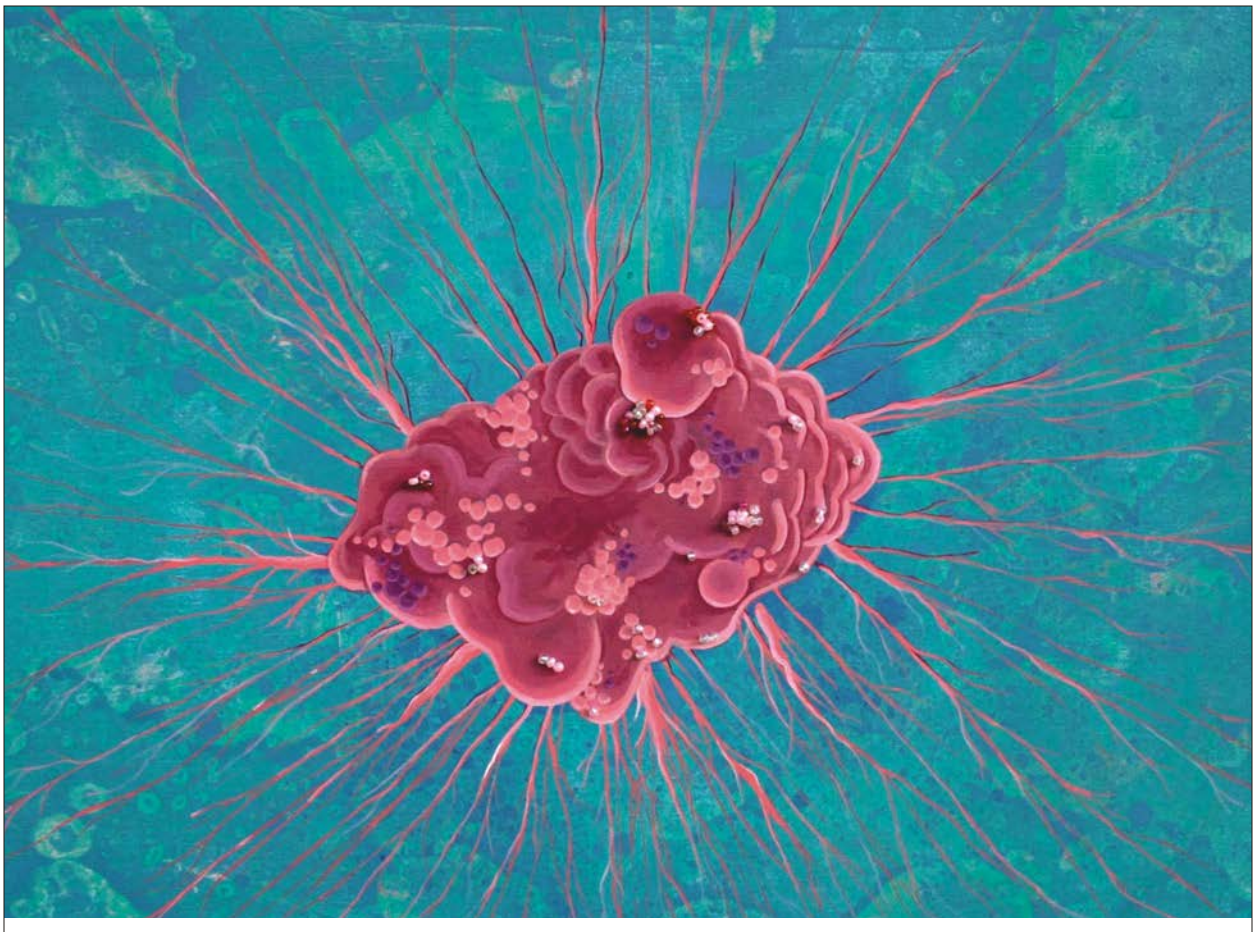

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Gastric Content of the Liquid Test Meals in Rats with Gastrointestinal Neoplasias Induced by N-methyl-N-nitrosoguanidine and 1,2-dimethylhydrazine

