EFFECTS OF AMINOBENZYL PENICILLIN(AB-PC), METHYLCHLOROPHENYL ISOXAZOLYL PENICILLIN (MCI-PC), AND 6-AMINOPENICILLANIC ACID (6-APA) ON THE CONTRACTILE RESPONSE OF GUINEA-PIG GALL BLADDER

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(Received July 5, 1983)

The present study was undertaken to investigate the effects of aminobenzyl penicillin (AB-PC), methylchlorophenyl isoxazolyl penicillin (MCI-PC), and 6-aminopenicillanic acid (6-APA) on the contractile response of guinea-pig gall bladder. Both AB-PC and MCI-PC remarkably decreased the contractile response induced by transmural electrical stimulation. 6-APA also reduced it, while its effect was of short duration. Neither AB-PC nor 6-APA affected the contractile response to exogenous acetylcholine, while MCI-PC remarkably reduced it. The reducing effect of MCI-PC is greater on the intramural electrical stimulation-induced contractile response than it is on the exogenous acetylcholine-induced contractile response. By the addition of AB-PC, the spontaneous contractile response of the tissue was enhanced phasically and then it disappeared with rapid lowering of the tonus level of the tissue. By the addition of MCI-PC, the tonus level in the spontaneous contractile response of the tissue decreased immediately, and then it increased with a so-called contracture-like response. In such a phenomena, the spontaneous contractile response of the tissue was not observed. Moreover, by the addition of 6-APA, the lowering of the tonus level of the tissue was caused promptly and the spontaneous contractile response was prevented completely. It appeared again, however, soon after with immediate recovering of the tonus level of the tissue. The effects of AB-PC, MCI-PC, and 6-APA on the spontaneous contractile response of the tissue mentioned above were also observed in the presence of tetrodotoxin. While the inhibitory effect on the spontaneous contractile response of the tissue and the remarkable change in the tonus level of the tissue induced by the addition of both AB-PC and MCI-PC were restored immediately by washing with normal Krebs solution, the reducing effect of these drugs on the transmural electrical stimulation-induced contractile response was not necessarily recovered immediately. From these results, the conclusion comes as follows: 1)AB-PC may affect not only on the muscle but also on the intramural cholinergic nerves. 2) MCI-PC may affect on the muscle, but its effect on the intramural nerves is also not likely to be negligible. 3) 6-APA may affect mainly on the muscle.

INTRODUCTION

ARATANI et al[1] reported that aminobenzyl penicillin (AB-PC) reduced the spontaneous contractile response of guinea-pig intestine and the blood pressure of a rabbit. They[2] also reported that methylchlorophenyl isoxazolyl penicillin (MCI-PC) diminished the spontaneous contractile response of rabbit intestine and the blood pressure of a rabbit. We can not yet, however, see the reports concerning the effects of these penicillins on the other organs which have smooth muscle.

It is demonstrated that the excretion of these penicillins into bile is carried out in good condition[3,4]. The present study was undertaken to in-

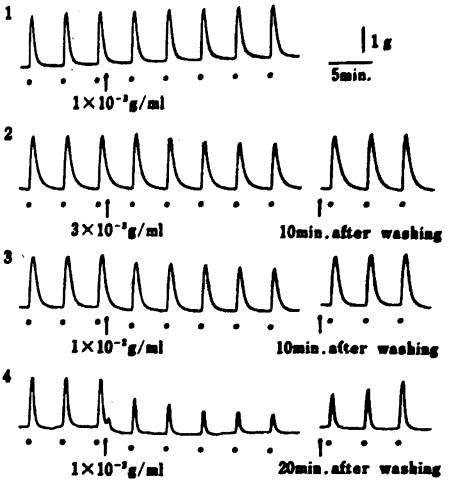
vestigate the effects of both AB-PC and MCI-PC on the contractile responses which were induced by both transmural electrical stimulation and exogenous acetylcholine, and which were induced spontaneously. The effects of 6-aminopenicillanic acid (6-APA), the basic structure of these penicillins, on these contractile responses were also investigated.

