Mechanical and Electrical Activity in the Duodenum of Diabetics With and Without Diarrhea

Pressures, Differential Pressures and Action Potentials

Vagn M. Drewes, MD

Duodenal motility was studied in diabetics with and without diarrhea. Diabetics with diarrhea had more and stronger pressure waves during fasting, more pressure waves after a test meal, and a total motor activity that was larger during fasting, after a test meal and after prostigmine. In addition, they had markedly more negative differential pressure waves in all periods, apparently because of a weaker reaction to intestinal distension. Maximal pressure appeared, on the average, shortly after the largest deflection in differential pressure. This difference was smallest in patients with diarrhea. An auxiliary finding was that the duration of action potential bursts increases after prostigmine.

Emphasis is placed on the importance of using a randomized, blind technic in evaluating the motility parameters registered, and, in addition, of employing in many cases, nonparametric statistical methods.

Disturbances in gastrointestinal function are common in patients with diabetes mellitus. Among the abnormalities seen, diarrhea is one of the most common. Most investigators believe that the increased incidence of diarrhea is due to alterations in the motility of the gastrointestinal tract (1–3), but actual motility studies are few (2, 3), and the pathogenesis of diarrhea is by no means clear.

The purpose of the present investigation was to determine if changes in gastrointestinal motility are present in diabetics with diarrhea, compared with diabetics without diarrhea. This was accomplished by simultaneous registration of intraluminal pressure variations, differential pressures and electrical action potentials. These studies were supplemented by short periods of cinematography.

From the Medical Department M, Århus Municipal Hospital and Medical Departments, Århus County Hospital, University of Århus, Århus. Denmark.

Address for reprint requests: Vagn M. Drewes, MD, Medical Department, Århus Amtssygehus, Århus, Denmark.

MATERIALS AND METHODS

Thirty-five patients divided into 2 groups were studied. One group consisted of 28 diabetics without diarrhea or other gastrointestinal symptoms. The average age of these patients was 44 years and the average duration of diabetes was 7 years. The other group consisted of 7 diabetics with diarrhea but without symptoms of other gastrointestinal disease. The average age of these patients was 48 years, and they had had diabetes on an average of 8 years. None of the patients studied had steatorrhea.

A special tube, described in detail elsewhere (4, 5), was used. The registering end was supplied with three openings in the same transversal plane. One opening led into an open, fluid-filled catheter. A small balloon protruded from another opening. This balloon was connected to another fluid-filled catheter in which there was a resting pressure of + 10 cm of water. Via these two catheters, pressure variations and differential pressures were measured, the latter with a modification of Ritchie et al's (6) technic. The third opening functioned as a suction-cup and contained two platinum electrodes (4). Pressure was transmitted to an electromanometer and potential variations to a universal amplifier where a time constant of 0.06 seconds and an upper limit frequency filter of 700 Hz were used in order to favorize registration of action potentials. These measurements were recorded on a Mingograf 81 together with a pneumogram (Fig 1), and a registration of the number of exposures was made in those short periods where cinematography was performed. The speed of the paper was 1 cm/sec.

Procedure

Subjects fasted from the evening before the studies were carried out. In the morning, the tube was passed through the mouth without anesthesia and inserted until the registering end was in the distal part of the duodenum. After a pause of one-half hour, activity was measured for 60 minutes during continued fasting, thereafter, for another hour after ingestion of a standardized, liquid test meal, and finally for one-half hour after intravenous administration of 0.005 mg prostigmine/kg body weight.

Tracing Evaluation

After all 35 patients had been studied, the tracings were evaluated and the various measurements performed. This was done randomly and blindly.

Enumeration of the number of pressure waves and measurements of the height and duration of the individual waves were carried out. Artifacts and pressure waves of less than 5 cm of water pressure were discarded. Thereafter, I determined for each individual person and for each individual 5-minute period, the number of pressure waves and their mean height and duration, together with an estimate of the total area of the pressure waves (the motility index)—ie, the sum of the numbers obtained by multiplying the height by the duration of each individual pressure wave.