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Abstract: We hypothesized that liquid test meal without a calorific value injected directly into the rats stomach by a sonde, may be emptied from the stomach both with and without gastrointestinal tumours at different rate. We tested hypothesis using the dye dilution test for gastric emptying. Intestinal tumours (adenoma, adenocarcinoma) in male Wistar rats at different dieting regime were experimentally induced by 1,2-dimethylhydrazine (DMH). Gastric and duodenal tumours in male Wistar rats at different dieting regime were experimentally induced by N-methyl-N-nitrosoguanidine (MNNG). We noticed statistically higher gastric content after applicating the test meal in the stomach of rats with duodenal tumours in comparison with the group of rats both with gastric tumours ($p<0.01$) or without gastric tumours ($p<0.001$). Remained gastric content of rats tested with intestinal tumours was not statistically significant in comparison with remained gastric content of rats with ($p = 0.901$) or without gastric tumours ($p = 0.406$). We postulate that the role of duodenal resistance in controlling liquid gastric emptying in rats has principle importance if the test meal is instillated into the stomach with or without tumours through a tube. The tumours of colon have no any effect on the stomach, particularly on gastric emptying of liquid meals instillated in rat stomach. Only duodenal tumours and duodenal pathohistological changes interfered gastric emptying.

Key words: N-methyl-N-nitrosoguanidine, 1,2-dimethylhydrazine, induced gastrointestinal tumours, noncaloric test meal, gastric emptying

Introduction

There is an increasing tendency to incriminate abnormalities in gastric emptying in the pathogenesis of gastrointestinal disease. Many disorders are also associated with delayed gastric emptying without evidence of structural gastric outlet obstruction. Benign and malignant tumours involving the gastrointestinal tract may cause disturbances in gastric motility, including delayed emptying. Numerous studies have also shown that distention of the colon or rectum include a decrease in gastric motility in animals and humans (Chanduri and Fink, 1991; Griffith *et al*., 1968; Tatsuta *et al*., 1990; Shih *et al*., 1985; Nomiyama, 1985; Minami and McCallum, 1984; Luie *et al*.,

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2000; Chin-Yen *et al*., 2000; Roland *et al*., 2001; Meeroff *et al*., 1980; Meddern *et al*., 1984; Reddy *et al*., 1983; Mistiaen *et al*., 1990; Di Baise and Quigley, 1998; Kent *et al*., 1975; Mollen *et al*., 2001; Watson and Love, 1987).

It remains unclear whether these inhibitory reflexes are neurally or humorally mediated or both (Di Baise and Quigley, 1990; Azpiroz and Malagelada, 1990; Shivshunker *et al*., 1983; Pearcy and Van Liere, 1926; Youmans and Meak, 1937; Bojö and Cassuto, 1992; Jansson, 1969; Zighelboim *et al*., 1993). However, infections, injury, toxins, malignancy and inflammatory processes stimulate mononuclear phagocytes and other cells to synthesize and release various proteins (Gue *et al*., 1994; Patton *et al*., 1987; Plata-Salamán *et al*., 1998; Mchugh *et al*., 1993; Robert *et al*., 1991), which reduced food intake and gastric emptying (Youle and Read, 1984; Van Wijk *et al*., 1992). Consequently, Chin-Yen Chen *et al*. (2000) also suggested that an unknown or unmeasured substance may release from hepatocellular carcinoma disturbed liquid gastric emptying in patients through either of these two pathways. Nevertheless, Nomiyama (1985) found, by use of acetaminophen absorption method, that gastric emptying in patients with early gastric cancer was rather rapid, if compared with emptying in healthy subjects. These differences may be caused by differences in the methods of the gastric emptying measurement and the test meal used (Tatsuta *et al*., 1990).

The emptying of liquids from the stomach is thought to be primarily a function of the pressure gradient between the stomach and duodenum. The rate of transfer of intragastric contents to the duodenum seems to depend on the balance between propulsive forces and the resistance offered by the distal antrum, the pylorus and the duodenum (Kelly, 1989). However, the increased intragastric pressure leads to more rapid gastric emptying of liquids. Hunt and McDonald (1951) described the emptying of stomach in human after a swallowed meal with that after a pectin meal instillated into the stomach through a tube. The slight accelerating of gastric emptying was found as the result of the absence of part of the receptive relaxation of stomach when swallowing was eliminated.

We also postulated that role of duodenal resistance in controlling liquid gastric emptying in rats has principle importance if the test meal is instillated into the stomach through a tube. It is also of interest to know whether the tumours of colon have an effect on the stomach, particularly on gastric emptying of liquid meals instillated in rat stomach. The role of duodenal resistance in controlling liquid gastric emptying in rats has not been extensively investigated.