MATERIALS AND METHODS

Guinea-pigs (250-300 g) were killed by a blow on the head and exsanguinated. The gall bladder was removed and divided into two approximately equal parts, longitudinally. One of these pieces was used in an experiment. The preparation was mounted in an organ bath which was filled with Krebs solution. As described by YOSHIDA et al[5], the fundus of the gall bladder was fixed with pins and the cervix end was connected with a silk thread to a force transducer. The mechanical responses of the gall bladder were recorded isometrically under a load of 1 g. Two 5 mm×5 mm silver plates coated with silver chloride was used as stimulus electrodes. As described by YOSHIDA et al[5], the electrodes were placed, one on the serosal side and the other on the mucosal side of the tissue and connected to a stimulator. Tissue was stimulated transmurally with rectangular pulses (50 volt, 0.5 msec, 30 Hz) for a period of 10 sec at intervals of 4 minutes. Both contractile responses to transmural electrical stimulation and exogenous acetylcholine were observed in 27℃ Krebs solution in order to prevent the appearance of spontaneous contractile response of the tissue. Observations relating to the spontaneous contractile response of the tissue was performed in 37℃ Krebs solution. The preparation was bathed in a Krebs solution which has the following composition (mM) : 133.5 NaCl, 4.7 KCl, 2.5 $CaCl_2$, 0.1 $MgCl_2$, 1.4 NaH_2PO_4, 16.3 $NaHCO_3$ and 7.8 glucose, perfused with 95% O_2 + 5% CO_2, pH 7.4.

The used drugs were : aminobenzyl penicillin Na salt (AB-PC), 1×10^{-4}g/ml-1×10^{-2}g/ml ; methylchlorophenyl isoxazolyl penicillin Na salt (MCI-PC), 1×10^{-4}g/ml-1×10^{-2}g/ml ; 6-aminopenicillanic acid Na salt (6-APA), 1×10^{-5}g/ml-3×10^{-3} g/ml ; tetrodotoxin, 1×10^{-7}g/ml ; acetylcholine chloride, 1×10^{-7}g/ml ; atropine sulfate, 1×10^{-6} g/ml. The concentrations indicate the final values in the organ bath. The concentrations of AB-PC and MCI-PC indicate the values which were converted to the potencies of antibiotic substances.

Fig. 1 Effects of aminobenzyl penicillin (AB-PC) on the transmural electrical stimulation-induced contractile response.
1-4 : effects of AB-PC (1×10^{-3}g/ml-1×10^{-2}g/ml). Each right side tracing of 2-4 shows the phenomenon after washing with normal Krebs solution. In all tracings, stimuli applied dots beneath each tracing.



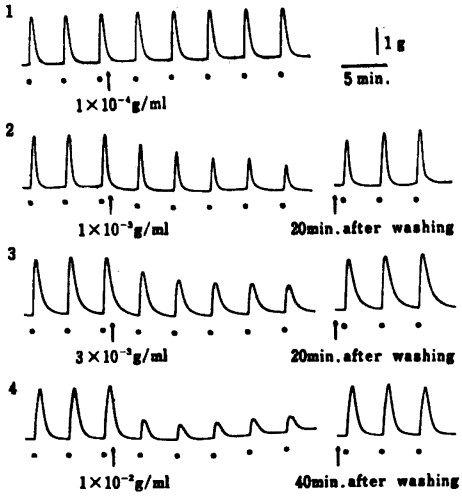
RESULTS

Effects of AB-PC, MCI-PC, and 6-APA on the Contractile Response Induced by Transmural Electrical Stimulation.

AB-PC (1×10^{-3}g/ml) did not affect the contractile response to transmural electrical stimulation (Fig. 1-1). AB-PC (3×10^{-3}g/ml) diminished it slightly (Fig. 1-2). AB-PC (1×10^{-2}g/ml) slightly reduced the tonus level of the tissue with decreasing the contractile response to transmural electrical stimulation. AB-PC, however, at this concentration remarkably reduced the contractile response to transmural electrical stimulation in three cases and showed only a very slight effect in three others (Fig. 1-3, 4). As shown in Fig. 1-4, the small phasic contraction was induced immediately after addition of AB-PC (1×10^{-2}g/ml) in two cases. It was not observed in four other trials. The effects of AB-PC on the contractile response and the tonus level of the tissue as mentioned above were recovered by washing with normal Krebs solution for 10 to 20 minutes (Fig. 1-2, 3, 4).

