Viscosity of gastric mucus in duodenal ulceration

JOHN R. N. CURT AND ROBERT PRINGLE

From the Department of Surgery, University of Dundee

SUMMARY A preliminary study of the rheological behaviour of visible gastric mucus in patients with duodenal ulcer and in controls indicates that duodenal ulceration is associated with an increase in the viscosity of visible gastric mucus.

The methods of measuring the viscosity of gastric mucin are described and the limitations of simple capillary viscometry are discussed.

Several theories are advanced which may account for the findings described in this investigation.

Very few studies of the viscosity of gastric mucus have been performed. Janowitz and Hollander (1954) measured the viscosity of cell-free canine gastric mucus using an Ostwald-Fenske viscometer. Zalaru (1966) determined the viscosity of human gastric mucus using a modification of the Ubbelohde viscometer. In both instances the viscometers used are ideally suited to the measurement of Newtonian fluids. In recent years a greater understanding of the problems of measuring viscosity has led to the development of instruments which provide a more accurate means of determining the behaviour of non-Newtonian substances. Since mucin is a suspension of macromolecules in a fluid matrix its behaviour is non-Newtonian and this must be taken into account when selecting an instrument to measure its viscosity. In this investigation the viscosity of gastric mucus in a group of patients with duodenal ulcer and in a group of controls was determined using a rotating cone-in-plate microviscometer.

PATIENTS AND METHODS

Ten patients with duodenal ulcer were investigated and 12 patients who had no history of gastric or duodenal disease or dyspepsia were used as controls. Each patient was fasted for 12 hours and the resting gastric juice was then aspirated and discarded. One hour later the stomach was again aspirated and the material obtained was centrifuged at 4,000 rpm for 15 minutes. The supernatant containing acid and the soluble gastric mucin was discarded and the residue of insoluble gastric mucus was used for the estimation of viscosity. Patients were asked to abstain from swallowing saliva or sputum during the hour preceding aspiration.

Viscosity was measured at 37°C in a Wells-Brookfield microviscometer (Fig. 1). The viscometer consists of a rotating cone-in-plate surrounded by a thermostatically controlled water jacket. Of the insoluble gastric mucus,

1.5 ml was placed in the head of the instrument (Fig. 2). Readings were made at 1.15, 2.30, 5.75, 11.50, 23.00, 46.00, 115.00, and 230.00 sec⁻¹ respectively. A rheogram was then constructed of the viscosity and shear rate of each specimen (Fig. 3). Duplicate measurements of viscosity were performed on each patient. Only clear specimens were used. Any specimen contaminated with bile or

FIG. 1. *The Wells-Brookfield microviscometer.*

FIG. 2. *The head of the instrument.*

blood was discarded as unsuitable since these contaminants would affect viscosity. The observations were made within a few minutes of obtaining the material as it was felt that delay might prejudice the accuracy of the viscosity measurement.

FIG. 3.

FIG. 3. *Rheogram of visible gastric mucus from a patient with duodenal ulceration. Viscosity is expressed in centipoises (Cp) and shear rate in inverse seconds (sec⁻¹).*

FIG. 4. *Composite rheogram of the mean results in duodenal ulcer patients and controls.*

RESULTS

The results are shown in Table I. In order to compare the results in the two groups the standard deviation was calculated for each shear rate. Since the numbers involved were small (27 patients) the 't' distribution was used to evaluate probability. The mean of the results in each group is shown in Figure 4.

The results of the present investigation have shown that the viscosity of visible gastric mucus is significantly greater in the group of patients with duodenal ulcer when compared with the control group. The difference is significant at all rates of shear smaller than 46.00 sec^{-1} ($P < 0.05$ at 29.00 sec^{-1} to $P < 0.001$ at 1.15 sec^{-1}).