The aim of the study was to find out if liquids, injected directly into the stomach by sonde, could be emptied at the same rate from a stomach with or without gastrointestinal disease. We tested this hypothesis using the dye dilution test for gastric emptying (Scarpignato *et al*., 1980; Mangel and Koegl, 1984) after Wistar rats by MNNG (Takahashi *et al*., 1986; Watanabe *et al*., 1992) for inducing gastroduodenal neoplasms and by DMH for inducing colon cancer (Hagihara *et al*., 1980; Seitz *et al*., 1984; Thurnherr *et al*., 1973).

Materials and Methods

Animals

Experiment 1

We used 70 male Wistar rats (Medical experimental Center, Medical faculty, Ljubljana, Slovenia, year 2003) weighing 150-200 g. The animals were fed pelleted Knapka food and maintained in macrolon cages at a constant temperature (22±2°C) and relative humidity (60±5%). All the animals were given N-methyl-N-nitrosoguanidine (MNNG; Fluka Chemie, Switzerland) at a concentration of 100 mg L^{-1} in a drinking solution (Takahashi *et al*., 1986; Watanake *et al*., 1992). We arbitrarily

divided the experimental animals into two groups. One group had MNNG diluted in tap water, while the other, in an 8% alcohol solution. The experimental animals drank MNNG solution for 29 weeks; after that they drank tap water for additional 29 weeks, at which time experiment was finished. 10 rats died before the end of experiment.

The experimental animals were observed daily and weighed every 4 weeks. Autopsies were performed on all except two animals. At the end of the 58 experimental weeks, the gastric emptying was performed.

Experiment 2

We used 120 male Wistar rats average weighing 233 g and maintained in animal rooms with constant temperature (22±2°C) and relative humidity (60±5%). Animals were divided into three groups, differing on dieting regimen. Animals in the group 1 (n = 30) were fed by pelleted food and tap water (control group), animals in the group 2 (n = 30) were fed by fat diet and tap water and animals in the group 3 (n = 60) were fed by pelleted food and 8% alcohol solution. Fat diet was prepared by addition of pork fat to the pelleted diet. Food and liquid consumption was measured daily. Prior to our study all animals were weighed and then weight was controlled every four weeks. 4 rats died before the end of experiment.

Animals were given a weekly injection of 1,2-dimethylhydrazine (DMH; Fluka Chemie, Switzerland), 20 mg kg^{-1} body weight for the initial 15 week (Hagihara *et al*., 1980; Seitz *et al*., 1984; *Thumherr* et al., 1973). We left the animals on the initial regime of diet for 14 weeks. After 29 weeks animals have been euthanised by carbon dioxide (CO_2) and gastric emptying tests have been performed.

Gastric Emptying Studies

The technique of Mangel and Koegel (1984) was used with modifications. Studies were performed on all rats with the exception of the rats which spontaneously died during the experiment.

During fasting the rats were maintained in wirebottomed cages to avoid coprophagy. The experiments were performed in a room with the same environmental conditions (temperature, noise and humidity) as those in the breeding area. All experiments were done in the morning.

The phenol red meal was prepared as follows: methyl cellulose was dissolved in water at about 80°C and prepared in a final concentration of 1.5%. The solution was stirred until dissolved and phenol red (50 mg/100 mL) was then added to the stirring solution.

Three mL of phenol red solution, maintained at 37°C was administered orally by sonde to the rats. The animals were killed 20 min after the instillation of the phenol red meal by means of CO_2 inhalation.

An incision was made for a middle laparotomy. The stomach was exposed and occluded at the pylorus and cardia. The stomach was then removed, cut along the greater curvature and washed out with 3 mL of 0.9% saline. The gastric content was placed in 100 mL of 0.1 N (normality) NaOH with 0.9% saline.

Trichloracetic acid (0.5 mL) (20% t vol^{-1}) was added to 5 mL of mixture. This sample was centrifuged at 2,500 rpm for 30 min. The supernatant was removed and 4 mL of 0.5 N NaOH added. Samples were then read on a colour spectrophotometer (MA 9502) at 560 nm.

