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A correlation between severity of migraine and delayed gastric emptying measured by an epigastric impedance method

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1 This study examined the ability of a bioimpedance method to detect the delay in gastric emptying which occurs during attacks of migraine.
2 In 64 non-migraineur control patients and 46 migraine patients outside an attack, gastric emptying rates were within the predicted normal range.
3 In contrast, rates in 14 migraineurs during 20 attacks were delayed during severe or moderate attacks and were significantly correlated with the intensity of headache, nausea and photophobia.
4 The epigastric impedance method was generally well tolerated by patients and appears to merit further investigation as a clinical method of monitoring gastric emptying of liquids.

Keywords gastric emptying epigastric impedance migraine

Introduction

The main practical reason for using bioimpedance methods for monitoring the volume of internal organs is their non-invasive nature. In addition, they are potentially highly sensitive and accurate (Brown, 1983; Schwann & Ferris, 1968). In recent years improvements in technology and electrodes has led to renewed interest in their capabilities. In cardiology for example, comparisons with established methods of measuring stroke volume have validated the bioimpedance approach in spite of the difficulty of calibrating the method with nomograms (Appel & Shoemaker, 1988; Bernstein, 1986).

In gastroenterology an epigastric impedance method produced comparable rates of gastric emptying with a scintigraphy method (Sutton *et al.*, 1985), dye dilution (McClelland & Sutton, 1985) and paracetamol absorption (Sutton, 1989). In healthy volunteers the method detected contractions and the stimulant effect of metoclopramide (McClelland & Sutton, 1985). In neonates it has detected the effect of increased viscosity on gastric emptying rates (Smith *et al.*, 1989).

Bioimpedance values at the surface bear a direct, linear relationship to the volume of internal organs provided that the specific impedance of the organ remains constant. Current densities are too small to produce deleterious tissue effects (Pethig, 1979). Brown (1983) has calculated that they are an order of magnitude less than would depolarise a neuronal synapse. Accordingly, it appears that epigastric impedance may be suitable for patients with marked symptoms of gastric malfunction, such as nausea and bloating. Indeed, it has been used in diabetic neuropathy patients with these symptoms, when it was found to detect unusually slow rates of gastric emptying (Gilbey & Watkins, 1987).

Gastric emptying is delayed during migraine attacks (Kaufmann & Levine, 1936) such that it reduces absorption of analgesics (Flavell-Matts, 1974). Accordingly, this study was designed to show whether an epigastric impedance method would detect delayed gastric emptying in migraine patients undergoing an attack.

Methods

Studies took place in the Institute of Neurological Sciences at The Southern General Hospital,

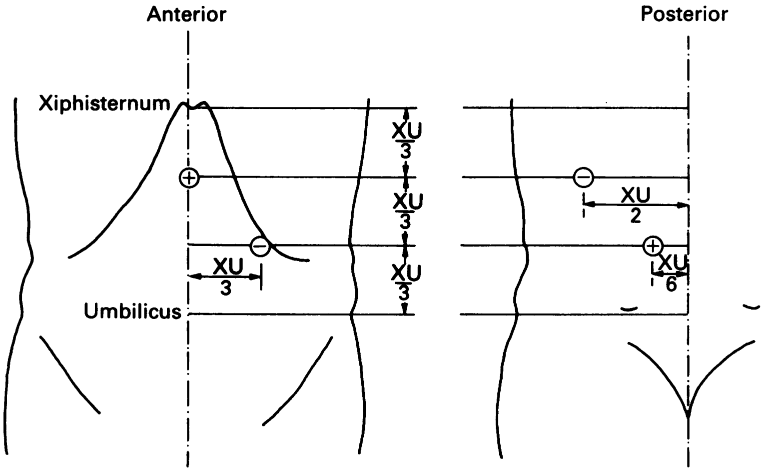

Figure 1 Electrodes were positioned by reference to the xiphisternum (X) and umbilicus (U). One of two input electrodes (+) was placed anterior to the stomach and one posteriorly. A similar configuration was used for detector electrodes (−).

Glasgow with the sanction of the institutional ethics review committee. Non-migraine controls were patients admitted to the institute for investigation of symptoms unrelated to the gastrointestinal tract. They had no history of recent trauma, spinal injury or psychiatric disorder known to be associated with delayed gastric emptying (Cooke & Christensen, 1978; Dubois, 1979; Malagelada, 1982).