MCI-PC (1×10^{-4}g/ml) had almost no effect on the contractile response to transmural electrical stimulation (Fig. 2-1). MCI-PC (1×10^{-3}g/ml and

Fig. 2 Effects of methylchlorophenyl isoxazolyl penicillin (MCI-PC) on the transmural electrical stimulation-induced contractile response.
1-4 : effects of MCI-PC (1×10^{-4} mg/ml-1×10^{-2}g/ml). Each right side tracing of 2-4 shows the phenomenon after washing with normal Krebs solution. In all tracings, stimuli applied at dots beneath each tracing.



3×10^{-3}g/ml) remarkably reduced the transmural electrical stimulation-induced contractile response and slightly reduced the tonus level of the tissue (Fig. 2-2, 3). As shown in Fig. 2-4, MCI-PC (1×10^{-2}g/ml) reduced still harder the contractile response to transmural electrical stimulation and slightly increased the tonus level of the tissue. These phenomena induced by MCI-PC were restored by washing with normal Krebs solution for 20 to 40 minutes (Fig. 2-2, 3, 4).

6-APA (1×10^{-5}g/ml) had almost no effect on the contractile response to transmural electrical stimulation (Fig. 3-1). 6-APA (1×10^{-4}g/ml) slightly diminished the transmural electrical stimulation-induced contractile response, but this effect was of short duration (Fig. 3-2). 6-APA (1×10^{-3} g/ml and 3×10^{-3}g/ml) significantly diminished the contractile response induced by transmural electrical stimulation, while these effects were also of short duration (Fig. 3-3, 4). Moreover, the effect of 6-APA (1×10^{-2}g/ml) on the contractile response was not studied owing to the poor solubility of 6-APA.

When the amplitude of transmural electrical stimulation-induced contractile response before treatment of AB-PC, MCI-PC, and 6-APA in each concentration was taken as 100%, its

Fig. 3 Effects of 6-aminopenicillanic acid (6-APA) on the transmural electrical stimulation-induced contractile response.
1-4 : effects of 6-APA (1×10^{-5}g/ml-3×10^{-3}g/ml). In all tracings, stimuli applied at dots beneath each tracing.

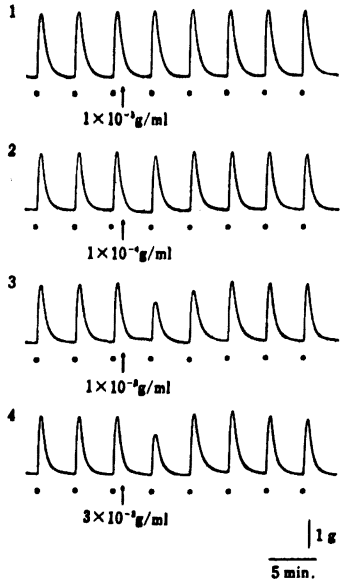
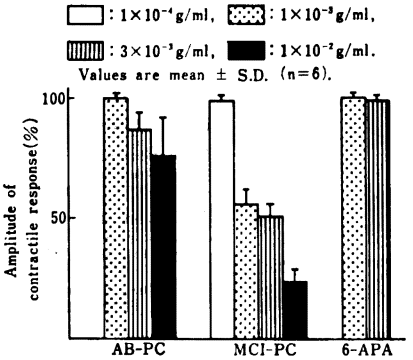


Fig. 4 Effects of aminobenzyl penicillin (AB-PC), methylchlorophenyl isoxazolyl penicillin (MCI-PC), and 6-aminopenicillanic acid (6-APA) on the transmural electrical stimulation-induced contractile response.
Each amplitude of transmural electrical stimulation-induced contractile response in the absence of AB-PC, MCI-PC, and 6-APA in each concentration was taken as 100%. Ordinate shows each amplitude of transmural electrical stimulation-induced contractile response at 15 min after addition of each agent which is registered as a relative contractile response of 100%.