The percentage of gastric remains was calculated as follows:

$$\% \text{ gastric remains} = \frac{\text{Absorption value for stomach}}{\text{Mean absorption value for test meal}} \times 100$$

Morphologic Evaluation

The gut and other visceral organs were examined macroscopically, fixed in a 10% neutral formalin and routinely processed for histopathological studies. Gastrointestinal lesions were classified histopathologically into neoplastic (dysplasia, papilloma, adenoma, squamous cell carcinoma, adenocarcinoma, sarcoma) and nonneoplastic (principally inflammatory) gastroduodenal diseases, following accepted histological criteria (Stinson *et al*., 1990).

Statistical Evaluation

The results of the analyses have been statistically processed with statistical programme STATGRAPHICS Plus 4.0. The statistical characteristic of differences between the arithmetic means among groups of laboratory rats has been checked with the analysis of variance (ANOVA and Duncan's test):

- The% gastric content at three dieting regime
- The weight of the rats at the end of experiment.

Statistically characteristic of differences of the gastric content between groups of laboratory rats with all pathohistological changes in the stomach, duodenum, small intestinum and colon have been evaluated by using the Student`s test.

Statistically characteristic of differences in the experimentally induced tumours by DMH and MNNG among groups of laboratory rats have been checked by estimate of the proportion of population: the differences between the proportions of two samples.

The significance of the percentage of the gastric content 20 min after the test meal has been evaluated by using the Student`s test.

Results

In both experiments (experiments 1 and 2) rats were drinking alcohol and in experiment 2 fat diet was given with the intention as well as to induce a higher number of tumours. Growth charts of rats in experiment 1 have been different, but there was no statistically significant difference in comparison with the control group ($p = 0.423$) (Fig. 1).

In experiment 2 we have observed the largest increase of body weight (Fig. 2) in the control group in comparison with group 2 (fat diet+tap water), but there was no statistically significant differences ($p = 0.777$). We have found statistically significant differences between control group and group 3 ($p = 0.038$) and between group 2 and group 3 ($p = 0.046$), at the end of experiment.

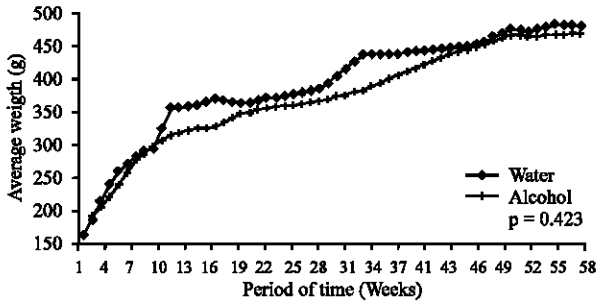

Fig. 1: Body weight gains of rats in the different MNNG-treated groups

Table 1: Effect of various test meals on gastroduodenal neoplasia induced by MNNG in rats*

Gastroduodenal lesions	Treatment (test meals)			
	Ethanol**	Water***	Total	p- value
Dysplasia	4	0	4[a]	a-b: p = 0.393
				a-c: p = 0.003
Papilloma	1	1	2[b]	
				a-d: p = 0.169
Carcinoma	5	11	16[c]	b-c: p = 0.000
				b-d: p = 0.566
Sarcoma	1	0	1[d]	
Total	11[A]	12[B]	23	c-d: p = 0.000
p- value	A-B: p = 0.791			

*70 rats at the beginning of experiment and 60 rats at the end of experiment,
**8.0 vol% of ethanol in tap water with MNNG (n = 30), ***Tap water with MNNG (n = 30)

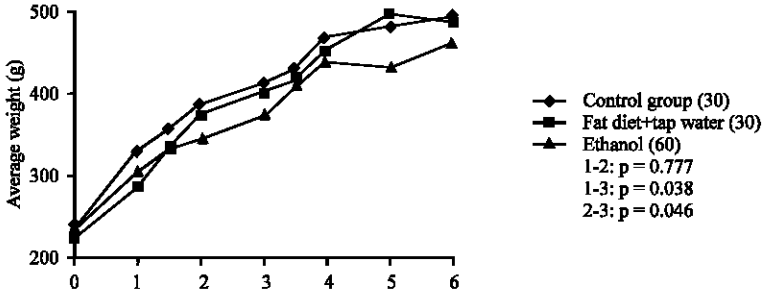

Fig. 2: Body weight gains of rats in the different DMH-treated groups

Table 1 shows tumours induced by MNNG in 60 rats. In the upper gastrointestinal tract, stomach and duodenum we observed 4 dysplasias, 2 papillomas, 16 carcinomas and 1 sarcoma or 23 pathological changes marked as tumours of the upper gastrointestinal tract. Pathohistological changes on stomach and intestine, including also 7 tumours of the liver and the gastric content are shown in Table 2.