DISCUSSION

The viscosity of a substance is defined as the ratio of shear stress to shear rate. Viscosity is therefore the resistance to shear (flow) of a fluid. By plotting shear stress and shear rate it is possible to study the behaviour of a substance. This graph is known as a rheogram. In the case of simple solutions the relationship between shear stress and shear rate is linear and the solution is known as a Newtonian fluid. This type of fluid can be investigated by using a capillary viscometer. Where the shear stress shear rate ratio is non-linear the behaviour of the substance is non-Newtonian. In order to measure with

FIG. 4.

TABLE I

COMPARISON OF VISCOSITY RESULTS EXPRESSED IN CENTI-POISES IN PATIENTS WITH DUODENAL ULCER AND CONTROLS AT DIFFERENT RATES OF SHEAR

Group	Shear Rate (Sec ⁻¹)							
	1.15	2.30	5.75	11.50	23.0	46.0	115.0	230.0
<i>Duodenal ulcer</i>								
1	280	200	92	76	51	32	19	10
2	216	120	50	32	21	14.5	9.6	8.4
3	90	50	32.5	18	12.5	10	10	7.8
4	300	150	70	42	28	15.5	14.2	9.6
5	290	160	80	53	36	27.5	20	10
6	300	180	80	44	30	23.5	17	10
7	460	280	98	52	30	17.5	9.4	6.7
8	58	26	11.2	5.6	3.6	2.8	2.9	1.7
9	130	70	36.8	24	17	13	9	10
10	170	95	46	33	22	18	15	10
Mean	229.4	133.1	59.7	38.0	25.1	17.7	12.6	8.4
<i>Control</i>								
1	120	75	48	35	30	25.5	20	10
2	90	50	32	20	15	12.5	10.4	9.2
3	76	38	18	10	7.5	4.7	2.8	2.9
4	60	35	28	25	23	18.5	12	8
5	168	84	44	27	18	12.7	8.6	6.9
6	90	52	28	17	11.5	8.5	6	6.3
7	90	50	32	20	15	12.5	10.4	9.2
8	50	30	10.4	7	5	3.6	2.6	2.6
9	60	35	48	40	30	31	18	10
10	150	75	36	21.6	14.3	10	6.5	5
11	50	30	12.8	8	4.5	3.2	2.2	2.1
12	12	9	4.8	3	2.5	1.6	1.3	1.2
Mean	84.6	46.9	28.5	19.5	14.8	12.3	8.4	6.1

precision the viscosity of non-Newtonian substances an instrument which measures both shear stress and shear rate must be used. There are several varieties of non-Newtonian behaviour. It can be a 'dilatant' material in which the viscosity increases as the shear rate increases. 'Plastic' and 'pseudo-plastic' materials are similar in behaviour in that the viscosity falls as the shear rate increases. However, in 'plastic' materials a certain force must be applied before any movement is produced. This force is known as the 'yield force' or 'yield value' of the substance.

Mucus is a non-Newtonian substance in that it shows a changing viscosity in response to changing rates of shear. It therefore behaves as a 'pseudo-plastic' material because its viscosity decreases with increasing rates of shear. It is also 'thixotropic' as the viscosity at any particular rate of shear depends on the amount of previous shearing it has undergone. This last characteristic is reversible and therefore differentiates 'thixotropy' from such other physical changes in mucus which might occur with degradation or increase in temperature. If these thixotropic materials are allowed to stand for a variable period the viscosity reverts to its former value. From the foregoing it is obvious that in order to measure the viscosity of a complex substance, such as mucus, a viscometer which measures shear stress at different rates of shear must be used.

Capillary viscometers cannot demonstrate the behaviour of the substance under examination and indeed they measure only one point on the viscosity curve. Blanshard (1955), in England, pioneered the use of the rotational cone-plate viscometer for studying the viscosity of sputum and he demonstrated that the viscosity decreased with increasing rates of shear. It has been shown in this investigation that visible gastric mucus has characteristics similar to sputum and behaves as a 'pseudo-plastic' substance.