amplitude after 15 min treatment of each drug in each concentration was registered as a relative contractile response of 100%. These results were observed as shown in Fig. 4. That is to say, the amplitude of transmural electrical stimulation-induced contractile response was 100±2% (n=6) in the presence of AB-PC (1×10^{-3}g/ml), namely almost equal to the value in its absence. It was reduced to 87±7% (n=6) in the presence of AB-PC (3×10^{-3}g/ml), and 76±16% (n=6) in the presence of AB-PC (1×10^{-2}g/ml). And also the amplitude of transmural electrical stimulation induced contractile response was 99±2% (n=6) in the presence of MCI-PC (1×10^{-4}g/ml), namely almost equal to the value in its absence. It was 56±6% (n=6) in the presence of MCI-PC (1×10^{-3}g/ml) and 51±5% (n=6) in the presence of MCI-PC (3×10^{-3}g/ml). And then it was 24±5% (n=6) in the presence of MCI-PC (1×10^{-2}g/ml). As shown in Fig. 4, the amplitude of the contractile response mediated by transmural electrical stimulation was 100±2% (n=6) in the presence of 6-APA (1×10^{-3}g/ml), and 99±2% (n=6) in the presence of 6-APA (3×10^{-3}g/ml). The two values were closely equal in the absence of 6-APA of the above concentration.

Effects of AB-PC, MCI-PC, and 6-APA on the Contractile Response Induced by Exogenous Acetylcholine (1×10^{-7}g/ml).

The exogenous acetylcholine (1×10^{-7}g/ml)-induced contractile response showed a following property. That is to say, the exogenous acetylcholine-induced contractile response was not affected by tetrodotoxin (1×10^{-7}g/ml), while it was remarkably inhibited by atropine (1×10^{-6}g/ml) (Fig. 5). Effects of AB-PC, MCI-PC, and 6-APA on the exogenous acetylcholine (1×10^{-7}g/ml)-induced contractile response showing such a property were observed as in Fig. 6 and 7.

AB-PC (3×10^{-3}g/ml and 1×10^{-2}g/ml) had almost

Fig. 5 Effects of tetrodotoxin and atropine on the exogenous acetylcholine (1×10^{-7}g/ml)-induced contractile response.

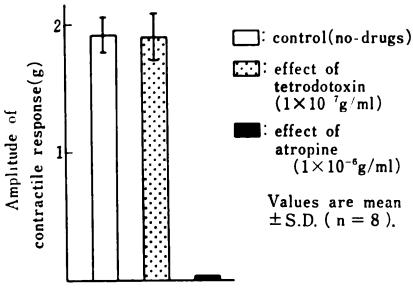


Fig. 6 Effects of aminobenzyl penicillin (AB-PC), methylchlorophenyl isoxazolyl penicillin (MCI-PC), and 6-aminopenicillanic acid (6-APA) on the exogenous acetylcholine (1×10^{-7}g/ml)-induced contractile response.

In all tracings, acetylcholine (1×10^{-7}g/ml) applied at a black triangle beneath each tracing. AB-PC, MCI-PC, and 6-APA in each concentration were given 15 min before addition of acetylcholine. Each left side tracing of 1-5 shows the contractile response in the absence of each agent, namely control. Each right side tracing of 1-5 shows the contractile response in the presence of each agent.

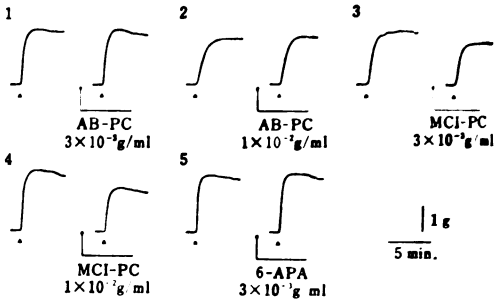
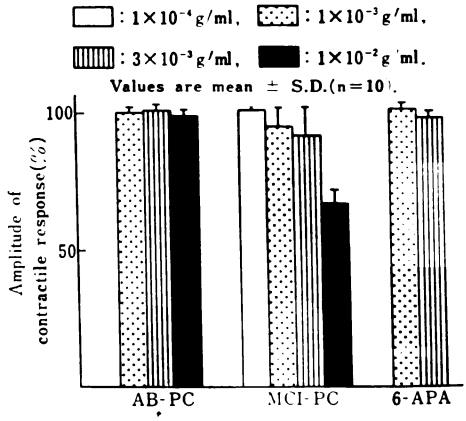


Fig. 7 Effects of aminobenzyl penicillin (AB-PC), methylchlorophenyl isoxazolyl penicillin (MCI-PC), and 6-aminopenicillanic acid (6-APA) on the exogenous acetylcholine (1×10^{-7}g/ml)-induced contractile response.