DMH induced intestinal tumours in 120 rats are shown in Table 3. We found 52 tumours (39 adenocarcinomas, 11 adenomas and 2 carcinomas of the Zymball gland). The highest number of tumours was observed in the group fed with the fat diet (27/30) and the lowest in group drinking alcohol (9/60).

We performed testing with measurable remained gastric content in 46 rats (120 rats were at the beginning of experiment and 116 rats were at the end of experiment), 18 with and 28 without intestinal tumours. We found 20 tumours in 18 rats (Table 4).

The remained gastric content in rats 20 min after the application of the noncaloric test substance (% of applied test meal) is shown in Table 5. Table 5 shows average gastric contents in rats without gastric tumours and with gastric tumours, with duodenal tumours, small intestinum tumours and tumours of colon and liver. The highest statistically significant of the gastric content was observed in rats with duodenal tumours in comparison with the gastric contents in rats without gastric tumours ($p<0.001$), with gastric tumours ($p<0.01$), with tumours in small intestinum ($p<0.01$) and tumours of colon ($p<0.001$) and of liver ($p<0.05$).

The gastric content was statistically significantly higher ($p<0.01$) in rats with duodenal tumours (62.8±19.6) comparing with rats which had only gastric tumours (24.1±17.7), (Fig. 3). Differences

Table 2: The gastric content 20 min after applicating the test meal in the stomach of the rats (% of applied test meal) with pathohistological changes of stomach and duodenum

No.	% of applied test meal	
1	20.2	Chronic superficial duodenitis
2	18.2	Fibrosis of fundic mucosa. Chronic superficial duodenitis
3	24.1	Chronic superficial duodenitis
4	24.1	Chronic antral gastritis with focal fibrosis of mucosa and sub. mucosa
5	22.9	Focal fibrosis of fundic and antral mucosa
6	13.8	No pathological changes
7	21.5	Chronic gastritis and focal fibrosis of antral mucosa Focal dysplasia (grade II) of nonglandular (squamous) mucosa Chronic superficial duodenitis
8	29.6	Chronic superficial duodenitis and focal fibrosis of antral mucosa
9	55.0	Focal regeneratory atypia of duodenal mucosa (in the vicinity of fibrosis)
10	27.1	Focal chronic gastritis of antral mucosa. Early adenocarcinoma of liver
11	64.4	Mild chronic gastritis of antral and fundic mucosa
12	(-)	No autopsy report
13	20.0	Focal fibrosis of fundic mucosa. Focal dysplasia and invasive squamous cell carcinoma of nonglandular mucosa
14	61.8	Mild chronic duodenitis with focal fibrosis of propria
15	10.3	Chronic duodenitis. Chronic gastritis and chronic erosion of antral mucosa
16	44.9	Focal fibrosis of submucosa of antral mucosa region Chronic duodenitis
17	24.4	Chronic gastritis of antral mucosa
18	16.9	Moderate dysplasia of squamous mucosa. Chronic antral gastritis with focal fibrosis of submucosa Early adenocarcinoma of antral mucosa
19	(-)	Advanced sarcoma
20	21.0	Chronic gastritis of antral mucosa. Liver cystadenoma
21	19.6	Chronic gastritis of antral mucosa
22	16.1	Focal fibrosis of antral and duodenal mucosa
23	34.7	Chronic gastritis of antral mucosa
24	19.6	Chronic gastritis of antral mucosa with focal fibrosis Squamous cell papilloma of nonglandular mucosa Adenocarcinoma (infiltrates muscularis propria) of antral mucosa
25	17.7	Moderate dysplasia of squamous mucosa. Early invasive cell carcinoma of nonglandular mucosa
26	23.5	Mild dysplasia of squamous mucosa
27	.6	Chronic gastritis of antral mucosa with focal fibrosis
28	27.8	Focal fibrosis of antral mucosa. Liver cystadenoma
29	11.4	Focal fibrosis of antral mucosa
30	20.2	Chronic gastritis of antral and fundic mucosa with focal fibrosis
31	27.6	Chronic gastritis of antral mucosa with focal fibrosis Liver hamartoma
32	52.6	Chronic duodenitis
33	10.2	Chronic gastritis of antral mucosa and erosion of fundic mucosa
34	21.0	Chronic gastritis of antral mucosa with focal fibrosis of antral and duodenal mucosa
35	38.8	Focal fibrosis of antral and fundic mucosa
36	(-)	Advanced autolysis. No tumor
37	22.9	Focal fibrosis of antral and fundic mucosa
38	1.6	Chronic gastritis of antral mucosa. Moderate dysplasia of nonglandular mucosa Early invasive squamous carcinoma
39	10.9	Chronic gastritis of antral mucosa. Focal dysplasia of fundic mucosa
40	8.3	Chronic gastritis of antral mucosa. Chronic duodenitis
41	(-)	Focal fibrosis of antral mucosa. Initial autolysis
42	59	Chronic gastritis and focal fibrosis of antral mucosa. Chronic duodenitis Advanced (Dukes B) adenocarcinoma of duodenum
43	7.6	Chronic gastritis of antral mucosa. Papillary cystadenoma of liver
44	6.5	Chronic gastritis of antral mucosa. Focal fibrosis of duodenal mucosa
45	76.2	Adenocarcinoma of antral mucosa
46	63.5	Focal fibrosis of antral mucosa. Gastritis cystica profunda of prepyloric region

