Drug-induced corrosive injury of the oesophagus

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Corrosive injuries of the oesophagus were quite common in previous years. The most common agent was lye but various organic and inorganic acids have also been responsible. Over a period of the last two years, five patients have been treated at the Ear Department of TYKS (Turku University Central Hospital) for fairly serious corrosive injuries of the oesophagus, subsequent to the consumption of drug tablets. The drug in question has been Cetiptin® tablets (AB Kabi), for which the chief indications are nocturia and urinary incontinence. The active ingredient in the tablet is emepronium bromide presented in 50 mg and 100 mg tablets. The manufacturer's recommended dosage is 100–200 mg three times daily, and in cases of nocturia a single dose of 200 mg in the evening. Emepronium bromide has an atropine-like effect as well as a hexamethonium type effect, blocking the transfer of stimuli both in nerve endings and in ganglia. According to the manufacturer, there are no side-effects worth mentioning.

Case reports

Case 1. The patient was a 31-year-old woman who had previously had urinary incontinence but had otherwise been in good health. The patient had taken Cetiprin® tablets from time to time. One evening after having taken one Cetiprin® tablet she got the feeling that the tablet had stuck behind her sternum. She failed, however, to drink any liquids following the consumption of the pill. On the following two days she began to experience pain in conjunction with eating and on the subsequent three days the pains became so severe that she was more or less unable to eat or drink anything. Even drinking water caused strong retrosternal pain. The patient came to the hospital out-patient clinic on the seventh day after taking the pill. At this time she was not even able to swallow her own saliva. Nothing abnormal was visible in her mouth or throat, and oesophageal X-rays were normal. Oesophagoscopy was performed and marked corrosive changes, partly fibrin-covered, partly ulcerative, were demonstrated (Fig. 1a). The mucous membrane of the lower third of the oesophagus was normal. The patient was treated with Gaviscon® powder. Symptoms did not disappear until a little more than a week after her visit to the hospital.

Case 2. The patient was a 29-year-old woman who had previously been in good health. She had been prescribed Cetiprin® tablets for the treatment of disturbances of urinary continence, and had taken the pills from time to time. One evening following consumption of one tablet, without water, she had the feeling that it had become stuck in her oesophagus. On the following day she began to have pain behind the sternum, and consumption even of liquid foods caused pain. Swallowing of water and saliva also caused feelings of pain. Nothing abnormal was visible in her mouth or throat when examined at the hospital out-patient clinic, and oesophageal X-rays were normal. Oesophagoscopy demonstrated marked corrosive changes in the middle third of the oesophagus (Fig. 1b), but the mucous membrane of the lower third of the oesophagus was
normal. The symptom of pain did not disappear until three weeks after the consumption of the CetiprinR tablet.

Case 3. The patient was a previously healthy 12-year-old boy who had gone to the doctor because of chest pain and fever. The symptoms were chiefly in conjunction with the act of swallowing. Chest X-ray was normal. Oedema of the mucous membrane of the middle third of the oesophagus was visible in the oesophageal X-ray, but no foreign body, hiatus hernia or reflux was visible. His symptoms were thought to have been caused by a foreign body which had already passed beyond the oesophagus. The patient went to the doctor again the next day. The fever had declined but the chest pains had markedly increased. The patient was sent to the out-patient clinic of the central hospital, on suspicion of a foreign body. The patient appeared to be in pain and was unable to swallow water; saliva flowed from the corners of his mouth. Oesophagoscopy was performed under anaesthesia and demonstrated very marked corrosive changes in the middle third of the oesophagus. The patient was prescribed cortisone and an antibiotic. It was not until this time that it became known that the patient had taken CetiprinR tablets, 50 mg three times daily for four days, for the prevention of enuresis. After six days, a further oesophagoscopy was performed when marked corrosive changes were still visible in the middle third of the oesophagus (Fig. 1c). Neither hiatus hernia nor reflux were found upon X-ray examination. The sedimentation rate was 43 mm at its highest.

Case 4. The patient was an 18-year-old woman who had consumed one CetiprinR tablet five days prior to coming to the hospital. The patient felt that the pill had become stuck in the oesophagus, but she had not taken any liquids following consumption of the pill. Retrosternal pains gradually began to appear and they were clearly related to swallowing. Finally the patient did not even dare to swallow water for fear of pain, and she was hospitalized. Upon admission the leucocyte count was 13,700/cu mm and the sedimentation rate 18 mm in the first hour. Neither foreign body, hiatus hernia nor reflux could be demonstrated upon X-ray. Upon oesophagoscopy, the middle third of the oesophagus was shown to be covered with fibrin, and ulcerative oesophagitis was present at various sites. The mucous membrane of the lower one-third was normal. The patient was treated with GavisconR powder and, for two weeks following oesophagoscopy, she had severe pains for which analgesics had to be taken. The oesophagus healed well without scar formation.