In 1908, Kaufmann first suggested the idea of investigating the qualities of gastric mucus in relation to the aetiology of peptic ulcer. Glass (1953) defined visible mucus as a complex gel composed of mucoid substance, water, electrolytes, enzymes, and shed cellular elements from the surface epithelial lining of the stomach. The mucinous fraction consists of polymers of glycoprotein molecules which, by their high molecular weight, impart high viscosity to gastric mucus. Waldron-Edward and Skoryna (1964) and many others demonstrated that the mucinous fraction has a relatively high blood group activity. Glass (1962) showed that the titres of blood group substances generally decrease with increasing acid secretion. The observations that duodenal ulcer is much commoner in blood group O individuals (Aird, Bentall, Mehigan, and Roberts, 1954) and in non-secretors of blood group substances in saliva and gastric juice (Clarke, Wyn-Edwards, Haddock, Howel-Evans, McConnell, and Sheppard, 1956) lend further support, if any is needed, to the need for further investigation of the so-called protective action of the 'mucous barrier'. The blood group substances in gastric mucus are mucopolysaccharides of high viscosity and are the only substances in the body containing L-fucose.

It is tempting to assume that the fucose content of gastric mucus is of importance in the aetiology of peptic ulceration, but Hoskins and Zamcheck (1965) found that the fucose content did not correlate with the subject's age, sex, or with the degree of gastric acidity. It is also known that Lewis (Le^a) substances in the surface epithelium of the gastric mucosa of non-secretors contain the same amount of L-fucose as the ABH blood group substances in secretors (Glass, 1962). Evans (1960) demonstrated that the quantity of blood group substances present in saliva is not related to the secretor status and/or ABO grouping. Most studies of gastric mucus have been biochemical and very few investigations of the physical nature of gastric mucin have been undertaken, especially with reference to the problem of duodenal ulcer. We feel that the viscosity of gastric mucus must be important in the concept of the 'mucous barrier' in that the more viscous the mucus

is, the more it clings to the mucosa. This fact was well demonstrated by Wolf and Wolff (1948) by direct observation of the gastric mucosa. The finding in this initial study that there is a significant increase in the viscosity of visible gastric mucus in patients with duodenal ulcer is totally unexpected and is very difficult to explain in terms of the theory of the protective action of gastric mucus. Consideration of the various factors involved leads to several possible explanations.

The increase in viscosity in patients with duodenal ulcer may be simply a defensive mechanism to protect the gastric mucosa from the hyperacidity which is present in these patients. Several workers (Bucher, 1932; Mahlo, 1938; Webster and Komarov, 1932) have shown that gastric mucus is rendered more viscous as acidity is increased. Miller and Dunbar (1933) suggested that the contact of gastric juice with the alkaline mucus produced isoelectric and acid mucinate resulting in an increase in viscosity and that this retards diffusion of hydrochloric acid and pepsin through the layer of mucus. This results in a progressive increase in pH towards the surface of the epithelial lining of the gastric mucosa. A second theory is that the duodenum is protected from ulceration in normal circumstances by gastric mucus washed off the gastric mucosa and if this mucus is very tenacious the duodenal mucosa is more readily exposed to the ulcerogenic properties of hyperacidity. The authors feel that the most likely and in many ways the most attractive explanation is that the presence of thick, tenacious mucus covering the antral mucosa may block the pH receptors and in doing so prevent the normal mechanism of inhibition of secretion from taking place. There is evidence to support this theory. Woodward, Lyon, Landor, and Dragstedt (1954) have shown that increasing acidification of the antral contents produces an inhibition of gastric acid secretion. Overholt and Pollard (1968) have shown by instilling 110 ml of acid solution into the stomach that there is a marked diffusion of H⁺ ions into the gastric mucosa of gastric ulcer patients, but no change in patients with duodenal ulcer. It is generally accepted that duodenal ulcer is associated with increased vagal tone (Dragstedt, 1954) resulting in hyperacidity and hypermotility of the stomach. If antral inhibition of gastric acid secretion is absent

due to a thick covering of viscid mucus then the first part of the duodenum would be exposed to the continual effect of undiluted gastric juice, especially when the stomach is empty.