Table 2: Continued

47	65.5	Focal fibrosis of antral and duodenal mucosa and antral submucosa
48	36.6	Adenocarcinoma of antral mucosa (submucosal invasion)
49	22.4	Gastritiscystica profunda of antram mucosa. Cystadenoma of liver
50	38.9	Chronic duodenitis. Adenocarcinoma of antral (prepyloric) mucosa (submucosal invasion)
51	25.0	Focal fibrosis of antral mucosa and submucosa and chronic erosion of antral mucosa
52	48.3	Focal fibrosis of antral and fundic mucosa
53	21.9	Focal fibrosis of antral mucosa. Adenocarcinoma of antral mucosa (submucosa invasion)
54	36.8	Chronic gastritis of antral mucosa. Advanced (Dukes B) adenocarcinoma of duodenum
55	80.5	Chronic gastritis and focal fibrosis of antral mucosa In nonglandular mucosa squamous papilloma and invasive squamous carcinoma (early) Advanced (Dukes B) adenocarcinoma of duodenum. Multiple papillary cystadenoma of liver
56	(-)	No autopsy report
57	12.7	Chronic gastritis of antral mucosa. Adenocarcinoma of antral mucosa (invasion of submucosa)
58	20.0	Adenocarcinoma of antral (prepyloric) mucosa (invasion of submucosa)
59	(-)	Chronic gastritis and focal fibrosis of antral mucosa
60	75.0	Advanced (Dukes B) adenocarcinoma of distal duodenum

Table 3: Experimentally induced intestinal tumours (and carcinoma of Zymball gland) by DMH in male Wistar rats*

Groups	Adeno = carcinoma (a)	Adenoma (b)	Carcinoma of Zymball gland (c)	Total
Control group (n = 30)	13	2	1	16
Fat diet+tap water** (n = 30)	20	6	1	27
Ethanol*** (n = 60)	6	3	0	9
Total (n = 120)	39 (A)	11 (B)	2 (C)	52
p-value	1-2: = 0.065	1-2: = 0.130	1-2: = 1.000	1-2: = 0.002
	1-3: < 0.001	1-3: = 0.740	1-3: = 0.157	1-3: < 0.001
	2-3: < 0.001	2-3: = 0.025	2-3: = 0.157	2-3: < 0.001

*120 rats at the beginning of experiment and 116 rats at the end of experiment,
**Pelleted food with addition of pork fat (30% energy value), ***8 vol% of ethanol in tap water

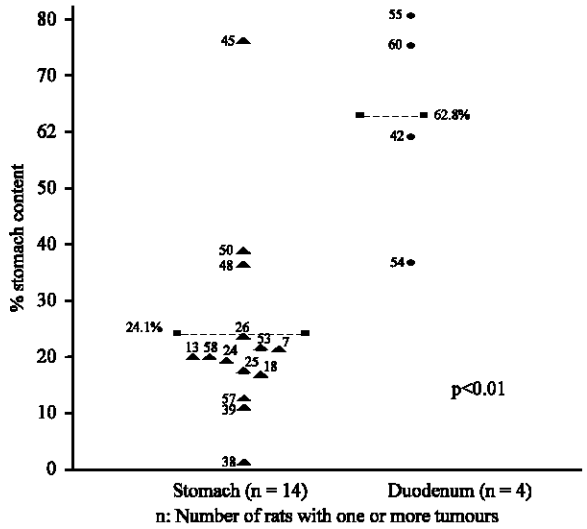

Fig. 3: The mark of rat (▲, ■) and the gastric content of the rats with tumours of the stomach and duodenum

have been statistically significantly higher considering all pathohistological changes only in stomach, only in duodenum or both with changes in stomach and duodenum (Fig. 4).

