Pharmacoradiography of the digestive tract
The effect of Bethanechol Chloride (Carbamylmethylcholine chloride) on the x-ray picture of the stomach and duodenal bulb

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消化管の薬理 X 線検査法
塩化ベサネコールの胃・十二指腸に及ぼす影響

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消化管の薬理X線検査法に塩化ベサネコールを応用し，胃・十二指腸に及ぼす影響を検討した結果秀れた効果を認めた．

X線学的には，胃の緊張，蠕動が昂進し，排出は促進され，又十二指腸球部の充満が良好となる．モルフィン，イミダリン，ワゴスチグミンの効果と比較検討を行ない，モルフインと略々同様で，イミダリン，ワゴスチグミンより優れた成績を得た．なお胃・十二指腸に対してブスコパンとは全く対照的な影響を与えた．診断上興味のあるX線写真を数例供覧した．筋肉内注射量は 1.5mg～2.5mgで必要かつ充分で重篤な副作用は経験しなかつた．

次で本剤経口投与により，胃下垂症及び慢性胃炎患者の治療を試み，自覚症状に対する効果を検討し満足すべき成績を得た．1日投与量はベサコリン末として 0.4～0.6 g で充分であつた．

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Content

Introduction

What is important in pharmacoradiography of the digestive tract is to get the most suitable medicament. The requirements should be as follows:

i) the effectiveness, ii) simplicity of application, iii) lack of side actions, iv) the induction of enough functional changes with small dosis in a short time, which could be determined radiologically and v) its economy.

The pharmacoradiography[1)2)3)] has been described in the text book of medical radiology, but it has not been generalized because of the difficulty of obtaining suitable medicament.

The medicaments which have been described are Morphine, Physostigmine, Insuline, Pilocarpine, Prostigmine etc. as stimulants of tone and peristalsis and Atropine, Adrenaline, Papaverine as spasmolytics[4)].

The pharmacoradiography or psychoradiography has been studied with our experience on 500 cases and reported by us since 1953[6)7)8)9)10)11)]. The Usefulness of Hyoscin-N-Butylbromide as spasmolytic on gastroduodenal deformities caused by hypertonus, partial or total spasm has been reported[8)9)]; on the other hand, the effectiveness of Morphine as stimulant on the hypotonic or atonic stomach and duodenum has been emphasized comparing with that of Vagostigmine and Imidaline[7)10)]. Although in daily diagnostic practice, the aim of our procedure has been the employment of spasmolytics for the hypertonic cases and the application of stimulants for the hypotonic cases, the majority of the differenciation has been practically for those cases with increased tonus of the wall of digestive tract, so that the spasmolytics have been more frequently applied.

From another point of view, the active change of the condition might be aimed at

essentially without considering the indication. It is essential in diagnostic radiology of the digestive tract to observe more widely and more deeply, changing its dimension, i.e., space, time and physiology. Pharmacoradiography is very important as one of such procedures.

Studying the pharmacoradiography with Morphine, Imidaline, Vagostigmine and Buscopan, Yamagishi concluded that more suitable medicament for pharmacoradiography is expected, since the progress of drugs is remarkable with the advancement of modern medicine[10]. He related to the effectiveness of Buscopan as spasmolytic for routine use in daily fluoroscopic room, and he found that Morphine was most effective as stimulant, which was very suitable for pharmacoradiography as many reports in foreign countries[4)12)]. Morphine is, however, restricted to be applied daily in our country, so its substitute as stimulant has been demanded.

Acetylcholine has not been applied to human body as stimulant of parasympathic nerve, because it is destructed by cholinesterase.

On the other hand, Major synthesized Bethanechol chloride with the suggestion of Sirmonart in 1935, which is stable against cholinesterase, safe for circulatory system with usual dosis, having stimulating action on digestive tracts.

As it was manufactured in Japan, the application to pharmacoradiography, especially the effect on x-ray picture of the stomach and duodenum has been studied. Because of its daily use in fluoroscopic room, about 1/3～1/2 of usual dosis in U.S. Pharmacopoeia XV, N.N.D. (1959) has been applied to pharmacoradiography with sufficient effect on x-ray picture of the stomach and duodenum.

As for the application of Bethanechol chloride to diseases of digestive organ, Machella[13)] found good results for disorders after vagotomy; epigastric fullness, hyposecretion, loss of appetite, nausea, vomiting and nutritional disturbance. Further, Stafford[14)], Grimson[15)], F. Stein[16)], W. Postlethwait[17)] and R. Dragstedt[18)] reported the effect on epigastric fullness of vagotomized stomach. J. Carson reported that it was effective to diminish the symptoms of Hirschsprung's disease.

The pharmacoradiographic application of Bethanechol chloride has never been reported. Further, the clinical effect on the gastroptotic patients by oral administration, will be reported later.