Each amplitude of exogenous acetylcholine-induced contractile response in the absence of AB-PC, MCI-PC, and 6-APA in each concentration was taken as 100%. Ordinate shows each amplitude of exogenous acetylcholine-induced contractile response at 15 min after addition of each agent which is registered as a relative contractile response of 100%.



no effect on the contractile response to exogenous acetylcholine (Fig. 6-1, 2., Fig. 7). MCI-PC (1×10^{-4} g/ml) had almost no effect on it (Fig. 7). MCI-PC (1×10^{-3}g/ml and 3×10^{-3}g/ml) had almost no effect on it in six cases and showed slight inhibitory effect in four others (Fig. 6-3). And MCI-PC (1×10^{-2}g/ml) decreased the contractile response induced by exogenous acetylcholine in all trials (Fig. 6-4). The amplitude of contractile response to exogenous acetylcholine in the presence of MCI-PC (1×10^{-3}g/ml) was eventually 87±7% (n=10) of the control measurement in its absence (Fig. 7). And also, in the presence of MCI-PC (3×10^{-3}g/ml), it was 82±10% (n=10) of the control measurement in its absence (Fig. 7). In the presence of MCI-PC (1×10^{-2}g/ml), it was reduced to 70±5% (n=10) of the control measurement in its absence (Fig. 7). Moreover, both 6-APA (1×10^{-3}g/ml and 3 ± 10^{-3}g/ml) did not affect the contractile response to exogenous acetylcholine (Fig. 6-5., Fig. 7).

Effects of AB-PC, MCI-PC, and 6-APA o the Spontaneous Contractile Response.

AB-PC (1×10^{-4}g/ml) had almost no effect on tl spontaneous contractile response of the tissue (Fi 8-1). By the addition of AB-PC (1×10^{-3}g/ml) the spontaneous contractile response of the tiss was enhanced phasically and then it disappear with a rapid lowering of the tonus level in tl spontaneous contractile response of the tissu while it appeared again soon after (Fig. 8-2). Tl same result was obtained by the addition of AB-P (3×10^{-3}g/ml) (Fig. 8-3). AB-PC (1×10^{-2}g/ml) sho ed close similarity to that described above, b it nearly prevented the spontaneous contracti response of the tissue (Fig. 8-4). The effect adding AB-PC (1×10^{-2}g/ml) in the presence tetrodotoxin (1×10^{-7}g/ml) was almost same as th observed by the addition of AB-PC (1×10^{-2}g/m in its absence (Fig. 8-4, 5). Effects of AB-PC me

Fig. 8 Effects of aminobenzyl penicillin (AB-PC) on the spontaneous contractile response of the tissue.
1–4 : effects of AB-PC (1×10^{-4}g/ml–1×10^{-3}g/ml).
5 : effect of AB-PC (1×10^{-3}g/ml) in the presence of tetrodotoxin (1×10^{-7}g/ml). Tetrodotoxin(TTX) which was indicated with an arrow was given 15 min before addition of AB-PC. Each right side tracing of 3–5 shows the phenomenon after washing with normal Krebs solution. In all tracings, AB-PC added at an arrow beneath each tracing.

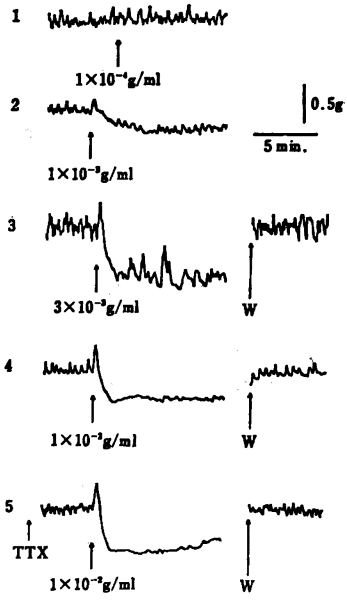


Fig. 9 Effects of methylchlorophenyl isoxazol penicillin (MCI-PC) on the spontaneous co tractile response of the tissue.
1–4 : effects of MCI-PC (1×10^{-4}g/ml–1×10^{-3}g/ml
5 : effect of MCI-PC (1×10^{-3}g/ml) in the pr sence of tetrodotoxin (1×10^{-7}g/ml). Tetrodotox (TTX) which was indicated with an arrow w given 10 min before addition of MCI-PC. Ea right side tracing of 3–5 shows the phenomen after washing with normal Krebs solution. In a tracing, MCI-PC added an arrow beneath ea tracing.

