amount, duration or latency period after completion of injection as compared with previously, in the spastic patients.

Registrations of clonus objectified clinical findings. In cases where the clonus remained following

Fig. 8. Spontaneous activity in the quadriceps, registered with electrodes, (*a*) before and (*b*) after injection of 60 ml of Chlormethiazole. The sections shown are representative of 20–30 min registration before and after injection.

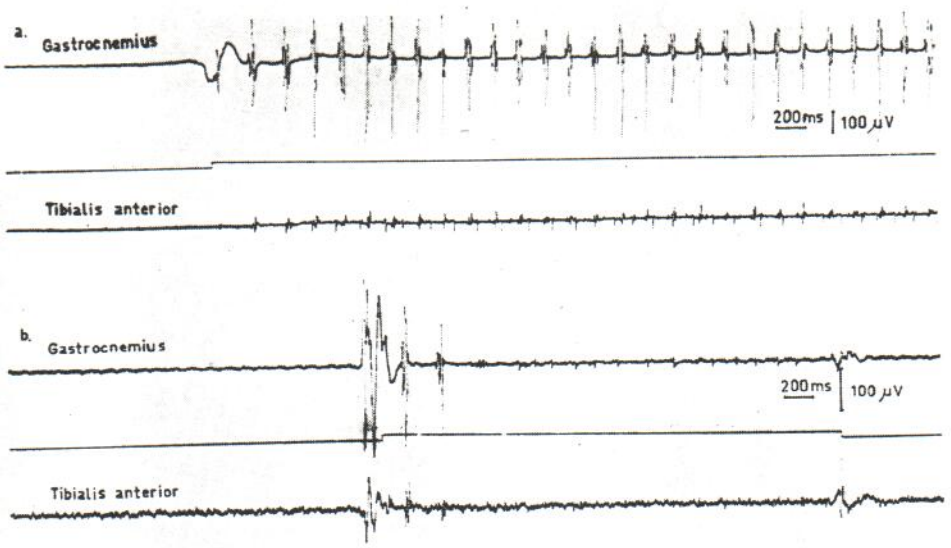

Fig. 9. Activity on application of skin electrodes during elicitation of clonus of the calf (*a*) before and (*b*) after injection of 60 ml of Chlormethiazole. Before injection an inexhaustible clonus was obtained without difficulty. After injection the most it was possible to elicit after repeated attempts was 2 consecutive contractions.

injection, there was no change either as to frequency or as to character (see Fig. 9).

Side-effects

One injection with Lidocaine and one injection with PLT 101 induced reduction in blood pressure of such an order as to compel the breaking off of the rest. Both these patients received Chlormethiazole injections without troublesome effects. Otherwise, less important side-effects were noted. In the case of Chlormethiazole they took the form of irritations, notably in the conjunctiva and the nasal mucous membrane, and in sporadic attacks of sneezing and coughing. Injections with Lidocaine brought feelings of swinging and giddiness and sporadic buzzing in the ears. Amobarbital, apart from drowsiness, brought no important changes.

DISCUSSION

Chlormethiazole has during recent years come more and more into use clinically on account of its anticonvulsant properties. This preparation has been shown also to posses inhibiting effects on other events within the central nervous system. It is sedative and hypnotic, with an inhibiting effect upon the respiratory centre and the thermoregulator centres as well as upon the vomiting centre (5). It can also, in cats and rats, reduce or suppress evoked cortical potentials (15, 16). It can also counteract chloral-induced hyperreflexia in dogs, block polysynaptic reflexes in dogs and block polysynaptic reflexes in decerebrated rats (14). Chlormethiazole has on the other hand no neuromuscular blocking effect.

In these tests it has been shown, among patients with clinical symptoms of spasticity and/or rigidity of different geneses, that the intravenous injection of Chlormethiazole in quantities not sufficient to have any appreciable effect upon the patient's degree of awakeness has a definite reducing effect upon pathologically increased muscular activity. EMG registration of this effect has shown reduction of spontaneous activity through rest and a reduction in muscular response through slow passive stretching. We have furthermore been able to show a significant raising of the threshold for pathologically exaggerative tendon reflexes following injection of Chlormethiazole. These changes could be demonstrated both in patients with purely cerebral lesions and in patients with spinal lesions, including advanced, of transverse type such as have led to total disappearance of voluntary activity and sensitivity below the level of the lesion. No difference was shown in degree of effect as between these two patient groups (see Fig. 10).

