Drug-induced esophageal damage (DIED) is far more common than one would expect from reports in the medical literature. The sequelae of this injury are poorly understood by many physicians. Fortunately, some patients recognize the etiologic or chronologic relationship of their esophageal symptoms to drugs they are taking and either stop the drug or alter the dosing schedule.

The most common types of DIED are the most acute and unfortunately are self-limited, lead to no serious sequelae and usually are asymptomatic within 10 days of stopping the offending drug.

The first report by Pemberton in 1970 concerned injury by oral potassium chloride, a medication produced in several formulations. After 26 years, potassium chloride in some solid forms remains one of the most potentially harmful substances when retained in fixed location within the esophagus, stomach, or small intestine.

An accurate history to determine the possibility of disordered swallowing, either neuromotor or obstructive in nature, in addition to patient education, patient compliance with dosing instructions and physician knowledge are essentials for the prevention of DIED. Awareness of the anatomical, pathological, pharmacological and gravitational factors that may strongly influence the risk of drug-induced injury is necessary for successful prevention. Since thousands of formulations of drugs have been prescribed by physicians or bought by patients at the pharmacy and grocery stores for several hundred years, why did the first report of drug-induced esophageal injury appear as late as 1970? Why is it a fact that in 1996, prescription habits and failure to inform patients of the risk of drug-induced injury occurs because of the lack of knowledge about its existence as a potentially lethal condition?

The predominance of elderly and female patients in most reports is readily explained by evaluating the frequency of underlying disorders that required potentially injurious medications as therapy. The elderly in general, take more drugs, are prone to have more motility disorders and obstructing lesions of the esophagus, spend more time in the recumbent position, produce less saliva and are more prone to forget dosing instructions even when physicians have properly given them. Age also tends to influence the type of drug injury that the patient will develop. Since cardiovascular disease is more common in the elderly, such contributing anatomical factors as a dilated aorta or enlarged heart (left atrium) compressing the esophagus can interfere with drug transit long enough for significant injury to occur. Cardiovascular disease increases the likelihood that potassium chloride or some formulation of quinidine will be the injurious agents. On the other hand, young patients are more likely to require medication for acne or urinary tract infections making antibiotics more common offending agents. In one review of 93 cases, the age range was 9 to 89 years with a mean age of 42 years. The mean ages for the various drugs that caused esophageal injury was: 30 years for antibiotics, 56 years for potassium chloride, and 64 years for quinidine.

Drugs appear to exert their most definitive and damaging effects by a direct action on the esophageal wall. This effect varies because of several factors that include the following: the chemical formula; concentration of the chemical(s) in the drug; its method of delivery, i.e. tablet, capsule, liquid; combination with agents to aid disbursement that may also slow transit; the duration of contact with mucosa (living cells of the esophagus); and the presence of pre-existing esophageal disorders that may alter passage to the stomach. The pH (degree of acidity) of some drugs is quite acid (ferrous sulfate, doxy- and tetracycline and ascorbic acid) while others that produce more severe injury and even death have neutral pH. Quinidine gluconate is said to have a pH near neutral when mixed with saliva but typically causes deep mural injury resulting in severe strictures that respond slowly to dilation therapy. Another important reason for the injury produced by quinidine gluconate (Quinaglute) likely is the size of the tablet which is 12 mm in diameter, about 50% of the normal esophageal lumen diameter.

In addition to size, other characteristics of drug formulation may predispose to injury. Gelatin capsules become very sticky or adhesive during dissolution when taken with inadequate liquids or are otherwise delayed in transit. Capsules taken by upright normal subjects are cleared normally from the esophagus (within 15 seconds) only if taken with water. If capsules become lodged in
the esophagus, they are difficult to displace even with repeated
swallows of water. Carlborg et al. have shown that doxycycline
capsules (Vibramycin) remain longer in the esophagus three
times as often as doxycycline in tablet form (Idocyclin).

The medicine, Fosamax, is given for osteoporosis, the bone-
thinning common among older women. It is hormone-free and is
often taken by those who are unwilling or unable to use estrogen
pills. Since it came on the market a year ago, it has been taken by
330,000 women in the United States and 110,000 others worldwide.
Fosamax can cause severe esophageal injury if it remains in contact
with the esophagus. Over 50 cases of injury are reported so far.

Most patients who suffer drug-induced esophageal injury
have no detectable esophageal disorder, neither neuromotor nor
obstructive. Therefore, the major responsibility for such injury
seems to fall squarely on the chemical content and formulation of
the drug and the manner in which the drug is taken by the patient.

Mechanisms of DIED - The Patient. The patient usually has
the capability to reduce or eliminate the risk of esophageal injury
by oral medication if he/she has been properly instructed and
cautioned by the physician. Certainly the physician is obligated to
inform the patient of the potential risks when prescribing drugs
likely to cause mucosal damage.

Forty-five of 112 patients (40%) with DIED reviewed by
Kikendall et al. revealed that there was a history of either taking
the drug with little or no fluid or just before going to bed. Forty-
nine percent could recall the sensation of the pill sticking in the
chest.

Guidelines for prevention of DIED should include the following:

1. All oral medications should be taken in the upright position
whenever possible.
2. The person should remain upright at least 10-15 minutes
after swallowing, to allow gravity to assist passage of
tablets or capsules.
3. At least 100 ml of fluid should be taken after each tablet
or capsule.
4. Special warnings should be stressed to all persons with
neuromotor or obstruction lesions of the esophagus and
in those with cardiomegaly or other forms of extrinsic
compression.
5. When the possibility of delayed passage of tablets or
capsules through the esophagus exists, due to motility
dysfunction, an obstructing lesion or required recumbency,
medications should be in liquid form or crushed and
dispersed in adequate volumes of fluid whenever possible.
6. Only physician awareness, education of the population of
the world, pharmaceutical success in producing safer
formulations and patient compliance with the simple
guidelines listed above are likely to ultimately reduce the
frequency of drug-induced esophageal damage.

