EDITORIAL

PEPTIC ULCER DISEASE AND ITS COMPLICATIONS

Peptic ulceration commonly involves the stomach, duodenum and lower oesophagus, and after gastric surgery, the gastro-enterostomy stoma. Collectively these afflictions go under the term peptic ulcer disease (PUD). This condition is common in East Africa, according to reports from Eldoret (1) and Nairobi (2) and a major cause of morbidity and mortality. Although the pathophysiology is still not fully understood we know that bacterial, host, environmental and pharmacological factors play a role in varying proportions in the causation and propagation of this disease and these can be classified as aggressive when they promote ulcer formation or defensive if they protect gastro-duodenal mucosa and advance healing (3). Aggressive factors which predispose to gastric and duodenal ulceration act by causing breakdown of the barrier that normally prevents irritation and autodigestion of the mucosa by the gastric secretions. Three of these are gastric acid, infection with *Helicobacter pylori* and use of non-steroidal anti-inflammatory drugs (NSAIDs). Gastric acid is produced by the parietal (oxyntic) cells in the glands of the body and fundus of the stomach, which also produce the intrinsic factor. These glands also contain chief (zymogen, peptic) cells which secrete pepsinogens. Infection with the bacterium *H. pylori* disrupts the protective barrier and predisposes to PUD while aspirin and other NSAIDs promote PUD by inhibiting the production of prostaglandins and a decrease in mucus and HCO_3 secretion. NSAIDs are widely used to combat pain in a variety of clinical settings.

Several mechanisms are important in the protection of the mucosa from ulceration, and they are either natural or pharmacological (4). The former include mucus, bicarbonate, prostaglandins, depth of the gastric pits and trefoil peptides, and together form the mucosal barrier. Mucus consists of a glycoprotein containing mucins which form a flexible gel coating the mucosa and is produced by glands in the pyloric and cardiac regions of the stomach which also produce bicarbonate. Prostaglandins stimulate mucus and HCO_3 secretion. The deep gastric pits play a protective role since hydrochloric acid with a pH of 1 produced deep in these pits is neutralised by mucus and HCO_3 before reaching the surface. There are also trefoil peptides in the mucosa which are protective. Drugs play a protective role by inhibition of gastric secretion, with the main ones in current use being H_2 histamine receptor antagonists, proton pump inhibitors, antibiotics against *H. pylori*, and misoprostol which is discussed below.

Because of our better understanding of the above, management of PUD has changed considerably and today PUD sufferers can look forward to better treatment and outcomes than did their counterparts of half a century ago. It is pertinent to review some of the factors which have changed our view of this disease. Long before current therapy was established the incidence of PU and admissions for uncomplicated DU had been dropping in the USA (3). This was due to better general health, protection of the stomach and duodenal mucosa through better eating habits, diet and campaign against ulcerogenic habits such as taking of alcohol and caffeine, reduced smoking and use of antacids. An even more important contributor to change of management of PUD was progress in the pharmaceutical research which led to introduction of newer and more effective remedies, aimed at reducing gastric acid secretion, which has long been known to be a major contributor to PUD. Three groups of these drugs are worth of mention. First was introduction of H_2-receptor antagonists like ranitidine and cimetidine which reduce gastric acid secretion as a result of histamine H_2 receptor blockade. Ranitidine was shown to give superior results over previous therapy in the treatment of peptic ulceration in Kenyans (5) and is still widely used. This was followed by the protein pump inhibitors such as omeprazole and esomeprazole which decrease gastric acid output by blocking ATP dependent hydrogen-potassium system, also known as the proton pump of the gastric parietal cell (6). Use of highly selective inhibitors of cyclo-oxygenase-2 such as celecoxib (Celebrex) in place of the more ulcerogenic non steroidal anti-inflammatory drugs was yet another pharmacological step in the reduction of peptic ulcer disease since they have been shown to have a lower risk of serious upper gastrointestinal events. However their use has been somewhat limited by concerns about their cardiovascular safety and are contraindicated in ischaemic heart disease, cerebro-vascular disease, peripheral arterial disease and heart failure (7).