Table 4: The mark of rat (in the bracket) and gastric content of rats (% of applied test meal) with induced intestinal tumours, 20 min after application of the test in relation to the type and the location of tumours and dieting regime

Location	Dieting regime	Adenocarcinoma	Adenoma	Total
Small intestinum	1. Control group	(4) 35*; (12) 20**		2
	2. Fat diet+tap water	(17) 42; (19) 18; (21) 23		3
	3. Ethanol	(43) 23; (46) 30		2
Colon	1. Control group	(5) 19; (8) 22; (12) 20**; (13) 22; (4) 35*; (11) 27		6
	2. Fat diet+tap water	(20) 36	(18) 18	2
	3. Ethanol	(27) 18; (31)10; (42) 14; (34) 16	(32) 42	5
Total		18#	2	20

Total number of rats with applied of test meals was 46: 18 rats with tumours and 28 rats without tumours
*, **: Rats with two tumours, #: 16 rats with 18 tumours

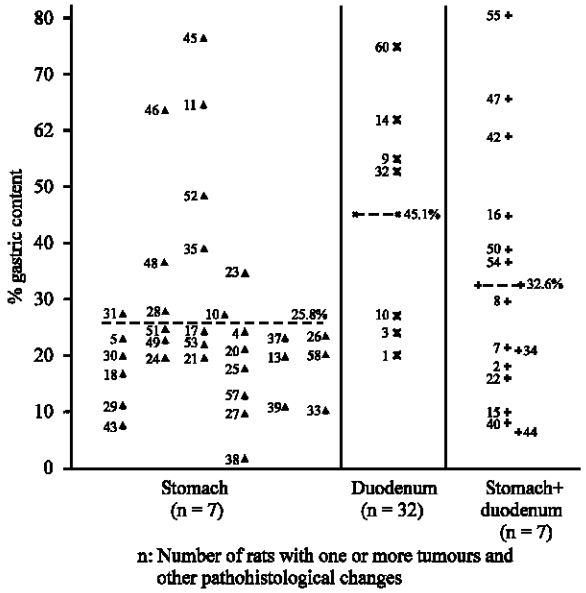

Fig. 4: The mark of rat (▲, x, +) and the average gastric content of the rats 20 min after applicating the test meal with all established pathohistological changes only in stomach, in duodenum and only both in stomach and duodenum

The remained gastric content in rats having pathohistological changes only in stomach (25.8±16.8) compared with changes in stomach and duodenum (32.6±22.9) was not statistically significantly different ($p = 0.258$) (Fig. 4). The remained gastric content in rats having pathohistological changes only in stomach (25.8±16.8) compared with changes in duodenum (45.1±21.3) was statistically significantly different ($p = 0.012$) (Fig. 4). In rats with liver tumours comparing with rats with gastric tumours, induced by MNNG, the gastric content was higher (30.6 compared with 24.1), but not statistically significant ($p = 0.486$) and the same is comparing with the rats without tumours (27.1), although DMH was used ($p = 0.537$). Differences were not statistically different.

Discussion

In the experiment by DMH, as described previously (Takahashi *et al*., 1986; Watanabe *et al*., 1992; Hagihara *et al*., 1980; Seitz *et al*., 1984; Thurnherr *et al* 1973) have artificially accelerated

Table 5: Gastric content of rats (% of applied test meal) in comparison with the location of tumours

