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Medical Memorandum

Renal Complications after Using Sulpenin

Combinations of penicillin and sulphonamides have been in clinical use for more than a year. No serious toxic effects have been reported, and the manufacturers know of only a few mild reactions occurring in a small number of instances. The following case report seems to be the first example of a serious toxic effect following the use of "sulpenin."

CASE REPORT

A married woman aged 73 was admitted to hospital on March 7, 1953, with the following history. In the previous ten days she had had "influenza," and mild bronchopneumonia, for which her doctor had prescribed sulpenin, the total amount given before admission being 28 tablets (14 g. sulphonamide). Twenty-four hours before admission she had suddenly developed epigastric pain, which had increased in intensity. It "spread through to the back," but did not radiate to the shoulders. The character of the pain was described as severe, with exacerbations. She had never had anything like this previously. Several times in the previous 24 hours she had vomited a small amount of mucoid fluid. Throughout this period she noticed a diminution in the quantity of urine passed, and what was voided was bloody (she admitted that she had not been drinking very much for the past two days). She had been constipated for five days. In 1916 laparotomy and appendicectomy had been performed, and in 1917 gastric ulcer had been diagnosed radiologically.

On examination she had the appearance of an ill, moderately dehydrated old lady. The tongue was dry and brown. The neck and chest, cardiovascular system, and central nervous system were all normal. Her blood pressure was 160/90 mm. Hg, pulse rate 80, temperature 99° F. (37.2° C.), and respirations 22. In the abdomen there was an upper right paramedian healed scar. Muscular movements were diminished, tenderness was acute in the epigastric area, but not in either loin, bowel sounds were diminished, no mass or abnormal viscus was palpated, and no fluid was detected. Rectal examination was normal. A straight x-ray film of the abdomen did not show air under the diaphragm or any intestinal abnormality. A diagnosis of anuria due to sulphonamide intoxication was made.

On March 8 the cystoscopy findings were: residual urine in the bladder 3½ oz. (100 ml.); some trigonitis; right ureteric orifice oedematous and blocked with bloody material, no efflux being present; left ureteric orifice oedematous without efflux. Attempted catheterization of the right ureter failed. There was a block 1.5 cm. from the vesical opening. A left ureteric catheter passed easily and was left *in situ*.

An indwelling gastric tube was left *in situ* for 24 hours, but yielded practically no material on aspiration. She was given oral fluids, 1 oz. (28 ml.) hourly for 12 hours, after which time the amount was doubled each 12 hours; 500 ml. of M/6 sodium lactate was administered intravenously. After the cystoscopy no urine was passed for 17 hours, at which time spontaneous diuresis took place. (The left ureteric catheter was left *in situ* for 72 hours, but no urine drained through it.) In the next 24 hours she passed 35 oz. (1 litre) of urine. She was discharged on March 13.

Investigations.—March 7: microscopy of urine removed from bladder on cystoscopy revealed it to be acid in reaction, with a microscopic haematuria. No sulphonamide crystals were seen. March 9: urine turbid, red-brown, pH 6.2; deposit abundant red blood cells, with no excess of leucocytes and no crystals seen; alkaline reserve, 40.4 vols. CO₂%. March 11: urine deep red, pH 5.6; still large numbers of red blood cells. On March 13 the report was similar. Intravenous pyelography showed good function on both sides, with normal renal outlines. The concentration of dye excreted was better on the left than on the right.

COMMENT

The simultaneous administration of two antibacterial agents is now an accepted principle of therapeutics. The drugs employed are many, proceeding from mixtures of synthetic agents, such as sulphonamides, to mixtures of sulphonamides with various antibiotics. Sulpenin is one of these; each tablet contains penicillin, 100,000 units, sulphadiazine, 0.25 g., and sulphamerazine, 0.25 g. The dose administered for infection of average severity is two tablets every four hours.

Garrod (1953) outlined the principles and the problems of this kind of therapy. He gives the following indications for its use: prevention of acquired resistance, achievement of synergism, prevention of toxic effects, mixed and double infections, and, rarely, the urgent undiagnosed case. The main difficulty is to avoid the production of resistant strains of infecting organism, but penicillin-sulphonamide mixtures tend to do this much less often than do other combinations.

This case emphasizes the fact that combinations of antibacterial agents do not abolish the capacity of the individual drugs to produce their specific toxic actions on the host. It seems likely that sulphadiazine was probably the responsible fraction, as its solubility in urine of pH 6-6.5 is less than half that of a comparable dose of sulphamerazine at that pH. Recent work has cast some doubt on the routine use of sulphonamide mixtures alone. Weinstein and Murphy (1952) state "that combinations of sulphonamides may have little clinical usefulness in many instances, since they are often not as effective as the single agents which compose them." This raises the question of what sulphonamide is best combined with penicillin. Of the sulphonamide preparations now available, sulphasomidine (6 (*p*-aminobenzene-sulphonamido)-2:4-dimethylpyrimidine), the isomer of sulphadimidine, would seem to be worth combining with penicillin. It has a greater solubility in acid urine than any other sulphonamide, the degree of acetylation is only 10-15%, the blood level remains consistently high, and side-effects are slight.

The clinical picture was not entirely typical in that no signs or symptoms referable to the loins were obtainable; a superficial examination suggested the presence of an intra-abdominal condition. A careful history provided the answer.

In the treatment—carried out along standard lines—it is significant to note that return of renal function occurred first on the non-catheterized side. Although the condition was what is often classified as an obstructive type of anuria, spontaneous diuresis occurred within 24 hours. The left ureteric catheter, *in situ* for 72 hours, did not drain urine in that period. It is possible that traumatic oedema of the ureteric mucosa, already partly damaged by a saturated solution of sulphonamide, was the cause of this depression of function. This experience would tend to support the view of those who recommend, after an initial cystoscopy, the application of the principles of the Bull regime to cases of sulphonamide anuria.

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