I. Pharmacoradiography of the digestive tract: the effect of Bethanechol Chloride on the x-ray picture of the stomach and duodenal bulb

1) Physical and chemical characteristics of Bethanechol Chloride with its pharmacologic action

Carbamylmethylcholine chloride.. $C_7H_{17}ClN_2O_2$.. (M.W. ..169, 69)

$$\left(\begin{array}{l} CH_3—CH—CH_2—N^+\ (CH_3)_3 \\ \quad\ |\ \\ \quad O—CO—NH_2 \end{array}\right) Cl^-$$

Bethanechol chloride is colorless or white crystal, or crystaline powder and has usually weak amine odor. It is stable in the air and the pH of 1% water solution is

5.565. It is well soluble in water, and 1 g is solved in 1 cc of water or 10 cc of alcohol. It is hardly solved by dehydrated alcohol and not solved by chloroform and ether. The melting point reaches to 217～221°C.

Since the discovery of stimulating effect on the parasympathic nerve by acetylcholine, many sorts of choline derivarates have been synthesized by Hant et al, which had not been used for treatment before Villaret in 1927. Acetylcholine is decomposed by cholinesterase in the body fluid, so that the effect disappears early. Its interest as stimulant of parasympathic nerve might be neglected clinically, but it has been noticed from physiological point of view. Hence, more stable Cholinesterase has been actively searched for, and Methacholine, Carbachol and Bethanechol have been synthesized and studied.

Acetylcholine has strong nicotinic action and this disadvantage was discussed, while Methacholine lost it but this was apt to be decomposed easily with cholinesterase. Carbachol is stable against cholinesterase with strong nicotinic action, i.e., with strong side action, and it is not antagonistic against Atropine. So it could not be clinically useful.

Bethanechol is stable against cholinesterase without nicotinic action, and its toxicity is weaker than Carbachol. The stimulating action of cholinester on parasympathic nerve has so strong effect on circulatory system that it is used to decrease the blood pressure, while Bethanechol at usual dosis has not any effect on circulatory system but strong action on digestive tract. The pharmacologic action of Bethanechol was studied by Molitor et al[20] in 1936 comparing with that of other cholinester. Starr[21] confirmed the stimulating action of this drug on digestive tract without any effect on circulatory system, giving it to the normal in 1940. W. Lee[22] reported that it increased the tone of atonic urinary bladder. Stafford[14] applied it to the treatment of postoperative epigastric fullness, and Machella[13] reported the good effect of Bethanechol on epigastric fullness, hyposecretion, loss of appetite, nausea, atonic symptom and hypoperistalsis after vagotomy, recording the gastric curve with balloon kymographic method of gastric movement. Stein[16] reported good result for adynamic ileus.

2) The objects and method of clinical experiment

i) The objects of experiment

The number of the patients examined reached to 64; 33 males and 31 females without particular meaning in their sexuality.

The age group of patients was 4 in tens, 18 in twenties, 18 in thirties, 12 in forties, 6 in fifties, 5 in sixties and 1 in seventies. The patients were examined from the youngest 15 to the oldest 71, and the number of cases was almost the same from twenties to forties.

The disease group was as follows; 23 cases of gastroptosis, 7 of gastritis, 7 of stomach ulcer, 2 of long stomach, 5 of duodenal ulcer, 1 of gastroduodenal ulcer, 1 of gastroduodenitis, one of duodenitis, 1 of pyloric stenosis and 1 of gastric polyp. Those cases were selected which had the functinal deformities caused by hypotonia or atonia of stomach, and the organic deformities or organo-functional deformities, in order to investi-

gate the effects of Bethanechol chloride on the tone, peristasis or emptying of the stomach, and filling of the duodenal bulb. As for control, 13 normal cases were examined. The comparative study with Morphine, Imidaline and Vagostigmine was practiced each on 30 cases.

The objects of Morphine group numbered 30; 22 males and 8 females. The diseases examined were 4 cases of stomach ulcer, 6 of duodenal ulcer, 3 of periduodenal adhesion, 3 of gastroptosis, 2 of prolaps of pyloric mucosa, 1 of stomach cancer, one of gastroduodenal ulcer and compared with 10 normal cases. The observation was repeated after 10~20 minutes of muscular injection of 4~5 mg of Morphinum hydrochloricum.

The objects of Imidaline group numbered 30; 20 males and 10 females. The age and sex incidence had no particular meaning. The diseases examined were 7 cases of duodenal ulcer, 5 of gastroptosis, 4 of stomach ulcer, 2 of periduodenal adhesion, 2 of gastroduodenal ulcer, 2 of stomach cancer, 1 of prolaps of pyloric mucosa and compared with 7 normal cases. After 10~20 minutes of muscular injection of 1 cc of 2% Imidaline, the effects were observed and compared.