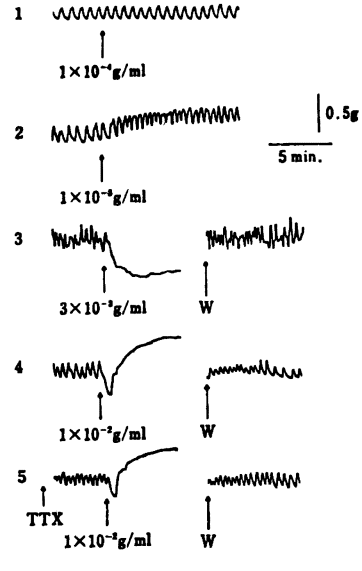
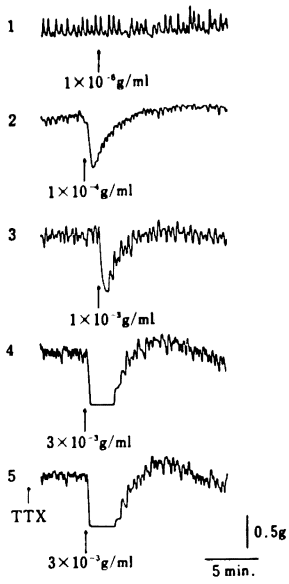


Fig. 10 Effects of 6-aminopenicillanic acid(6-APA) on the spontaneous contractile response of the tissue.
1-4 : effects of 6-APA (1×10^{-5}g/ml-3×10^{-3}g/ml).
5 : effect of 6-APA (3×10^{-3}g/ml) in the presence of tetrodotoxin (1×10^{-7}g/ml). Tetrodotoxin (TTX) which was indicated with an arrow was given 10 min before addition of 6-APA. In all tracings, 6 APA added at an arrow beneath each tracing.



tioned were recovered immediately by washing with normal Krebs solution (Fig. 8-3, 4, 5).

MCI-PC (1×10^{-4}g/ml) had almost no effect on the spontaneous contractile response of the tissue (Fig. 9-1). Following addition of MCI-PC (1×10^{-3} g/ml), the frequency of spontaneous contractile response of the tissue increased with raise of the tonus level of the tissue (Fig. 9-2). By the addition of MCI-PC (3×10^{-3}g/ml), the spontaneous contractile response of the tissue was prevented with rapid lowering of the tonus level of the tissue, while it was recovered immediately by washing with normal Krebs solution (Fig. 9-3). By the addition of MCI-PC (1×10^{-2}g/ml), the tonus level in the spontaneous contractile response of the tissue was decreased immediately, and then it was increased gradually with a so-called contracture-like response (Fig. 9-4). As shown in Fig. 9-5, these results produced by MCI-PC (1×10^{-2}g/ml) were also observed by its addition in the presence of tetrodotoxin (1×10^{-7}g/ml). Then, effects of MCI-PC on the spontaneous contractile response of the tissue were restored immediately by washing with normal Krebs solution (Fig. 9-3, 4, 5).

6-APA (1×10^{-5}g/ml) had almost no effect on the spontaneous contractile response of the tissue (Fig. 10-1). As shown in Fig. 10-2, 3, following the addition of 6-APA (1×10^{-4}g/ml and 1×10^{-3}g/ml), the lowering of the tonus level of the tissue was caused promptly and the spontaneous contractile response was prevented completely. But, it appeared again soon after with immediate recovering of the tonus level of the tissue. 6-APA (3×10^{-3} g/ml) showed close similarity to that described above (Fig. 10-4). There was a little difference, however, from the change in tonus level of the tissue, namely the tonus level of the tissue was rapidly decreased by the addition of 6-APA (3×10^{-3}g/ml) and then it was immediately increased over the state before its addition. After that, it tends to decrease gradually (Fig. 10-4). As shown in Fig. 10-5, the same view was demonstrated by the addition of 6-APA (3×10^{-3}g/ml) in the presence of tetrodotoxin (1×10^{-7}g/ml).