The equipment has been described previously (McClelland & Sutton, 1985; Sutton, 1989). It provided a 4 mA peak to peak current oscillating at 100 kHz which was applied through two silver-silver chloride input electrodes. Two similar electrodes were placed on the skin of the abdomen and back to detect current fluctuations. Electrode positions are described in Figure 1. Separate input and output electrodes provide a more stable electrical contact with the skin due to less susceptibility to polarization effects and local current distortions than a common input-output array (Schwann & Ferris, 1968).

After amplification current fluctuations were displayed on a Bryans flatbed chart recorder. This produced traces similar to Figure 2. The trace is broadened by respiratory movements which occasionally include sharp spikes due to coughing etc. Two such spikes are visible in Figure 2 before the impedance increase due to the gastric filling. Traces return to baseline levels provided that the patient maintains his position.

All assessments were made after a minimum of a 4 h fast, by the same investigator (RB) in the 45° semi-recumbent position. The test 'meal' consisted of deionised water-orange flavoured

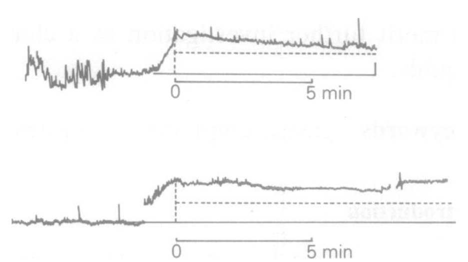

Figure 2 Epigastric impedance recordings. The y axis represents overall impedance (ohms). Time 0 is the point of maximal impedance increase due to the ingestion of orange squash. The upper trace records a normal gastric half emptying time of 7–8 min. The lower trace shows no tendency to revert to baseline, typical of delayed gastric emptying during a severe migraine attack.

squash (Quosh®) in the ratio 5:1 by volume. This has an osmolarity in the range 230–240 and a conductivity of 1.10 mSiemen (Sutton, 1989).

The size of deflection was measured on the chart by a ruler. The lower margin of the respiratory fluctuations was used throughout. The last point at which it recrossed the 50% full level was designated the 50% emptying time (*t*50%). This was measured along the x axis from the impedance peak, i.e.; the moment of maximum filling. A minimum of 10 min steady baseline record was obtained before the test meal was drunk, and, wherever possible, on return to baseline when the stomach had emptied. However, during several migraine attacks the trace did not return to baseline and recordings ceased after 30 or 60 min depending on the comfort of the patient. Such a recording is illustrated by the lower trace in Figure 2.

The intensity of attacks was judged subjectively on a 4 point scale: none, mild, moderate, severe. Nausea and photophobia were similarly assessed. Signs of pallor, neck stiffness etc were recorded by the observer.

Results

Summary demographic data for the 64 non-migraineur control patients and 46 migraineurs outside an attack are listed in Table 1 with group mean gastric *t*50%. There was a preponderance of females in the migraineur controls which was also found in the patient group. All gastric *t*50% results in these two groups were less than 30 min.

Subjective ratings of the severity of 20 migraine attacks in 14 patients with observer's comments and gastric *t*50% results are listed in Table 2. Pain ratings moderate or severe and the presence of nausea, vomiting or photophobia were associated with gastric *t*50% greater than 30 min in 12 of 13 attacks and in the 13th it was 29 min. When pain was recorded as mild *t*50% remained below 30 min, although on one occasion which included nausea, it reached 29 min.

Two patients were monitored during both severe to moderate and mild headache and produced gastric *t*50% in excess of 30 min only during the more severe attacks. In one patient two of five assessments were severe and showed markedly delayed gastric emptying which could only be classified as *t*50% greater than 60 min because there was no tendency to return to baseline. The patient had a normal emptying pattern during mild attacks.

Spearman's rank correlation coefficients and their statistical probabilities for *t*50% *vs* the intensity ratings of the three main symptoms severity ratings were as follows: pain intensity $r_s = 0.84$ ($P < 0.01$), nausea and vomiting $r_s = 0.52$ ($P < 0.05$), photophobia $r_s = 0.52$ ($P < 0.05$).

Discussion

We have found a significant correlation between the intensity of the migraine attack and gastric emptying times. This was most evident for pain intensity but included nausea or vomiting and photophobia. Outside an attack the 46 migraineur controls were indistinguishable from non-migraineur controls.

Our mean value for controls (9 ± 5 min, $n = 64$) is comparable with published values, although few are available for similar liquid meals. The meal is acid (pH 2.6–2.7) and acid delays gastric emptying (Hunt & Knox, 1972). Using a scintigraphy method Dooley and his colleagues (1984) found that water acidified with HCl to pH 2.0 emptied more slowly than water at neutral pH (respective $t_{1/2}$ mean values of 11 ± 2.1 and 2.2 ± 0.7 min, $n = 7$). By computerised ultrasound imaging Bateman & Whittingham (1982) concluded that cooling large volume liquid meals retards gastric emptying, but their slowest $t_{1/2}$ was 24.9 min ($n = 8$).