Obviously a great deal of research must be undertaken into the physical behaviour of the various components of gastric mucus and the relevance of this behaviour to the pathogenesis of duodenal ulcer.

REFERENCES

- Aird, I., Bentall, H. H., Mehigan, J. A., and Roberts, J. A. F. (1954). The blood groups in relation to peptic ulceration and carcinoma of colon, rectum, breast, and bronchus. *Brit. med. J.*, 2, 315-321.
- Blanshard, G. (1955). Viscometry of sputum. *Arch. Midx. Hosp.*, 5, 222-241.
- Bucher, R. (1932). Das Wesen der Schutzwirkung des Magenschleims. *Dtsch. Z. Chir.*, 236, 515-559.
- Clarke, C. A., Edwards, J. W., Haddock, D. R. W., Howel-Evans, A. W., McConnell, R. B., and Sheppard, P. M. (1956). ABO blood groups and secretor character in duodenal ulcer. *Brit. med. J.*, 2, 725-731.
- Dragstedt, L. R. (1954). The etiology of gastric and duodenal ulcers. *Postgrad. Med.*, 15, 99-103.
- Edward, D. W., and Skoryna, S. C. (1964). Properties of gel mucin of human gastric juice. *Proc. Soc. exp. Biol. (N.Y.)*, 116, 794-799.
- Evans, D. A. P. (1960). The fucose and agglutinin contents of saliva in subjects with duodenal ulcers. *J. Lab. clin. Med.*, 55, 386-399.
- Glass, G. B. J. (1953). The derivation and physiological significance of the glandular mucoprotein in human gastric juice. *J. nat. Cancer Inst.*, 13, 1013-1024.
- (1962). Biologically active materials related to gastric mucus in the normal and in the diseased stomach of man. *Gastroenterology*, 43, 310-325.
- Hoskins, L. C., and Zamcheck, N. (1965). Studies on gastric mucus in health and disease. II. Evidence for a correlation between ABO blood group specificity, ABH(O) secretor status, and the fucose content of the glycoproteins elaborated by the gastric mucosa. *Ibid.*, 48, 758-767.
- Janowitz, H. D., and Hollander, F. (1954). Viscosity of cell-free canine gastric mucus. *Ibid.*, 26, 582-591.
- Kaufmann, J. (1908). Lack of gastric mucus (amylorrhoea gastrica) and its relation to hyperacidity and gastric ulcer. *Amer. J. med. Sci.*, 135, 207-214.
- Mahlo, A. (1938). *Der Magenschleim*, Stuttgart, F. Enke.
- Miller, C. O., and Dunbar, J. M. (1933). Change in viscosity of mucin pH. *Proc. Soc. exp. Biol. (N.Y.)*, 30, 627-629.
- Overholt, B. F., and Pollard, H. M. (1968). Acid diffusion into the human gastric mucosa. *Gastroenterology*, 54, 182-189.
- Webster, D. R., and Komarov, S. A. (1932). Mucoprotein as a normal constituent of gastric juice. *J. biol. Chem.*, 96, 133-142.
- Wolf, S., and Wolff, H. G. (1948). Studies on mucus in the human stomach: estimation of its protective action against corrosive chemicals applied to the gastric mucosa and attempts at quantitation of gastric mucin by two chemical methods. *Gastroenterology*, 10, 251-255.
- Woodward, E. R., Lyon, E. S., Landor, J., and Dragstedt, L. R. (1954). The physiology of the gastric antrum: experimental studies on isolated antrum pouches in dogs. *Ibid.*, 27, 766-785.
- Zalaru, M. C. (1966). Research on the viscosity of gastric juice (Rumanian). *Med. interna (Buc.)*, 18, 89-98.