DISCUSSION

Using the same stimulus condition as described in the present study, YOSHIDA et al[5] reported a contractile response induced by transmural electrical stimulation. This contractile response was inhibited by atropine (1×10^{-6}g/ml) and tetrodotoxin (1×10^{-7} g/ml), enhanced by physostigmine (1×10^{-7}g/ml), and was unaffected by guanethidine (1×10^{-6}g/ml). Consequently, they suggested that the transmural electrical stimulation-induced contractile response was mediated by intramural cholinergic excitatory nerves, that is, it may be induced by release of acetylcholine from the ending of intramural cholinergic nerves. And also the same view was demonstrated by LEE et al[6]. On the other hand, the exogenous acetylcholine-induced contractile response was unaffected by tetrodotoxin (1×10^{-7}g/ml), while it was inhibited by atropine (1×10^{-6}g/ml) (Fig. 4). It thus can be considered that this contractile response is induced by the action of acetylcholine to the muscle, regardless of intramural nerves.

AB-PC (1×10^{-3}g/ml) had almost no effect on the transmural electrical stimulation-induced contractile response, while AB-PC (3×10^{-3}g/ml and 1×10^{-2}g/ml) reduced it respectively (Fig. 1, 4). The exogenous acetylcholine-induced contractile response was almost unaffected by the addition of

AB-PC (1×10^{-3}g/ml, 3×10^{-3}g/ml, and 1×10^{-2}g/ml) (Fig. 6, 7). Therefore, these results suggest that the reducing effect of AB-PC on the transmural electrical stimulation-induced contractile response is mediated by the action of AB-PC on the intramural cholinergic nerves. MCI-PC reduced both of intramural electrical stimulation-induced contractile response and exogenous acetylcholine-induced contractile response (Fig. 2, 4, 6, 7). This reducing effect was greater on the former contractile response than on the latter contractile response (Fig. 4, 7). These results alone are, however, based on the failure to estimate whether MCI-PC acts on the muscle in the gall bladder wall, the intramural nerves or both of them. The transmural electrical stimulation-induced contractile response was decreased by the treatment of 6-APA, while the decreasing effect of 6-APA was of short duration (Fig. 3). After 15 min treatment of 6-APA, both of transmural electrical stimulation-induced contractile response and exogenous acetylcholine-induced contractile response were unaffected by 6-APA (Fig. 4, 7). Since the decreasing effect of 6-APA on the transmural electrical stimulation-induced contractile response which was of short duration was not investigated at this time, it can not be discussed here. 6-APA, however, may have little effect on both intramural nerves and muscle in the gall bladder wall 15 min after the treatment of 6-APA.

By the addition of AB-PC, MCI-PC, and 6-APA, the spontaneous contractile response of the tissue was affected with the remarkable change of the tonus level of the tissue as shown in Fig. 8, 9, 10. In particular, by the addition of AB-PC (1×10^{-2} g/ml), the spontaneous contractile response was enhanced and then it was prevented with a lowering of the tonus level of the tissue (Fig. 8). And also, it was almost prevented with a lowering of the tonus level of the tissue by the addition of MCI-PC (3×10^{-3}g/ml) and was almost abolished with a shifting to the contractile response like a contracture after rapid lowering of the tonus level of the tissue by the treatment of MCI-PC (1×10^{-2}g/ml) (Fig. 9). Moreover, the spontaneous contractile response of the tissue was immediately inhibited with a rapid lowering of the tonus level of the tissue by the addition of 6-APA (1×10^{-3}g/ml and 3×10^{-3}g/ml), while it appeared again soon after (Fig. 10). These results were also obtained in the presence of tetrodotoxin (Fig. 8, 9, 10). Therefore, it is possible that each phenomenon which is induced by each adding of AB-PC (1×10^{-3}g/ml), MCI-PC (1×10^{-3}g/ml), and 6-APA (3×10^{-3}g/ml) may be mediated by each of their action on the muscle in the gall bladder wall, and not on the intramural nerves. In addition, the manner of the action of AB-PC, MCI-PC, and 6-APA on the spontaneous contractile response of the tissue differs from one another as mentioned above. It thus seems likely that the mechanism of their action on the muscle differs from one another. We can not yet explain these differences. Analysis on these differences will be reported in the near future.

Moreover, in 37℃ Krebs solution, the remarkable change of the tonus level of the tissue was observed by the addition of AB-PC, MCI-PC, and 6-APA (Fig. 8, 9, 10). On the other hand, in 27℃ Krebs solution, such a remarkable change of the tonus level of the tissue was not observed by the addition of these drugs (Fig. 1, 2, 3). Thus, the effects of these drugs on the tonus level of the tissue may depend on the temperature.