As far as the differential pressure waves are concerned, I divided the material into five subgroups—those waves that were completely positive, those that were completely negative, those that were first positive and then negative, those that were first negative and then positive and finally those that were more complex. Thereafter, I counted the number during the period of fasting, the period after the test meal and the period after prostigmine.

As previously described (4), approximately 120 action potential bursts which were representative and as evenly distributed as possible were chosen from each patient. The height and duration of these waves were measured, and the mean values calculated for each patient for each of the three periods (4).

Finally, I measured the durations between the middle of the action potential bursts, the maximum of the accompanying pressure wave and the maximal oscillation of the accompanying differential pressure wave. Here I calculated the mean values for each patient for each period.

Statistical evaluation was done with the help of the following nonparametric tests: Mann-Whitney U test, Wilcoxon matched-pairs signed-ranks test, Kruskal-Wallis one-way analysis of variance, Sign-test, and χ^2 test (7, 8).

RESULTS

The number of pressure waves in diabetics with diarrhea was significantly greater than the number in diabetics without diarrhea both during fasting and after the test meal, but no difference could be demonstrated after prostigmine (Table 1).

The average height of the waves was greater during fasting in diabetics with diarrhea. There was no difference after the test meal and after prostigmine (Table 1). The average duration was the same in all three periods (Table 1). The motility index, which has been defined previously, was greater in diabetics with diarrhea in all three periods (Table 1).

Results of the enumeration of differential pressure waves is shown in Table 2. The number is given as the median of 1-hour values and the original figure from the prostigmine period was therefore multiplied by two. As shown in the table, no difference in the number of various types of differential pressure waves in the 2