The real revolution in the understanding and management of PUD occurred 25 years ago when Marshall and Warren (who spent an agonising period trying to prove their discovery to sceptical and unconvinced medical colleagues)

showed the link between the bacteria *H. pylori* and PUD (8). Their work profoundly changed our knowledge of and approach to PUD, introducing antibiotic therapy to the management of the disease and drastically reducing complications (9). In Kenya, Ogutu *et al* (10) showed the association between PUD and *H. Pylori.* Early in the 1980s upper GI endoscopy was introduced in Kenya and it proved safe and more accurate than both clinical examination and barium meal for diagnosing of diseases of the upper GIT (11,12). Duodenal ulcer was confirmed by endoscopy as the commonest lesion in patients presenting with dyspepsia in Nairobi (2). Where this facility is available, patients get diagnosed earlier and treatment saves them from potentially complicated PUD.

These positive developments have been countered to some extent by factors that tend to worsen PUD, the so called aggressive factors. First is the widespread use of NSAIDs in treating musculoskeletal conditions and their excessive use as analgesics, second is the increased use of aspirin in prevention of cardiovascular complications, and third is that people live longer, and in advanced age use more NSAIDs. NSAIDs relieve pain and inflammation by inhibition of prostaglandin synthesis whose side effect is weakening of the gastric mucosal defence to resist luminal irritants. Nitric oxide (NO) counters this and plays a protective role. While neutrophil adherence to the endothelium of the gastric capillaries may be critical in NSAID injury, NSAIDs may also induce activity of inflammatory mediators, tumour necrosis factor TNFa and leucotrienes. NSAID- induced ulcers can be treated by stopping the NSAIDs or when this is not advisable, by treatment with the prostaglandin agonist misoprostol. Misoprostol, a synthetic prostaglandin analogue has antisecretory and protective properties, promoting healing of gastric and duodenal ulcers. It can prevent NSAID- associated ulcers its use being most appropriate for the frail or elderly from whom NSAIDs cannot be withdrawn. It is sometimes combined with NSAIDs like diclofenac or naproxen (7).

Due to these factors PU has increased in the older generation in the developed countries but is uncommon in the young. Not so in Africa. In this issue, Dakubo *et al* (13) writing from Ghana in West Africa found that most of their patients were young, confirming a similar earlier finding in West Africa (14) and East Africa where patients with perforated duodenal ulcer were on average 20 years younger than those reported from America (15,16). This indicates that there are factors other than age which predispose to PUD and low socio-economic status seems to be one such factor. Apart from poverty and malnutrition, African patients report to hospitals late often with the disease advanced or complicated, and in any case most of the health facilities they attend are poorly equipped and understaffed. In addition there is widespread use and abuse of NSAIDs, sometimes self prescribed. The result of all this is that PUD is common and where PUD is high, so will the complications. The three classical surgical complications of PUD are haemorrhage, perforation and pyloric stenosis.

Carswell and Zarezaev (17) reviewed these complications in a series from Kampala which is typical of many African countries. Gastric outlet obstruction was the commonest, but this was because it was the least serious of the three complications, since it took some time, often months to develop, and allowed patients to present themselves to the hospital. Moreover its diagnosis, in well established form, was difficult to miss (18). Haemorrhage had a high chance of under-treatment due to deprived health facilities and there were many preventable deaths. The current accepted treatment for haemorrhage is upper GI endoscopy with injection with vasoconstrictors after resuscitation. Endoscopic facilities are not widely available and in many places on the continent and open surgery is still recommended. Post surgery, medical treatment with PPls is advised as recurrence is not uncommon (19).

Perforation remains a major problem because of widespread use of NSAIDs and high prevalence of PUD particularly in rural areas. Very few cases were seen by Carswell and Zarezaev (17), but they were convinced most of the patients were dying untreated.

Perforated peptic ulcer is often missed, and patients will succumb either acutely or due to subsequent complications. In Kampala even those correctly diagnosed and treated, had a high mortality. The standard treatment for perforation is laparotomy and closure by an omental patch. Few surgeons will advocate vagotomy or some other anti-ulcerogenic treatment after this, particularly now that there are effective drugs to treat those with residual PUD symptoms after surgery. Closure of perforated DU is an operation that lends itself very well to laparoscopy which, in experienced hands, is quicker, less traumatic and relatively easy to do and will in time replace open surgery. It is already practised in Kenya.

The paper from West Africa (13) highlights the fact that this problem is still common, affecting mainly the young and has serious complications often leading to death. Clinicians must pay special attention to a disease that need not be such a great public health issue as it is at the moment.

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