In over 100 bioimpedance estimations in 76 normal volunteers Sutton (1989) found only one *t*50% greater than 30 min. This exception was confirmed by simultaneous scintigraphy, the volunteer being anxious and therefore slightly stressed (Sutton *et al.*, 1985). Rainbird and her colleagues (1987) found epigastric impedance *t*50% values in medical student volunteers that were consistently less than 20 min, without circadian variation. Moreover, *t*50% in a supine posture did not increase beyond 30 min. In dia-

Table 1 Gastric emptying in migraineur and non-migraineur controls

Patient group	n	*Median age (years)*	*% female*	*Mean gastric t50% (± s.d.) (min)*
Non-migraineur				
1st assessment	64	31	47	8.7 (4.9)
2nd assessment	10	22.5	50	12.3 (5.9)
3rd assessment	7	23	55	10.0 (7.0)
Migraineur outside an attack	46	25.5	76	10.1 (5.3)

There was no significant difference between non-migraineurs, including repeated assessments, and migraineurs outside an attack.

Table 2 Gastric emptying times and subjective ratings of pain, nausea and photophobia during 20 migraine attacks

Patient	*Sex*	*Age (years)*	*Pain score*	*Photo-phobia*	*Nausea vomiting*	*Gastric t50% (min)*	*Gastric t50% rating 1–3*	*Observer comments*
1	F	39	3	1	3	>60	3	Pain 24 h constant
1			3	2	2	>60	3	Pain 48 h constant
2	F	16	3	2	3	>30	3	Vomited during test
3	F	43	3	3	3	>30	3	Dizzy, drank 300 ml only
4	F	23	3	3	3	>30	3	Distressed, drank 200 ml
5	M	48	2	3	2	>30	3	Stiff neck & shoulders
6	F	43	2	0	1	>30	3	None
7	F	23	2	1	1	50	3	Stiff neck & shoulders
8	M	24	2	2	2	>30	3	Stiff neck & shoulders
9	F	42	2	1	1	>30	3	None
1			2	3	3	29	2	Loss of balance
10	F	27	2	1	1	>30	3	Attack had lasted 24 h
11	M	34	2	0	1	>30	3	Stiff neck & shoulders
1			1	0	2	12	1	Pain 'almost gone'
1			1	2	1	22	2	Pain 24 h, subsiding
11			1	0	1	29	2	Mild attack
12	M	47	1	0	0	12	1	Headache began 24 h ago
12			1	0	0	9	1	None
13	F	44	1	0	0	17	2	Pallor ++
14	F	14	1	0	0	6	1	Mild attack, wearing off

Spearman's rank coefficient, $r_s = 0.84$ for gastric *t*50% *vs* pain intensity ($P < 0.01$), $= 0.52$ for nausea and vomiting ($P < 0.05$) and 0.52 for photophobia ($P < 0.05$).
Further refinement of gastric rating stratification did not change the value of r_s.

betic patients with autonomic neuropathy a similar threshold of 30 min separated patients with and without symptoms of gastric involvement (Gilbey & Watkins, 1987).

In theory, impedance methods are highly accurate and sensitive (Brown, 1983; Geddes & Baker, 1967; Murray, 1981) but a possible source of error is that gastric secretions may reduce the conductivity of gastric contents. This would reduce total surface impedance and, in this system, produce an artificially rapid emptying rate. However, Sutton (1989) found that blocking acid secretion with histamine H_2-receptor blockers did not increase *t*50% in normal volunteers and there was no correlation between *t*50% and the conductivity of gastric aspirates. Possible explanations may be that the simple, crystalline test 'meal' does not provoke sufficient secretions. Alternatively, the current pathway may be circumferential rather than through the stomach, at least until a threshold of total gastric conductivity is reached.

A second source of error may be fluctuations in skin conductivity related to stress during migraine attacks. For example, sweating would reduce the resistance at the surface but, from the use of silver-silver chloride electrodes in other monitoring systems, this effect appears to be overcome by the excellent contact provided by correctly applied electrodes. Blood flow through the skin may also fluctuate during stress, but this would produce very small changes compared with the increases seen during gastric filling, which are of the order of an ohm. The stressed volunteer reported by Sutton *et al.* (1985), whose delay in gastric emptying was detected by both bioimpedance and scintigraphy suggests that stress will not impair the ability of epigastric impedance to monitor the volume of the stomach.