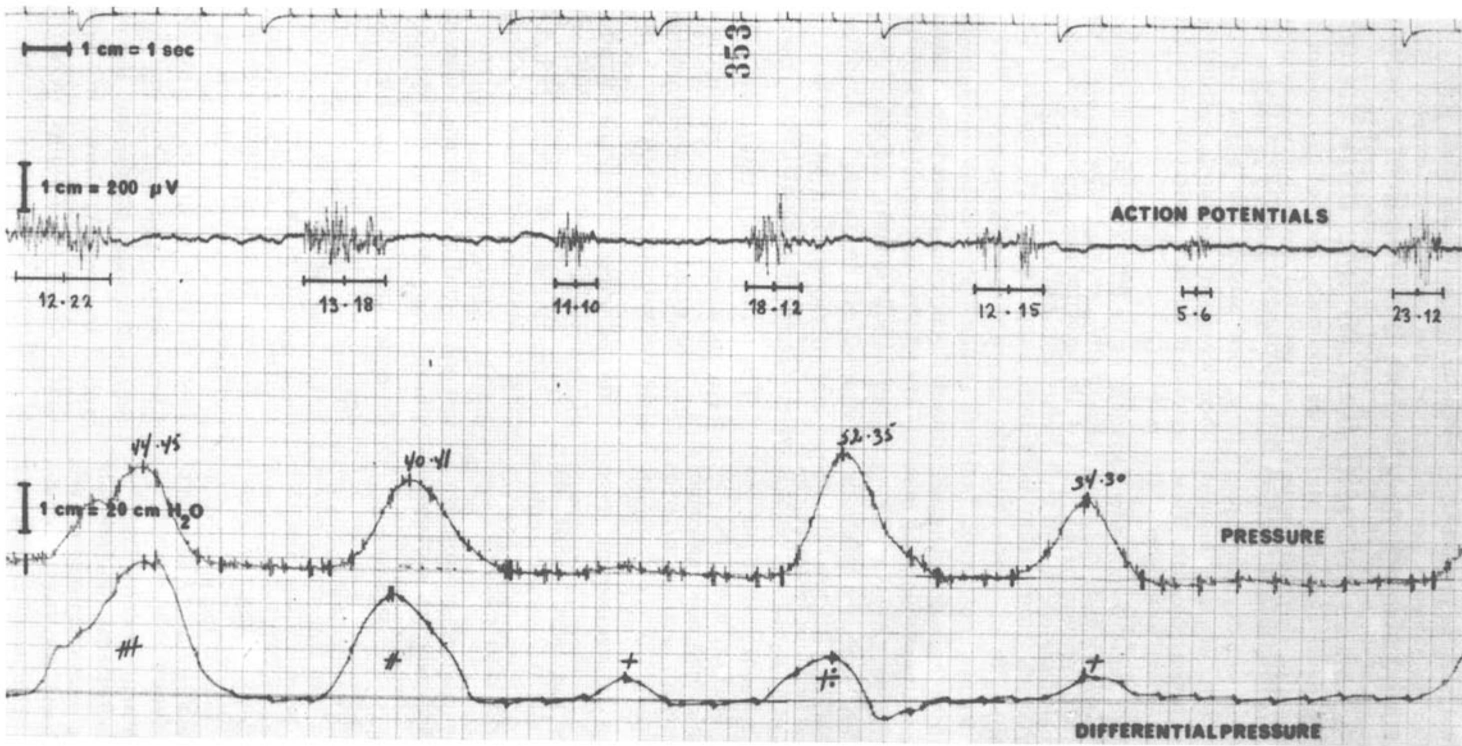

Fig 1. Action potentials, pressure waves and differential pressure waves.

Table 1. Pressure Waves in Diabetics With and Without Diarrhea

Pressure waves	Period of evaluation	Diabetics		Significance of difference between medians (*P*)
		With diarrhea	Without diarrhea	
Waves/5 min	Fasting	16.5	11	<0.01
	After test meal	24	21	<0.01
	After prostigmine	26.5	24	>0.05
Average height (cm of water)	Fasting	21	18	<0.05
	After test meal	24	24	>0.05
	After prostigmine	32	31	>0.05
Average duration (seconds)	Fasting	4.2	3.9	>0.05
	After test meal	4.6	4.4	>0.05
	After prostigmine	4.8	5.0	>0.05
Motility index	Fasting	1450	1050	<0.01
	After test meal	3250	2550	<0.05
	After prostigmine	5600	4450	<0.05

Median value for 5-minute periods.

Table 2. Differential Pressure Waves in Diabetics With and Without Diarrhea

Subgroup of differential pressure waves	Subperiod	Diabetics		Significance of difference between medians (*P*)
		With diarrhea	Without diarrhea	
Positive	Fasting	128	171	>0.05
	After test meal	127	207	>0.05
	After prostigmine	158	196	>0.05
Negative	Fasting	61	18	<0.01
	After test meal	97	25	<0.001
	After prostigmine	94	44	<0.01
Positive negative	Fasting	1	18	>0.05
	After test meal	4	30	>0.05
	After prostigmine	56	54	>0.05
Negative positive	Fasting	7	6	>0.05
	After test meal	20	15	>0.05
	After prostigmine	24	22	>0.05
Complex	Fasting	1	0	>0.05
	After test meal	0	0	>0.05
	After prostigmine	2	2	>0.05

Median values for 1-hour period.

groups of diabetics could be demonstrated, except that there were many more purely negative differential pressure waves in the diabetics with diarrhea. The increased appearance of negative differential pressure waves in diabetics with diarrhea was found in all three periods (Table 2).

The average duration of the action potential bursts was longer after prostigmine than during fasting ($P<0.05$) and after the test meal ($P<0.001$). The respective median values for the entire group of 35 individuals was 1.16, 1.06 and 1.05 seconds. No difference was found between diabetics with and without diarrhea, and no differences were found between the average heights of the action potential bursts.

The maximum height of the pressure waves appeared, on the average, slightly later than the maximal amplitude of the differential pressure wave in both the diabetics without diarrhea ($P<0.001$) and diabetics with diarrhea ($P<0.05$). The average time difference was less in individuals with diarrhea than in those without diarrhea ($P < 0.05$). In both cases, the time differences were, however, quite small—0.01 and 0.11 seconds, respectively.

In several patients, cinematography was performed, but for only short periods of time. Examination of the films has not contributed to the understanding of the differences shown between diabetics with and without diarrhea.

DISCUSSION

There are only a few studies of gastrointestinal motility in diabetics with diarrhea (2–4, 9–14). Furthermore, in the majority of existing reports, either only a very few patients have been investigated (10, 11) or intestinal motility has been estimated using only transit times or more or less quantitative measures with the help of radiologic technics (12–14). The results of many of these motility studies have been directly contradictory, and with few exceptions, have contributed little to the understanding of the pathogenesis of so-called diabetic diarrhea.