The inhibitory effect to the spontaneous contractile response and the remarkable change of the tonus level of the tissue which are considered to be induced by the action of AB-PC (1×10^{-2} g/ml) and MCI-PC (1×10^{-2}g/ml) on the muscle as mentioned previously were restored immediately by washing with normal Krebs solution (Fig. 8, 9), while the reducing effects of these drugs on the transmural electrical stimulation-induced contractile response were not restored immediately by washing with normal Krebs solution. That is to say, the reducing effect induced by AB-PC (1×10^{-2} g/ml) was recovered by washing within approximate 10-30 min with normal Krebs solution, and that by MCI-PC (1×10^{-2}g/ml) was recovered by washing with approximate 40 min with normal Krebs solution (Fig. 1, 2). Thus, these results may support that both AB-PC and MCI-PC act on the muscle in the gall bladder wall but also on the intramural nerves. When either of AB-PC or MCI-PC was given to man per oral administration at a dosage of 500 mg, namely at a clinical dosage, the concentration of each drug in the blood was observed by several investigators[7-10]. That is to say, the highest concentration of AB-PC in the blood was 4.4 μg/ml (ICHIKAWA et al)[7] and 3.4 μg/ml (HIGUCHI et al)[8]. And also that of MCI-PC in

the blood was 4.64 μg/ml (SHIODA et al)[9] and 3.0-3.5 μg/ml (ŌKUBO et al)[10]. The concentrations of these drugs in the blood were remarkably lower than those used in our study. As shown in our study, AB-PC, MCI-PC, and 6-APA at low concentration had almost no effect on the contractile response of the tissue, but these drugs at high concentration, although there were few exceptional cases, had effect on it remarkably. This result is compatible with the observations of ARATANI et al[1,2]. ARATANI et al[1] suggested that AB-PC showed cholinergic action to the organ which has smooth muscle. ARATANI et al[2], again, suggested that MCI-PC acted mainly paralytically on that organ, but its cholinergic action to that organ was also not likely to be negligible. In the present study, such a cholinergic action of these drugs was not observed. The conclusion comes as follows: 1) AB-PC may affect not only on the muscle but also on the intramural cholinergic nerves. 2) MCI-PC may affect on the muscle, but its effect on the intramural nerves is also not likely to be negligible at this time. 3) 6-APA may affect mainly on the muscle.

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モルモット胆のうの収縮に及ぼす aminobenzyl penicillin(AB-PC), methylchlorophenyl isoxazolyl penicillin (MCI-PC), 及び 6-aminopenicillanic acid (6-APA) の影響

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モルモット摘出胆のうの収縮反応に及ぼす aminobenzyl penicillin (AB-PC), methylchlorophenyl isoxazolyl penicillin (MCI-PC), 及び 6-aminopenicillanic acid (6-APA) の影響について検討した。

経壁電気刺激により誘発される収縮反応に対し AB-PC 及び MCI-PC は, 抑制的に作用した。6-APA もまた, それを抑制したが一過性であった。外来性 acetylcholine により誘発される収縮反応に対して AB-PC 及び 6-APA は, ほとんど影響を与えなかったが, MCI-PC は抑制的に作用した。MCI-PC の抑制作用は, 外来性 acetylcholine により誘発される収縮反応に対するよりも, 経壁刺激により誘発される収縮反応に対して著しかった。自動運動に対し AB-PC は, 一過性に運動を亢進させた後, tonus の低下と共に自動運動の消失を来たした。MCI-PC を作用させると tonus の低下を来たした後, 拘縮様の収縮反応に移行し, 自動運動は消失した。さらに 6-APA を作用させると, tonus の低下を来たし, 自動運動は消失したが, 一過性であった。上述の自動運動に及ぼす3薬物の影響は, tetrodotoxin 存在下でも同様に観察された。これらの成績より, 1) AB-PC は, 筋及び壁内 cholinergic nerves の両者に対して作用を及ぼすものと思われる。2) MCI-PC は, 筋に対して作用を及ぼすが, 壁内神経に対する作用も無視できないように思われる。3) 6-APA は, 主として筋に対して作用を及ぼすものと思われる。