The objects of Vagostigmine group numbered 30; 13 males and 17 females. The diseases examined were 4 cases of gastric ulcer, 2 of duodenal ulcer, 5 of gastroptosis, 2 of periduodenal adhesion, 1 of stomach cancer and compared with 16 normal cases. They were observed repeatedly 10-20 minutes after muscular injection of 0.5 mg of Vagostigmine.

ii) The method of experiment

The procedure practiced was as follows. The mucosal pattern of the stomach is radiographed as usual[8)9)], then 300 cc of barium mixture is given to the patient, and the fluoroscopy and radiography of the stomach and duodenum is exercised in each position. Three hours after the injection of barium meal, the contrast medium is given again when the stomach is completely empty. Confirming that the finding is not changed comparing with that of first fluoroscopy, x-ray film is taken in erect position, and at the same time, 1.5 mg~2.5 mg of Bethanechol chloride is injected subcutaneously in proportion to the body weight, and after that fluoroscopy and radiography are practiced after 5, 10, 15, 20, 25 and 30 minutes.

According to U.S. Pharmacopoeia XV, N.N.D. (1959), the maximum dosis is 30 mg, prohibiting administration of more than 120 mg in 24 hours, and its usual dosis is described as 5~10 mg.

The dosis we used was 1/3~1/2 of the indicated dosis, i.e., 1.5 mg~2.5 mg showed sufficient effect, thus it could be considered as optimal dosis to be used in the fluoroscopic room. In employing 5 mg, palpitation, flush, heavy perspiration and increase of pulse were observed, while side actions were slight with 1.5 mg~2.5 mg. This should be emphasized in the procedure in the fluoroscopic room. Further, the change of findings comparing with that before administration, if present after 20 minutes, was radiographed and recorded. Some cases showed strong influences even after 1 hour.

3) The results obtained (shown in Table 1)

i) The effective time

The effect on the stomach and duodenum was demonstrated after 5–10 minutes in all case. The remarkable effect disappeared after 30 minutes in almost all cases except one even after 1 hour. The relatively short duration of the influence of this drug was demonstrated radiologically.

ii) Side actions

Perspiration was observed in almost all cases. This degree was strong in 3 cases, moderate in 5 cases, mild in 19 cases and none in 3 cases. One case complained of flush, palpitation and pulse increase, relieved rapidly with subcutaneous injection of 0.6 mg of atropine. The perspiration disappeared, however, in 5 minutes, and it could be a good indication of the response to the drug, thus it was rather useful in fluoroscopic procedure. No case was experienced which needed the interruption of fluoroscopy or injection due to serious side actions. The local pain through injection was very slight.

4) The comparison with the effects of Morphine, Imidaline and Vagostigmine will be described in the following each section.

5) The effects on the x-ray picture of the stomach

i) The tone of the stomach

The effect on the tone of the stomach was studied by means of our measurement of tone-angle of the stomach. The tone increased in 48 of 64 cases (75.0%), did not changed in 12 cases (18.8%) and decreased in 4 cases (6.2%), thus the hypertonic action of this drug was demonstrated.

Table 1: The Effects of Bethanechol Chloride on the X-ray Pictures of the Stomach & Duodenal Bulb

		Stomach										Duodeum Filling of the bulb		
		Tonus			Peristalsis			Emptying						
	No. of Cases	increased	no change	decreased	increased	no change	decreased	accelrated	no change	delayed	undetermined	improved	no change	inhibited
Normal	13	11	2	0	11	1	1	8	1	2	2	8	3	2
Gastroptosis	23	18	4	1	16	5	2	20	2	1	0	15	5	3
Gastritis	7	4	1	2	5	0	2	5	2	0	0	4	2	1
Stomach Ulcer	7	4	3	0	3	2	2	2	3	2	0	1	2	4
Duodenal Ulcer	5	4	0	1	3	2	0	3	1	0	1	2	2	1
Long Stomach	2	1	1	0	1	0	1	1	0	1	0	1	1	0
Stomach Cancer	2	1	1	0	0	2	0	0	2	0	0	1	1	0
Gastroduodenal Ulcer	1	1	0	0	0	1	0	0	1	0	0	0	0	1
Gastroduodenitis	1	1	0	0	1	0	0	0	0	0	1	1	0	0
Duodenitis	1	1	0	0	1	0	0	1	0	0	0	0	1	0
Pyloric Stenosis	1	1	0	0	1	0	0	0	1	0	0	0	1	0
Gastric Polyp	1	1	0	0	1	0	0	0	1	0	0	0	1	0
Total	64	48	12	4	43	13	8	40	14	6	4	33	19	12

The comparison of the effect with other medicaments used for pharmacoradiography was as follows; 8), 10)

With Morphine (3～5 mg), the tone increased in 23 of 30 cases (76.6%), did not change or decreased in 7 cases (23.4%), while with Vagostigmine it increased in 14 of 30 cases (46.6%) and did not change or decreased in 16 cases (53.4%). On the other hand, with Imidaline, it increased in 16 of 30 cases and did not change or decreased in 46.6%. On the contrary, with Buscopan, it increases in 16 of 300 cases (5.3%), did not change in 38 cases (12.7%) and decreased in 246 cases (82.2%).