Case 5. The patient was a 27-year-old woman who took CetiprinR pills for relief of urinary incontinence. One evening, after having taken one tablet without fluids she had a feeling that the tablet had lodged in her throat. On the following two days, she began to feel retrosternal pains of increasing magnitude, and these were clearly related to the act of swallowing. Finally the pain was such that she did not even dare swallow water. Oesophagoscopy, performed at the hospital out-patient clinic, demonstrated fairly marked corrosive changes but the lower one-third of the mucous membrane was normal. Neither hiatus hernia nor reflux could be demonstrated upon oesophageal X-ray. The pains gradually eased within two weeks.

Discussion

CetiprinR tablets are known to cause ulceration of the oral mucosa, in patients such as the elderly or mentally retarded, who have retained the tablet in
Partly fibrin-covered, partly ulcerative corrosive changes in the middle third of the oesophagus, as seen at oesophagoscopy (Cases 1, 2 and 3).
their mouths for some time before swallowing (Strouthidis et al., 1977). Similar cases of corrosive injury to the oesophagus have also been described in the literature (Kavin, 1977; Kenwright and Norris, 1977). Other drugs are known to cause lesions of the oesophagus when the tablet or capsule lodges in the oesophagus (Carlborg, 1976). The patients described above were all young people who had taken one or only a few Cetiprin<sup>R</sup> tablets. In four of the cases, the patient had taken the tablet in the evening and immediately felt that it had lodged in the oesophagus. The motility of the oesophagus is slow in the evening, especially at night, and tablets that are taken without fluids can lodge in the oesophagus for long periods (Carlborg, 1976). The patients described had taken the tablets for relief of urinary incontinence and this is apparently the reason for taking the tablet without fluids.

The subjective symptoms of all patients were similar. Retrosternal pains occurred and increased a few days after consumption of the tablet and its subsequent lodgement in the oesophagus. They were clearly related to the act of swallowing and, as a result of the pain (initially) solid foods and, later on, liquid foods also were either difficult or impossible to swallow. The youngest patient developed a pyrexial reaction, and one patient had a leucocytosis of up to 13,700/cu mm; the sedimentation rate of one patient rose to 43 mm in the first hour. Pain on swallowing continued for 2–3 weeks after impaction, but none of the patients developed permanent stricture of the oesophagus.

To our knowledge none of the patients had had previous functional disorders of the oesophagus, nor did any of them have any kind of stricture. Oesophagoscopy was performed in all cases and the results were similar: there was a marked corrosive injury to the middle third of the oesophagus, which was partly ulcerative and partly fibrin-covered, but the mucous membrane of the lower third of the oesophagus was normal in all patients. X-ray of the oesophagus was performed on all patients, but neither hiatus hernia nor gastrooesophageal reflux was shown in any of the cases. Recently two cases have been presented in the literature in which Cetiprin<sup>R</sup> was suspected of having caused iatrogenic reflux oesophagitis (Shepperd, 1977). None of the patients reported vomiting. Both oesophagoscopy and X-ray studies showed that a local corrosive injury was present and there was no indication of a reflux disease process.

Apparently Cetiprin<sup>R</sup> is not the only drug which can cause irritative changes in the oesophagus (Carlborg, 1976). The author has seen patients with corrosive injuries to the oesophagus caused by doxicyclin (Vibramycin<sup>R</sup>) and alprenolol-chloride (Aptin<sup>R</sup>). In each of these cases the tablet or capsule had been consumed in the evening or night without fluids, and the tablet or capsule had lodged in the oesophageal mucosa, thus causing chemical injury. In these cases, however, the symptoms were not as marked as in the cases following the consumption of Cetiprin<sup>R</sup>. One often hears a patient describing how an aspirin tablet has lodged in the oesophagus and caused some pain. In such cases the physician may doubt the patient’s story, even though such an event has occurred as described.

**Summary and Conclusions**

Five patients are described who had retrosternal pains following the consumption of Cetiprin<sup>R</sup> tablets. The pains increased so markedly within a few days that, initially, solid foods and, subsequently liquid foods also were impos-
sible to swallow. Typically the history was of the consumption of a tablet in the evening or night without fluids and the pains lasted for 2–3 weeks. A marked corrosive injury of the middle third of the oesophagus was shown at oesophagoscopy in each case, but the mucosa of the lower one-third of the oesophagus was normal. Gastro-oesophageal reflux was not demonstrated radiologically in any of the patients. None of the patients developed a stricture of the oesophagus. The most likely alternative in the differential diagnosis was a foreign body. Oesophagoscopy should be performed on any patient in whom such pains persist for more than 4–5 days, even if the X-rays are normal.

The physician should advise his patients to take tablets or capsules with fluids. This is especially important if the drug is taken in the evening or at night. Cetiprin® tablets should be taken in the evening while the patient is still upright, and should be taken with fluids. If a corrosive injury does develop, we suggest that treatment should be with cortisone and with agents which protect the oesophageal mucous membranes.

REFERENCES


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