Without gastrointestinal tumours[A] (n = 28) I.	Gastric tumours[B] (n = 14)II.	Duodenal tumours[C] (n = 4)II.	Small intestinum tumours[D] (n = 7)I.	Colon tumours[E] (n = 13)I.	Liver tumours[F] (n = 7)II.
27.1±9.6	24.1±17.7	62.8±19.6	27.3±8.7	23.0±9.4	30.6±23.1

p<0.001: C-A; C-E; p<0.01: C-D; C-B; p<0.05: C-F

I. Without gastrointestinal tumours and with small intestinum and colon tumours, where tumours were induced by DMH

II. Gastric, liver and duodenal tumours were induced by MNNG

n. Number of rats with one or more tumours (dysplasia, papilloma, squamous cell carcinoma, adenocarcinoma, sarcoma)

incidence intestinal tumours (adenoma, adenocarcinoma). Gastric and duodenal tumours were induced by MNNG. Changed dieting regime including fat and ethanol, which in animal experiment also accelerated colonic cancer (Seitz *et al*., 1984), but there was no direct evidence for gastric and intestinal cancer in alcohol consumption (Cerar and Pokorn, 1996). We induced 4 dysplasias, 2 papillomas, 16 carcinomas, 1 sarcoma, 39 adenocarcinomas, 11 adenomas by using these two methods.

In our research we noticed no statistically significant differences in gastric content, 20 minutes after the application of the test pectin meal in stomachs of rats without tumours or with tumours or other pathohistological changes in gastrointestinal tract (Table 5). We noticed statistically higher content in rats with duodenal tumours in comparison with the group of rats with gastric tumours ($p<0.01$) or without gastric tumours ($p<0.001$).

We also found that there was not a great difference in the rate of emptying between the rats having the gastric neoplastic and those with inflammatory disease (Fig. 4). This finding also confirms the previous work of Nomiyama (1985) who had been using the acetaminophen absorption method to discover that gastric emptying in patient with early gastric cancer had been rather rapid, in comparison with emptying in healthy subjects. On the other hand, delayed gastric emptying has been demonstrated for a variety of infiltrative diseases (Chanduri and Fink, 1991; Tatsuta *et al*., 1990; Shih *et al*., 1985; Di Baise and Quigley, 1998; Pokorn and Cerar, 1996; Minami and McCallum, 1984). This includes lymphoma, carcinoma, Whipple's disease and disease produce granulomas in the gastric wall. However, in our study all animals with a prolonged gastric emptying with neoplasia had advanced carcinomas of the duodenum (Fig. 3).

Gastric mucosal abnormalities can affect gastric emptying. Diseases of the gastric musculature, including the inflammatory and endocrine myopathias, muscular dystrophies and infiltrative disorders, can result in significant gastroparesis (Chanduri and Fink, 1991). However, the most patients with gastroparesis have a delay in the emptying of solid food, but the rate of liquid emptying is preserved. This observation suggests that the factors that regulate the fundic tone are preserved longer in most patients with gastroparesis (Reynolds, 1989).The proximal stomach has two remarkable motor properties that allow careful regulatation intragastric pressure during gastric filling, namely receptive relaxation and accommodation (Kelly, 1989). The proximal stomach relaxes to receive the bolus of ingested food from the esophagus; hence the term receptive relaxation (Cannon and Lieb, 1987). The emptying of liquids from the stomach is thought to be primarily a function of the pressure gradient between the stomach and duodenum. Liquid entering the fundus trigger vagally mediated initial receptive relaxation, so that the fundus plays a key role in the gastric emptying rate for liquids (Kelly, 1989).

Accommodation to distension is a process whereby the stomach accepts increasing volumes without greatly increasing the intragastric pressure. The slight shortening of the time for gastric emptying could be accounted for as a result of the absence of the part of receptive relaxation of the stomach when swallowing is eliminated (Hunt and MacDonald, 1951). In the present research, an

increased gastric emptying especially the initial emptying (Kelly, 1989) of liquid might also be explained by the abolition of receptive relaxation or of the change in the fundic tone as the intragastric injection of the liquid test meal occurs, that raises the intraluminal pressure, elevated the pressure gradient between the stomach and duodenum and allow more liquids into the duodenum. (Azpiroz and Malagelada, 1985 and 1987). It is likely that similar gastric content observed in rats both with and without tumours means a poor and equal compliance for proximal stomach accommodation during gastric emptying.

However in our experiment abnormally slow gastric emptying in the rats with duodenal tumours compared with the emptying with and without tumours on the stomach may be caused by quit mechanically duodenal resistance in controlling liquid gastric emptying in the rats. The gastric content after the quickly injected liquid test meal without calorific value was the same regardless the presence of gastric tumours or tumours of lower intestinal tract. Only duodenal tumours and duodenal pathohistological changes interfered gastric emptying.

We also did not find an inhibited gastric emptying in the rats with intestinal and liver tumours compared to the control rats without tumours.

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