In summary, the hypertonic action of Bethanechol chloride on the stomach as compared with that of Vagostigmine, Imidaline or Buscpoan was so strong as to be almost equivalent to the effect of Morphine.

Further, it should be emphasized that in cases of gastroptosis the tone increased in 18 of 23 cases (78.8%).

ii) The peristalsis of the stomach

With Bethanechol chloride, the peristaltic movement of the stomach increased in 43 of 64 cases (67.2%), did not change in 13 cases (20.3%) and decreased in 8 cases (12.5%). In comparison, with Vagostigmine it increased in 12 of 30 cases (40%), did not change or decreased in 18 cases (60%) and with Imidaline it increased in 15 of 30 cases and did not change or decreased in 15 cases (50%), while with Morphine it increased in 20 of 30 cases (66.6%) and did not change or decreased in 10 cases (33.4%). It was demonstrated that Bethanechol had more evident action on the peristalsis of the stomach than any other medicament, Vagostigmine, Imidaline and Morphine. Further, hyperperistalsis was observed in 16 of 23 cases (69.6%).

On the other hand with Buscopan, the peristalsis increased in 32 of 300 cases (10.7%), did not change in 142 cases (47.0%) and decreased in 127 cases (42.3%), showing remarkable contrast.

iii) The emptying of the stomach

With Bethanechol chloride, the emptying of the stomach was accelrated in 40 of 64 cases (62.5%), did not change in 14 cases (21.9%) and delayed in 6 cases (9.4%) with the undetermined 4 cases (6.3%). The accelration of emptying was observed in 20 of 23 cases of gastroptosis. Whereas, with Buscopan, the emptying was accelrated in 43 of 300 cases, did not change in 149 cases (49.7%) and delayed in 108 cases (36%).

Thus Bethanechol chloride accelrates the emptying of the stomach, especially of the patient with gastroptosis, hypotonia or hypoperistalsis.

6) The effect on the x-ray picture of the duodenal bulb;

The filling of the duodenal bulb

The duodenal bulb was observed in erect, supine and prone position with the aids of serial and spot radiography.

In employing Bethanechol chloride, the filling of duodenal bulb was improved in 33 of 64 cases (51.6%) with no change in 19 cases (29.7%) and was inhibited in 12 cases