The next issue of CSD News will contain Part II on Diagnosis and
Treatment of DIED. For emphasis, the Guidelines for Prevention
shown above will also appear with Part II.

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HELICOBACTER PYLORI: ROLE IN CAUSATION OF PEPTIC ULCERS AND OTHER CONDITIONS

UMESH CHOUDHRY, M.D.

Recent discoveries have provided information that establishes a bacterium, Helicobacter pylori (Hp), as the cause of peptic ulcer disease in a large majority of patients. This discovery has now been well reported by the media. Hence, a large proportion of the population has become aware of this association. Aggressive reporting, however, may have created some confusion in the minds of some patients. The following article is aimed at clarifying some of these issues.

Scientists have known about the existence of Hp for several decades. However, its role in causation of disease in the stomach and duodenum was not reported until late 1980's. These bacteria infect the gastrointestinal tract of humans in childhood. The prevalence is related to living conditions of patients in their early years. About 65% of the elderly population carry this bacteria. As living conditions in the western society improved in the last century the younger population had a very low prevalence of infection with this organism.

Hp infection is associated with several widely different outcomes, some of which are clinically important. All infected patients have an acute inflammation in their stomach called acute gastritis. The patients then progress to a chronic gastritis of the lower most part (antrum) of their stomach. A proportion of these patients then go on to develop peptic ulcers, most commonly duodenal and less often gastric or stomach ulcers. In some patients there is a progression of the antral gastritis to involvement of the entire stomach. With prolonged infection some of these patients may have atrophy or thinning of the inner lining of the stomach wall. Several other factors such as smoking, high salt diet, etc. are also associated with this type of gastritis. At this time little is known about how Hp and other factors interplay in the progression to atrophic gastritis. An early age of onset of infection and more severe mucosal damage may, however, be important. Over time, atrophic gastritis results in decreased acid production by the stomach (hypochlorhydria). A small proportion of patients with atrophic gastritis Type III and hypochlorhydria may subsequently develop stomach cancer, a form of cancer whose incidence has generally declined and is relatively low in the United States excluding the African Americans and native Alaskans. It is pertinent to note that of the three sub-types of atrophic gastritis (I, II, and III), only Type III is associated with gastric cancer.

A recent research study from Europe which received some attention in the general press raised some concerns about the long term use of the acid suppression medication, omeprazole, in patients with H. pylori infection. We believe that the evidence at this time is not convincing as this study compared populations of two different countries who may have completely different risk factors at play. The specific sub-type of atrophic gastritis (Type I) associated with omeprazole use is not considered to be associated with increased risk of developing gastric cancer. Further research will be needed before we can recommend that every patient who requires prolonged omeprazole therapy be tested for Hp.

As scientists acquire more information about this organism it appears that all strains may not be responsible for disease. Already significant information about how Hp actually causes inflammation is becoming available. This holds promise for identifying and eradicating more virulent strains in the future. For the purpose of this discussion it is sufficient to say that chemical mediators produced by the bacteria alter hormonal balance in the stomach and may cause increased acid secretion.

Lastly, a word about who needs to be treated or investigated for this bacterial infection. Since the prevalence of this bacteria in the younger or middle age group is relatively low, mass screening of the population is not recommended. Patients undergoing endoscopic or radiographic evaluation who are found to have any of the lesions associated with this bacteria should be tested for this bacterial infection. This is best done by obtaining biopsies from the stomach. A blood test is also available but is less specific for active infection. A simple breath test will become available in the near future.

Things To Remember

1. OFFICE HOURS: 8:00 a.m. 'til 4:40 p.m. Monday through Friday.

   Our office is closed on weekends and some holidays so it is important to make sure any medication refills are called to us during our regular office hours.

   Also, our emergency telephone number for after hours is (813) 974-2201. Please remember these calls will be responded to by one of our gastroenterology residents who will in turn contact the appropriate attending physician on call.

2. BILLING: Our patients who have problems with their physician or facility fee bills should contact Laura Fusner, Financial Specialist, at the University of South Florida Medical Clinics at (813) 974-4659 between the hours of 9:00 a.m. and 4:00 p.m. Monday through Friday.

   It is the patient's responsibility to get authorizations or pre-certifications from their insurance company before any treatment occurs. Laura is available to help with insurance authorizations when problems arise.

   For those patients who are from out-of-town, a new toll-free number has been added for you to call with billing questions. The number is 1-888-873-3627. This number is for calls originating in Florida and is only for billing questions and help with insurance authorizations.

3. DILATIONS: For our patients who receive periodic esophageal dilations: Please try to anticipate and contact our office at least 2 to 3 weeks in advance of your need for dilation, if at all possible. We have been having to schedule return cases 3 to 4 weeks in advance due to our heavy patient load. We do not want any of you to suffer unnecessarily, so please help us with your appointment needs.

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CONTINUING MEDICAL EDUCATION

During the past six months, members of the Center for Swallowing Disorders staff have continued their active participation in graduate medical education at regional, national, and international meetings and by contributions to the medical literature.

Lecture Presentations by CSD Staff

April 11, 1996: Toxin to Medicine: Botulism to Botox. Internal Medical Grand Rounds, University of South Florida College of Medicine. Tampa, FL. (Boyce)

15. October 12, 1996: 1) Anatomy and Physiology of the Esophagus, 2) GERD and the Role of 24 Hour pH Monitoring. SGNA Course. H. Lee Moffitt Cancer Center and Research Institute. Tampa, FL. (Choudhry)

Contributions To Medical Literature and Clinical Research Abstracts