There is thus a reduction of pathologically increased reflexes, both poly- and monosynaptic, without corresponding inhibition of the voluntary motor system. On the other hand, in 2 patients with only rigidity and normally elicitable quadriceps reflex, there was no change in the reflex threshold value following Chlormethiazole injection. The action of the preparation in regard to effect on spasticity can thus be regarded as a

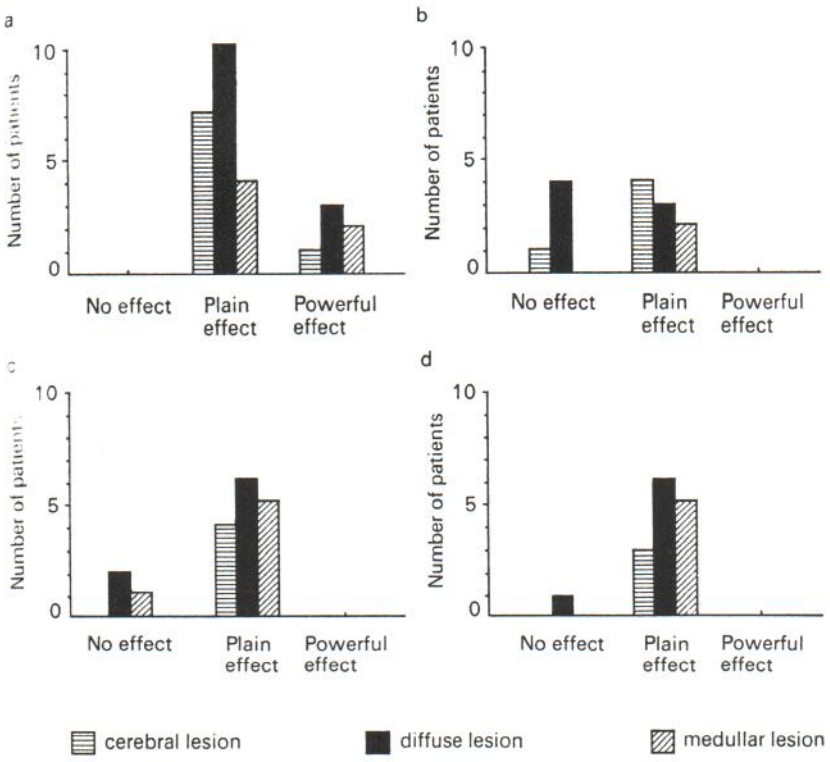

Fig. 10. Comparative distribution in patients with cerebral and spinal lesions respectively of the effects of different preparations upon rigidity: (*a*) Chlormethiazole, (*b*) Lidocaine, (*c*) Amobarbital and (*d*) PLT 101. Differences are inappreciable.

reduction of the pathological raised gamma system activity, in which, to judge from the positive results at the examination of patients with advanced or possibly total spinal transverse lesion, part of the effect described can take place at spinal or periferal level.

Rigidity, in animals, has been described as assuming two entirely different forms: alpha rigidity and gamma rigidity (7). It would naturally therefore be of interest to put Chlormethiazole to animal tests to discover differential effect on these two types of rigidity. In man, there is at present no possibility of studying such a differentiation, as methods used in animal experiments cannot be adapted to clinical use, and the two types of rigidity cannot therefore at present be established in homo.

Because of the importance of this area of investigation in the course of years a number of methods have been tried to bring about decreased spasticity and rigidity. Among these, for instance, have been: neuro-muscular blocking preparations such as curare; cryotherapy, possibly with blocking effect on the muscle spindles and the dermal receptors (9, 13); phenol blocking of the peripheral nerves and intrathecal (11, 18) muscular vibration (8); as well as various preparations with inhibitory effects upon the polysynaptic reflexes (for summary see Pedersen (17)). In the last of these groups Chlormethiazole can be included, the reducing effect of which upon spontaneous spasms together with improved capacity for movement—resulting from decreased rigidity and spasticity without corresponding change in voluntarily generated activity—can justify its clinical use at least for provisional purposes.