Fig. 1a

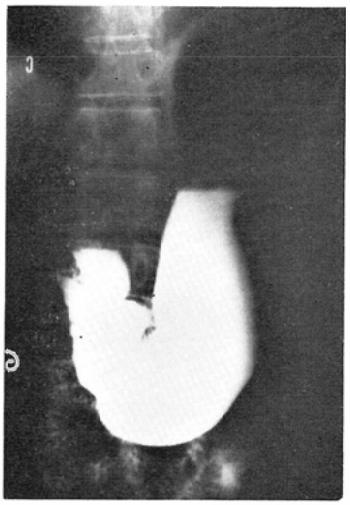


Fig. 1b

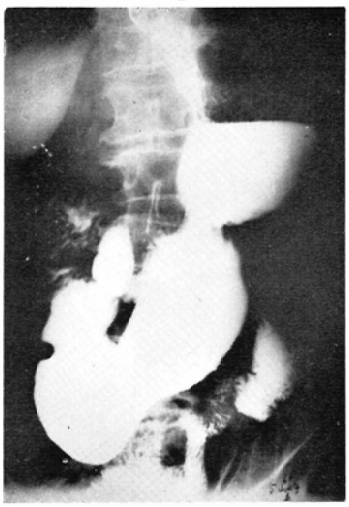


Fig. 2a

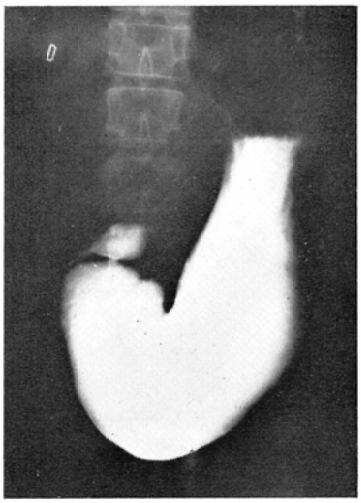


Fig. 2b

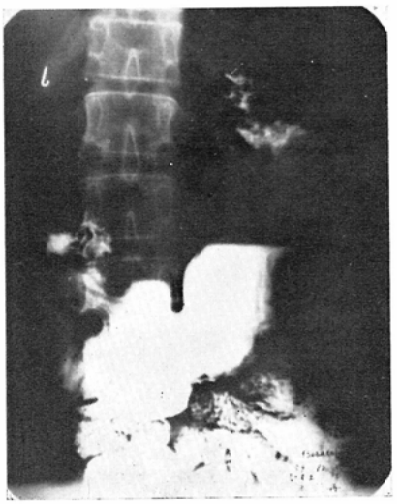


Fig. 3a

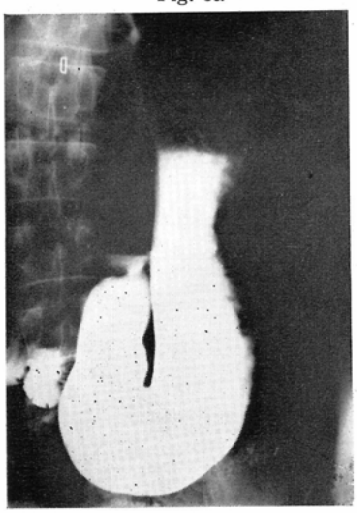


Fig. 3b

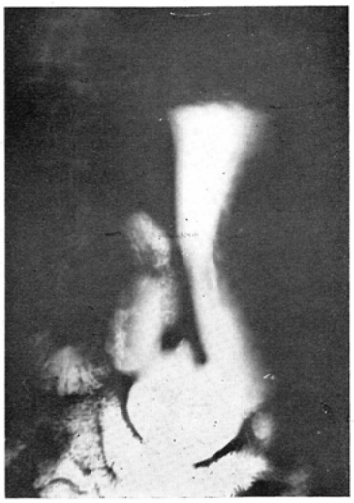


Fig. 4a

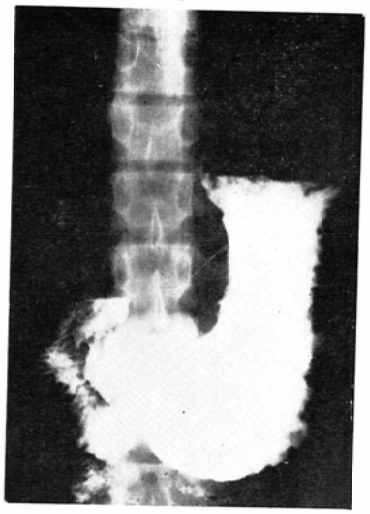


Fig. 4b

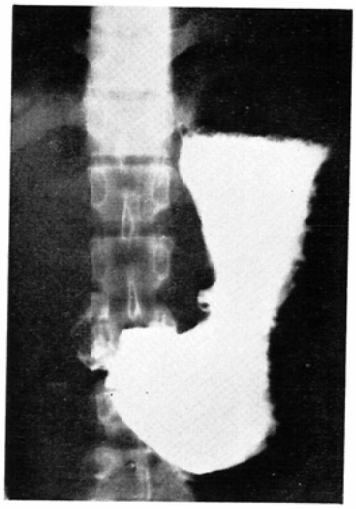


Fig. 5a

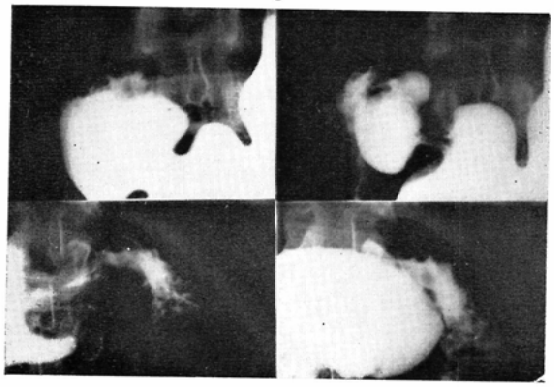


Fig. 5b

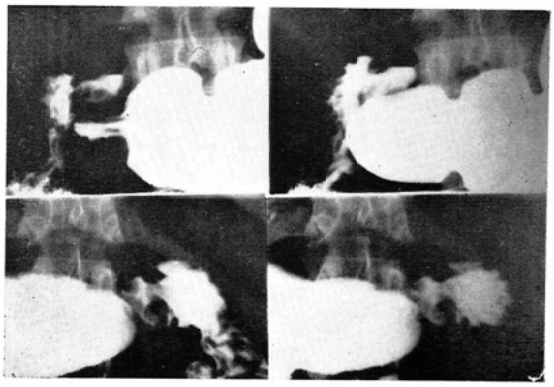
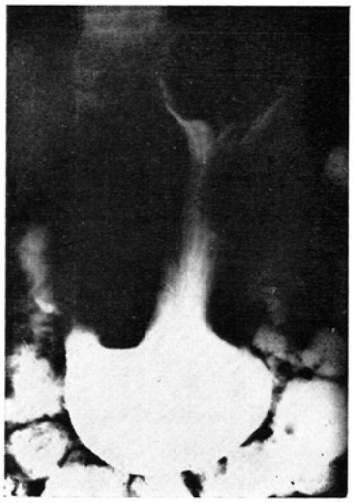