A completely non-invasive method may be used repeatedly, which is essential for monitoring the progress of disease or the effect of treatment. Epigastric impedance requires subjects not to move the torso and to swallow a test meal of at least 300 ml which we thought might prove difficult for patients experiencing nausea and bloating. In the event patients tolerated these restrictions well although one who experienced dizziness and one who was distressed could not swallow more than 300 and 200 ml.

While the nature of the experiment precluded making measurements by a second method by which to confirm individual results, the correlation with severity of attack suggests that epigastric impedance differentiates normal from abnormal results. This combined with its non-invasiveness and relatively undemanding methodology leads us to conclude that its potential as a clinical monitoring technique is worthy of further exploration.

References

Appel, P. L. & Shoemaker, W. C. (1988). Non-invasive monitoring systems for acute care. *Anesthesiology*, **68**, 43–46.

Bateman, D. N. & Whittingham, T. A. (1982). Measurement of gastric emptying by real time ultrasound. *Gut*, **23**, 524–527.

Bernstein, D. P. (1986). Continuous, non-invasive, real-time monitoring of stroke volume and cardiac output by thoracic electrical bioimpedance: Theory and rationale. *Crit. Care Med.*, **14**, 898–901.

Brown, B. H. (1983). Tissue impedance methods. In *Imaging with non-ionising radiations*, ed. Jackson, D. F., pp. 85–110. Guildford: Surrey University Press.

Cooke, A. R. & Christensen, J. C. (1978). Motor functions of the stomach. In *Gastrointestinal disease*. 2nd edition, eds Sleisenger, M. S. & Fordtran, J. S., p. 637. Washington: W. B. Saunders and Co.

Dooley, C. P., Reznik, J. B. & Valenzuela, J. E. (1984). Variations in gastric and duodenal motility during gastric emptying of liquid meals in humans. *Gastroenterology*, **87**, 1114–1119.

Dubois, A. (1979). Pathophysiology of gastric emptying; methods of measurement and clinical significance. *J. clin. Gastroenterol.*, **1**, 256–266.

Flavell-Matts, S. G. (1974). Metoclopramide in the treatment of migraine. *Practitioner*, **212**, 887–890.

Geddes, L. A. & Baker, L. E. (1967). The specific resistance of biological material; a compendium of data for the biomedical engineer and physiologist. *Med. and Biol. Eng.*, **5**, 271.

Gilbey, S. G. & Watkins, P. J. (1987). Measurement by epigastric impedance of gastric emptying in diabetic autonomic neuropathy. *Diabetic Medicine*, **4**, 122–126.

Hunt, J. N. & Knox, M. T. (1972). The slowing of gastric emptying by four strong acids and three weak acids. *J. Physiol. (London)*, **222**, 187–208.

Kaufman, J. & Levine, I. (1936). Acute gastric dilatation of the stomach during an attack of migraine. *Radiology*, **27**, 301–302.

Malagelada, J.-R. (1982). Gastric emptying disorders. Clinical significance and treatment. *Drugs*, **24**, 353–359.

McClelland, G. R. & Sutton, J. A. (1985). Epigastric impedance; A non-invasive method for the assessment of gastric emptying and motility. *Gut*, **26**, 607–614.

Murray, P. W. (1981). Field calculations in the head of a newborn infant and their application to the interpretation of transcephalic impedance measurements. *Med. Biol. Eng. Comput.*, **13**, 538–546.

Pethig, R. (1979). *Dielectric and electronic properties of biological materials*. Chichester, UK: John Wiley and Sons.

Rainbird, A. L., Pickworth, M. J. W., Lightowler, C., Mitchell, M. & Wingate, D. L. (1987). Effect of posture and cold stress on gastric emptying measured by the method of epigastric impedance. *Pharm. Med.*, **2**, 35–42.

Schwann, H. P. & Ferris, C. D. (1968). Four electrode, null techniques for impedance measurements with high resolution. *Rev. Sci. Instrumen.*, **39**, 481–485.

Smith, H. L., Hollins, G. W., Newell, S. J. & Booth, I. W. (1989). Epigastric impedance studies: A clinically useful method for measuring gastric emptying in children. *Gut*, **29**, 1475–1476.

Sutton, J. A. (1989). *Epigastric impedance; A novel, non-invasive method of measuring gastric emptying*. M.D. Thesis, London University.

Sutton, J. A., Thompson, S. & Sobnack, R. (1985). Measurement of gastric emptying rates by radioactive isotope scanning and epigastric impedance. *Lancet*, **i**, 898–900.

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