The present study showed that intestinal motility was altered in diabetics with diarrhea compared with diabetics without diarrhea. Diabetics with diarrhea had more and stronger pressure waves during fasting, more pressure waves after a test meal and a greater total amount of motor activity—judged from the previously mentioned motility index—during fasting, after a test meal and after prostigmine.

In addition, it appeared that there was not only a quantitative change in pressure variations in the intestine, with an increased number of pressure waves of increased strength, but also a change in the character of the motility as manifested by a marked increase in the number of negative differential pressure waves. Thus, not only were there quantitative variations from the normal, but there was also an altered reaction pattern. This was also evidenced by the, admittedly quite small, differences between the average distances between the pressure waves and the differential pressure waves.

No comparable published reports are available on studies of diabetics with diarrhea where pressure variations in the intestine were measured with the use of open catheters and the results given. However, there are studies where intestinal motility has been estimated on the basis of pressure variations in balloon catheters and where, in addition, balloon catheters have been used to investigate the reaction of the intestine to distension. Whalen et al (2) studied 8 diabetics with diarrhea during fasting and compared them with 12 control subjects. These investigators were unable to demonstrate significant differences in intestinal tone, the fraction of time occupied by phasic small waves or the frequency and duration of large waves.

At first sight, these results seem to indicate that changes in intestinal motility did not occur, but this kymographic study can obviously not be compared to that portion of the present study where motility was estimated by measuring intraluminal changes in pressure. This is also the case in the work of McNally et al (3) who studied 8 control subjects, 24 diabetics without diarrhea and 4 diabetics with chronic diarrhea during fasting. Neither were these investigators able to demonstrate changes in the frequency of small waves in the small intestine in the 4 diabetics with diarrhea; however, they indicated that there was an increased number of large waves and that the amplitude of these waves appeared to be increased.

In both studies (2, 3), the reaction of the intestine to distension was also investigated. Whalen et al (2) studied this by distending a thick-walled, rubber balloon in the jejunum. In 4 diabetics with diarrhea, they found that none of these patients felt pain even when the balloon was distended far beyond the point that produced pain in the 8 control subjects ($P<$ 0.01). This was interpreted to show decreased or absent visceral pain response in the jejunum in diabetic diarrhea. McNally et al (3) investigated the volume which could be injected into the balloon before the small bowel wall contracted. Among the diabetics studied, this volume was largest in the 4 that had diarrhea. These findings can probably be related to my finding of an increased occurrence of negative differential pressure waves in diabetics with diarrhea. All three findings can be explained by the observation that the response of the small bowel to distension is reduced in diabetics with diarrhea, so that the bowel wall in these patients can be distended to a greater degree without producing a reaction.

Whalen et al's (2) work should also be noted, because nonparametric statistical methods were used as in the present study. Admittedly, this is not necessary in all cases, but preliminary studies and studies of the values given in the literature showed very clearly that conditions for the use of more conventional methods were not present in many cases (5). For instance, it became apparent that the number of pressure waves per time unit was neither distributed normally nor distributed according to any other commonly known distribution—unless very long periods of registration were used. A more or less corresponding situation was present as far as several other parameters were concerned—eg, height of pressure waves and motility index. There can be no doubt that this is of great importance and that nonparametric statistical methods should be used to a greater degree. These methods have, up to now, only seldom been used in motility studies.

In the present investigation, a randomized blind technic was used in evaluating the registration curves after all of them had been recorded. All investigators of motility know that evaluation of curves is very difficult and can be quite subjective. This not only makes it difficult to compare results obtained by various groups, but also the curves evaluated by the same investigator. This is particularly the case with precise motility studies—eg, measurements of the duration of pressure waves; but it is also the case with comparisons between the number of pressure waves, and with comparative evaluations of action potential bursts. The time factor, in particular, but also the possible knowledge of the origin of the individual curves and numerous other factors, usually make it advisable to use a randomized, blind technic in comparative investigations, unless a mechanical reading makes this superfluous. To date, there are practically no clinical studies which fulfill these criteria.

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