Fig. 6a

Fig. 6b



(18.8%). The comparison with other medicaments was as follows; with Morphine, the filling of the duodenal bulb improved in 18 of 30 cases (60%) with no change in 7 cases (23.3%) and was inhibited in 5 cases (16.6%); with Imidaline, it was improved in 18 of 30 cases (60%) with no change in 10 cases and was inhibited in 2 cases (0.66%); with Vagostigmine, it was improved in 12 of 30 cases (40%) with no change in 12 cases and inhibited in 6 cases (20%). On the contrary, with the spasmolytic, Buscopan, the filling of duodenal bulb was improved in 336 of 500 cases (67.2%). The effect of Buscopan on the filling of the duodenal bulb was most excellent, but in cases of gastroptosis, Bethanechol chloride was very effective in 15 of 23 cases (65.2%), while Buscopan was effective in 13 of 19 cases of gastroptosis.

7) Case Presentation (see illustrations)

Case No. 1 (Fig. 1a,b)…Fig. 1a showed the normal stomach and duodenum. The tone, peristalsis and emptying of the stomach markedly increased 10 minutes after the injection of Bethanechol Chloride (Fig. 1b).

Case No. 2 (Fig. 2a,b)…The increased tone, peristalsis and emptying of the stomach (Fig. 2b) after the injection of Bethanechol Chloride are compared with the findings without the injection (Fig. 2a).

Case No. 3 (Fig. 3a,b)…Fig. 3a revealed gastroptosis. See marked effect after the injection (Fig. 3b).

Case No. 4 (Fig. 4a,b)…Fig. 4a without the injection showed a small niche on the lesser curvature of the stomach. While in Fig. 4b, it was clearly demonstrated 10 minutes after the injection of Bethanechol Chloride.

Case No. 5 (Fig. 5a,b)…The niche and deformity of the duodenal bulb without the injection (Fig. 5a) were more clearly demonstrated with the injection (Fig. 5b).

Case No. 6 (Fig. 6a,b)…The lesser curvature of the antrum was linear and rigid suggesting malignancy (Fig. 6a). After the injection of Bethanechol Chloride, it remained unchanged, thus revealing the range of carcinomatous invasion (Fig. 6b).

8) Summary

1. The usefulness of Bethanechol Chloride for pharmacoradiography was demonstrated.

2. Bethanechol chloride gave strong effects on the x-ray pictures of the stomach and duodenum. The tone of stomach and peristalsis increased and the emptying of stomach was accelrated. In comparison with other stimulants, Morphine, Imidaline and Vagostigmine, the effect was as strong as Morphine and stronger than Imidaline and Vagostigmine. It showed remarkable contrast to Buscopan.

3. As for the effect on the x-ray picture of the duodenal bulb, the filling was frequently improved, thus it was useful in serial pharmacoradiography with rapid and strong changes of the bulb. While with Buscopan, the filling time of duodenal bulb was prolonged without marked changes, so that it was very convenient to be investigated. The comparison with such effect was very interesting.

4. The application of Bethanechol Chloride to pharmacoradiography demonstrated

more clearly the organic lesions, and the range of wall invasion because of the deepening of the peristaltic wave.

5. In cases of gastroptosis, it was very effective on the tone and peristaltic movement, emptying of the stomach and filling of the duodenal bulb.

6. As for side actions, perspiration which could be important sign of the action was observed in short duration without particular disturbances, the local pain being very slight. Those cases which needed the interruption of fluoroscopy have never been experienced.

7. Our usual dosis was 1.5 mg～2.5 mg which was 1/3～1/2 of the usual dosis in U.S. Pharmacopoeia. It might be sufficient for pharmacoradiography in daily practice.

II. The Effects of Bethanechol Chloride orally administered at Out-patient Clinic.

1) Oral administration of Bethanechol Chloride

i) The objects of clinical experience

The patients treated were those who visited the out-patient clinic of the Fujikura Densen Co. as shown in Table 2. Seven cases of Gastroptosis, 12 cases of Gastritis, and one patient of constipation were treated. The course of those who suffered from gastritis was chronic with subjective symptoms as shown in Table 2 except 3 cases of subacute gastritis. The age and sex distribution is shown in Table 2 & 3. Fluoroscopy of G.I. tract was carried out on 12 cases of 20 patients, and all cases of gastroptosis were radiologically confirmed.

ii) Method of administration

0.4～0.6 g of Besacolin Powder (20～30 mg of Bethanechol Chloride) was administrated orally in 2～3 times daily 30～60 minutes before meal.

The combination with other medicaments was avoided as far as possible in order to judge the net effect. The exceptional cases are shown in Table 2.

iii) The period of administration

As a rule, the administration was supressed with clinical recovery of subjective symptoms of the patient. As shown in Table 2, the period ranged from 2 days to more than 100 days. The average peroid was from 5 days to 1 month.

