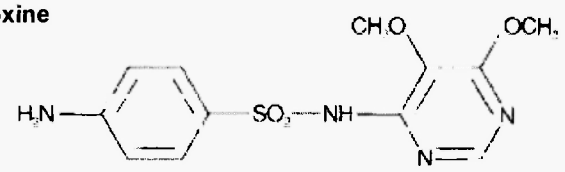
LETTER

Sudden Enlargement of the Prostate in a Patient Taking Fansidar® for Malaria

In most developing countries, adverse drug reactions are seldom reported /1/. Severe drug reactions associated with the administration of *N*-(5,6-dimthoxy-4-pyrimidinyl) sulfanilamide (sulfadoxine) and 2,4-diamino-5-(*p*-chlorophenyl)-6-ethylpyrimidine (pyrimethamine) as Fansidar® (Fig. 1) have included Stevens-Johnson syndrome, toxic epidermal necrolysis, hepatic necrosis, hematological complications and renal failure /2/. We present here a case of acute prostate enlargement in a patient taking Fansidar® for malaria chemoprophylaxis.

Sulfadoxine



Pyrimethamine

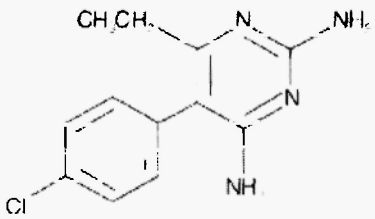


Fig. 1: Chemical structure of sulfadoxine and pyrimethamine, the two major components of Fansidar®.

A 65 year-old previously healthy man taking Fansidar® for malaria prophylaxis suddenly presented with dysuria, frequency and urgency of urination on the second day. On examination, he was restless, weak, with normal and stable vital signs and afebrile. Complete blood count values were within normal ranges. Blood chemistries were also within normal ranges. Urinalysis was normal and 24-hour urine culture

returned negative bacterial growth. X-ray examination of the abdomen and kidney, urethra and bladder was normal. Pelvic ultrasound revealed prostate enlargement that was confirmed on rectal digital examination to be smooth, enlarged and tender. However, prostate enzyme assay was normal.

Fansidar® was withheld and an indwelling catheter placed. The patient was started on antibiotics (ampicillin plus cloxacillin), nitrofurantoin and ascorbic acid. Fluid intake was maintained at 3 l/ day and urine output monitored through an indwelling catheter. Three days later the patient's condition improved. The catheter was removed and he started passing urine without pain. Repeated digital examination on the fifth day and two weeks later showed that the prostate had gone back to normal.

Both sulfadoxine and pyrimethamine are folic acid antagonists. Sulfadoxine inhibits the activity of dihydropteroate synthase while pyrimethamine inhibits dihydrofolate reductase. Sulfadoxine and pyrimethamine are active against the asexual erythrocytic stages of *Plasmodium falciparum*. After administration of one tablet, peak plasma levels for pyrimethamine reach approximately 0.2 mg/l, and sulfadoxine about 60 mg/l, within 4 hours. With one tablet per week, steady-state plasma concentrations are reached of about 0.15 mg/l for pyrimethamine after about 4 weeks and about 98 mg/l for sulfadoxine after about 7 weeks, the recommended adult dose for malaria prophylaxis. Only about 5% of sulfadoxine appears in the plasma as its acetylated metabolite and 2-3% as the glucuronide, while pyrimethamine is transformed to several currently unidentified metabolites. Both pyrimethamine and sulfadoxine are eliminated mainly via the kidneys.

We were not able to determine whether the present side effect was due to the sulfadoxine or pyrimethamine component of Fansidar®, or their metabolites. We do not know whether this is the presentation of the early phase of renal failure seen in patients taking Fansidar® in the elderly that has not been previously reported. Fansidar® has also been reported to be associated with hepatitis, pancreatitis, nephritis and polyneuritis during clinical trials. Clinical studies of Fansidar® did not include sufficient numbers of subjects aged 65 years and above to determine their response to Fansidar® and whether they respond differently from young adults /2/.

To the best of our knowledge, this is the first report of possible Fansidar®-induced acute prostate enlargement, calling for vigilance in the subtropics, Africa and Asia where malaria is endemic.

Blessing C. Ajuonuma[1,4], *Mary Uchechi Ajuonuma*[1,4], *Adanma Uzo-Ngerem*[2,4], *Margaret K. Ajuonuma*[2,4], *Fidelis O. Ajuonuma*[5], *Chika L. Chukwu*[3] *and Louis C. Ajonuma*[5]

[1]School of Nursing, Lyceum Northwestern University, Dagupan City, The Philippines, [3]Department of Medicine, Federal Medical Center, Owerri, Imo State, Nigeria, [2]Department of Internal Medicine, De LaSalle University Medical Center, Dasmarinas, Cavite, The Philippines, [4]School of Pharmacy, Lyceum Northwestern University, Dagupan City, The Philippines and [5]St Mary's Maternity Hospital, Amakohia, Etiti, Imo State, Nigeria
e-mail: Louisca@alumni.cuhk.net

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