Usually desirable, in the case of the patients here concerned, is a training up of the performance capacity of the voluntary muscles. In this form of therapy there is always the possibility that the increase in the muscular strength might bring with it a troublesome increase both in rigidity and in spasticity. Besides which the training up itself could be appreciably hampered by involuntary spasms and rigidity. These arguments considered, it could be of great interest to perform a study accompanied by training of spastic musculature over a period of one to two hours during which the spasticity and the rigidity induced for instance by Chlormethiazole were reduced or brought down to a minimum. Such a study is now actually going on.

The results we have obtained from the testing of the effect on spasticity and rigidity of Amobarbital injected intravenously do not differ qualitatively from the results obtained with Chlormethiazole. There appears however to be a quantitative difference in the sense that, with the use in

each case of injection quantities determined by onset of drowsiness, there is a tendency for Chlormethiazole to have a better effect on rigidity and spasticity than Amobarbital. This tendency is most marked in the test of pathological raised tendon reflexes. Chlormethiazole brought here a significant raise of threshold values, which was not the case with Amobarbital. With regard particularly to the difficulty of determining grades of drowsiness, but also with regard to differences between injection volumes per minute and injection speeds in terms of mg/min, no difference between Amobarbital and Chlormethiazole could be found, such as could be substantiated by evidence.

The results we obtained in the case of Amobarbital can well correspond with earlier animal tests in which it was found that barbiturates have an inhibitory effect on the patellar reflex (10, 21) as well as with the marked hypnotic effects found by other authors (2, 12) which accompany dosages of such an amount as to induce obvious changes in spasticity.

Our tests with Lidocaine intravenously showed no effect upon the patellar reflex. Parallelly, the effect on spasticity was extraordinarily slight. This result corresponds well with the unimportance, previously established, of the effect of this preparation on mono- and polysynaptic reflexes (3). On the other hand, in a number of patients it was shown to have a reducing effect upon muscular resistance to slow passive stretching. This result may possibly be a consequence of the great reduction, testified by the above authors, of the cortical facilitating effect on the spinal motor neurone.

While all patients examined displayed reduced rigidity on injection of Chlormethiazole, injection of Lidocaine evinced effects in some cases and no effect in others. No tendency towards differentiation of effect could be found with Lidocaine in a division of patients into those with purely cerebral lesions and those with purely medullary.

Our reasoning as above concerning Chlormethiazole should apply also to PLT 101, as in this investigation we were unable to find any difference between the two preparations, whether qualitatively or quantitatively.

SUMMARY

The occurrence of reducing effects upon spasticity and rigidity was studied in 33 patients, in each of whom was tested one or more of the following preparations: Chlormethiazole, Lidocaine, Amobarbital and PLT 101 (a preparation related on Chlormethiazole) in intravenous injection. All preparations were shown to have a reducing effect on rigidity. Chlormethiazole, Amobarbital and PLT 101 also had reducing effect on spasticity.

Also performed was a comparison between the effects of different preparations tested, in pairs, upon the same patient. It could be evinced here that Chlormethiazole, given in a quantity sufficient to induce perceptible drowsiness, had a significantly better reducing effect on rigidity than Lidocaine given in standard dosage. Comparison with Amobarbital, also given in a dosage to bring about incipient drowsiness, showed that Chlormethiazole had possibly the better effect on rigidity ($p = 0.06$). As to effect on rigidity, no certain difference between Chlormethiazole and PLT 101, given similarly as to dosage and to injection speed, could be shown. In spasticity, no difference appeared between the effects of Chlormethiazole, Amobarbital and PLT 101. Results are discussed in respect to differences between injection volume and injection speed.

An objectification of changes in the threshold for the elicitation of stretching reflex was performed. A significant increase could be shown here in spastic patients following injection of Chlormethiazole, in non-spastic patients no change in threshold values could be demonstrated. Injection with Lidocaine produced no change at all. No significant difference was shown with Amobarbital ($0.05 < p < 0.10$).

Parallelly with reduction of involuntary activity, improvement in voluntary movement capacity was received. It should be possible to make clinical use of this effect, for instance in the training up of spastic and rigid patients in whom involuntary activities are in sufficient amount to block or to impede seriously the motions desired.

ACKNOWLEDGEMENTS

This investigation has been supported by grants from the Swedish Medical Research Council and the Astra Pharmaceutical Company.

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Key words: Electromyography; muscle relaxants; spasm.

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