2) Clinical Results: The Effect on the subjective symptoms

The criteria of the effect were classified as follows;

i. Symptoms disappeared···marked effect
ii. Symptoms recovered···considerable effect } effective
iii. Slight effect
iv. No effect

As shown in Table 2, Besacolin was markedly effective in 7 of 20 cases, considerably effective in 7 cases, slightly effective in 2 cases and not effective in 4 cases. It was effective in 14 of 20 cases (70%).

The disappearing rate of subjective symptoms reached to 60.7% in all cases as shown in Table 4. As for each symptom, which disappeared after the treatment, it is shown

as follows; loss of appetite…77.8%, epigastric fullness…55.6%, feeling of stagnation…50%, epigastric pain…50%, nausea…80% and constipation…40%. The effect was remarkable especially on loss of appetite, epigastric fullness and nausea. Further, as shown in Table 5 & 6, the disappearing rate of subjective symptoms was 71.4% in cases of gastroptosis, while it was 43.5% in cases of chronic gastritis revealing the complexity of types of chronic gastritis. The period for the disappearing of symptoms was mostly within 5 days in cases of gastroptosis and gastritis.

During the administration of Besacolin, no important side action was found even in case treated over 3 months. The change of blood pressure was never noticed.

3) Summary

1) Giving orally Bethanechol Chloride (Besacolin) to 20 cases of visiting patients, the subjective symptoms were observed. It was effective in 14 of 20 cases, especially on loss of appetite and epigastric fullness.

2) The disappearing rate of subjective symptoms was 71.4% in cases of gastroptosis.

Table 2a

Case No.	Sex	Age	Clinical Diagnosis	subjective symptoms	x-ray Diagnosis
1	M	34	Gastroptosis	loss of appetite, epigastric fullness and nausea	Gastroptosis
2	M	42	〃	loss of appetite, epigastric fullness, nausea and pain	〃
3	F	28	〃	epigastric fullness, pain and tendency of constipation	〃
4	F	33	〃	epigastric stagnation, nausea and tendency of constipation	〃
5	F	26	〃	epigastric fullness and pain	〃
6	F	21	〃	loss of appetite, nausea, cranial dullnes and dizziness	〃
7	M	28	〃	loss of appetite, epigastic fullness	〃+Gastritis
8	M	20	Chronic Gastritis	epigastric fullness, stagnation, pain and alternative constipation and diarrhea	Gastritis
9	M	46	〃	epigastric stagnation, narrowing feeling of oesophagus and vomiting	
10	M	52	〃	loss of appetite and stagnation	
11	M	20	〃	loss of appetite and nausea	
12	M	31	〃	loss of appetite, stagnation feeling	
13	M	31	〃	epigastric fullness, dullness & loss of appetite	
14	M	28	〃	loss of appetite, stagnation & constipation	
15	F	18	Gastritis	loss of appetite and cranial dullness	
16	F	20	〃	loss of appetite and cranial dullness	
17	F	23	Chronic Gastritis	loss of appetite and dullness	
18	M	24	〃	loss of appetite and tendency of constipation	
19	M	46	Gastritis	epigastric fullness	
20	F	23	Constipation	constipation	

Table 2b

Case No.	Daily Dosis	Period (days)	Effect	Side Action	N.B.
1	0.4 g 0.6 g	3d 14 } 17	marked	—	appetite increased after 5 d.
2	0.4 0.6 0.4	3 30 68 } 101	considerable	—	appetite increased in 3 d., symptoms disappeared in 5 d.
3	0.6	30	considerable	—	recovered in 5 d., soft stool
4	0.4 0.6	2 6 } 8	considerable	—	symptoms recovered in 3 d. but tendency of constipation
5	0.4 0.6	1 4 5	considerable	—	recovered in 1 day, epigastric pain disappeared
6	0.6	16	marked	—	appetite increased in 2 d., nausea disappeared in 7 d. other symptom in 14 d.
7	0.6	14	no	—	
8	0.4 0.6	2 20 } 22	slight	—	
9	0.6	10	no	—	
10	0.6	14	considerable	—	appetite increased in 2 d., no stagnation in 5 d., combination with vitamine B & liver treatment
11	0.6	30	considerable	—	appetite increase in 2 d., nausea recovered in 21 d. combination with multi-vitamine & liver treatment
12	0.6	12	no	—	
13	0.4 0.6	2 3 } 5	marked	—	appetite increase in 2 d, symptomless in 3 d.
14	0.6	6	marked	—	symptomless in 2 d., soft stool in 4 d. liver treatment
15	0.6	2	marked	—	symptomless in 2 days
16	0.6	4	marked	—	appetite increase in 2d., symptomless in 3 d., combination with acid inhibitor and liver treatment
17	0.6	40	slight	—	combined with liver treatment
18	0.4 0.6	2 7 } 9	considerable	—	appetite increase in 2nd ingest. constipation not relieved
19	0.2 (once)	6	marked	—	symptomless after lst ingestion
20	0.4 0.6	2 6 } 8	no	—	

Table 3 Sex and Age Distribution

age	—20	21—30	31—40	41—50	total
male	2	3	3	4	12
female	2	5	1	0	8
total	4	8	4	4	20

Tabel 4 Observation of Subjective Symptoms (20 Cases)

subjective symptom	No. of cases	Disappeared within						Completely disappeared	recovered	slightly recovered	not effective
		1d.	3d.	5d.	1w.	2w.	3w.				
loss of appetite	13	2	7	1	0	0	0	10	0	1	2
epigastric fullness	9	1	2	2	0	0	0	5	2	1	1
feeling of stagnation	6	0	2	1	0	0	0	3	0	1	2
feeling of heaviness	1	0	1	0	0	0	0	1	1	0	0
epigastric pain	4	1	0	1	0	0	0	2	1	1	0
nausea	5	0	1	2	1	0	0	4	1	0	0
vomiting	1	0	0	0	0	0	0	0	0	0	1
feeling of narrowed oesophagus	1	0	0	0	0	0	0	0	0	0	1
dullness	2	0	1	0	0	0	0	1	0	1	0
cranial dullness	2	0	1	0	0	1	0	2	2	0	0
dizziness	1	0	0	0	0	1	0	1	1	0	0
tendency of constipation	5	1	0	1	0	0	0	2	0	0	3
alternative constipation and diarrhea	1	0	0	0	0	0	0	0	0	0	1
total	51	5	15	8	1	2	0	31	8	5	11

Table 5 Gastroptosis

subjective symptom	No. of cases	Disappeared within						completely disappeared	recovered	slightly recovered	not effective
		1d.	3d.	5d.	1w.	2w.	3w.				
loss of appetite	4	0	2	1	1	1	0	3	0	0	1
epigastric fullness	5	0	0	2	0	0	0	2	2	0	1
feeling of stagnation	1	0	1	0	0	0	0	1	0	0	0
feeling of heaviness	1	0	1	0	0	0	0	1	0	0	0
epigastric pain	2	1	0	0	0	0	0	1	1	0	0
nausea	4	0	1	2	0	0	0	4	0	0	0
vomiting	0	0	0	0	0	0	0	0	0	0	0
feeling of narrowed oesophagus	0	0	0	0	0	0	0	0	0	0	0
dullness	0	0	0	0	0	0	0	0	0	0	0
cranial dullness	1	0	0	0	0	1	0	1	0	0	0
dizziness	1	0	0	0	0	0	0	1	0	0	0
tendency of constipation	2	1	0	0	0	0	0	1	0	0	1
alternative constipation and diarrhea	0	0	0	0	0	0	0	0	0	0	0
total	21	2	5	5	1	2	0	15	3	0	3

The result is interesting, because suitable treatment for gastroptosis is not known as yet. In cases of chronic type of gastritis, the course and symptoms are so complicated that the combination with other medicament should be considered.

3) As for the mode of administration, it may be given 0.4～0.6 g daily in 2～3 times

Table 6 Chronic Gastritis

subjective symptom	No. of cases	Disappeared within						completely disappeard	recovered	slightly recovered	not effective
		1d.	3d.	5d.	1w.	2w.	3w.				
loss of appetite	7	1	4	0	0	0	0	5	0	0	2
epigastric fullness	2	0	1	0	0	0	0	1	0	1	0
feeling of stagnation	5	0	1	1	0	0	0	2	0	1	2
feeling of heaviness	0	0	0	0	0	0	0	0	0	0	0
epigastric pain	1	0	0	0	0	0	0	0	0	1	0
nausea	1	0	0	0	0	0	0	0	1	0	0
vomiting	1	0	0	0	0	0	0	0	0	0	1
feeling of narrowed oesophagus	1	0	0	0	0	0	0	0	0	0	1
dullness	2	0	1	0	0	0	0	1	0	0	1
cranial dullness	0	0	0	0	0	0	0	0	0	0	0
tendency of constipation	2	0	0	1	0	0	0	1	0	0	1
alternative constipation and diarrhea	1	0	0	0	0	0	0	0	0	0	1
total	23	1	7	2	0	0	0	10	1	3	9

especially for gastric symptoms. It should be given at least for one week.

4) Any grave side action has never been experienced.

5) The recurrence of subjective symptoms has not been noticed except one case which recurred 10 days after finishing the prolonged treatment.

Conclusion

The diagnostic as well as therapeutic value of Bethanechol Chloride was studied and demonstrated with excellent results.

The pharmacoradiographic application of Bethanechol Chloride in comparison with other medicaments is of keen interest, because the most suitable medicament has not yet been obtainable.

The muscular injection of 1.5 mg～2.5 mg of Bethanechol Chloride may be safe and sufficient for diagnostic purpose.

Further, the therapeutic effects of Bethanechol Chloride through oral administration were observed with considerable success. It is recommended to prescribe 0.4～0.6 g of Besacolin powder in 2～3 times daily.

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