The patient went on to make an uneventful recovery after seven days of intravenous ceftazidime alone. A specimen of cerebrospinal fluid taken during single drug treatment contained 31.5 mg ceftazidime/l. The specimen was sterile on culture and both inhibited and killed the standard inoculum of salmonella in vitro at a dilution of 1/32 (table). The concentration of ceftazidime and the inhibitory dilution were both twice that obtained with the lower dose of the drug, and in retrospect there was probably no need to have increased the dose when chloramphenicol was discontinued.

Comment

These findings are clear evidence of antagonism between the bacteriostatic agent chloramphenicol and the bactericidal ceftazidime and support the view that such combinations are undesirable in the treatment of meningitis. When a cephalosporin such as ceftazidime is used to treat Gram negative meningitis it should not be combined with chloramphenicol.

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Reversal of liver damage due to long term methyltestosterone and safety of non-17 α -alkylated androgens

Long term androgen treatment may lead to various patterns of liver damage including cholestasis, peliosis hepatis, nodular regenerative hyperplasia, and primary hepatic tumours.^{1,2} In 1977 we described a series of patients with liver damage due to long term methyltestosterone.³ We now report a follow up study of some of these patients (those traceable) after they had stopped this drug, as well as a survey of patients receiving long term treatment with non-17 α -alkylated androgens, which are said to be free from hepatotoxicity.

Patients, methods, and results

We studied 42 patients (34 female to male transsexuals and eight impotent men). None took excess alcohol (>80 g/day). All were examined physically, and blood was taken for liver function tests. Liver scintiscans with sulphur colloid labelled with technetium-99m were performed in most patients. The series was divided into three groups (table). Tests of significance were derived from the binomial test.

Group 1—Six patients had taken methyltestosterone (50 mg thrice daily) alone for a mean of 1.3 (SD 0.6) years. During treatment all had had abnormal liver function and four abnormal liver scans. Liver biopsy in two had shown sinusoidal dilatation, hepatic vein lesions, and cholestasis. When restudied two to four (mean 4.1) years after stopping methyltestosterone all six patients

had normal liver function and liver scans, although in one uptake of colloid into the spleen was still slightly increased.

Group 2—Eighteen patients originally given methyltestosterone 50 mg thrice daily had been changed to an alternative androgen preparation. Fifteen had received methyltestosterone for between three months and five years (mean 2.3 (1.3) years) before being transferred to sublingual testosterone 30 mg thrice daily for one to four years (mean 3.15 (1.4) years) before reassessment. Eight of these patients had had abnormal liver function and scans, and five of these eight had shown androgen related changes on liver biopsy. Liver function and scans were normal in all eight when reviewed during treatment with sublingual testosterone. A further three of these 15 patients had had only abnormal liver function during treatment with methyltestosterone, which returned to normal with sublingual testosterone. Liver function and scans had been normal in four of the 15 patients and remained so during treatment with sublingual testosterone, although in one patient the scan showed increased uptake of colloid into the spleen. The other normal liver scans remained unchanged. The remaining three of the 18 patients had received methyltestosterone for a mean 2.8 years and were then given a parenteral non-17 α -alkylated androgen for a mean of 4.5 years. One patient had normal liver function and scan while taking both methyltestosterone and Sustanon 250 (testosterone propionate 30 mg, testosterone phenylpropionate 60 mg, testosterone isocaproate 60 mg, and testosterone decanoate 100 mg/ml). The two others had had abnormal liver function and scans, which returned to normal during treatment with either Sustanon 250 or testosterone oenanthate.

Group 3—Eighteen patients were treated solely with sublingual testosterone 30 mg thrice daily for between 10 months and six years (mean 3.1 (1.8) years). They all had normal liver function, but four had slightly enlarged spleens with increased uptake of colloid on scintiscanning.

Comment

These results suggest that liver damage induced by methyltestosterone is reversible, in agreement with occasional previous reports. We found no evidence of hepatic damage due to long term treatment with non-17 α -alkylated androgens, which are traditionally regarded as free from hepatotoxicity. Electronmicroscopical abnormalities in the bile canaliculi and increased retention of sulphobromophthalein have, however, been described,⁴ although they appear to be much less common than with 17 α -alkylated compounds. Recently bile duct proliferation, peliosis, and cholangiocarcinoma were reported in a series of patients treated with non-17 α -alkylated androgens.⁵ The importance of the abnormal spleen image found in some of our cases is not clear, although peliosis may affect the spleen and spare the liver.

Although our findings are reassuring, we recommend careful long term surveillance of patients taking non-17 α -alkylated androgenic and anabolic steroids; isotopic or ultrasound imaging is advisable in addition to liver function tests.

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Patients with abnormal liver function and isotope liver scans during treatment with methyltestosterone (MT) and after stopping treatment (group 1) or substitution of a non-17 α -alkylated androgen (group 2). Group 3 were given testosterone only

	Group 1			Group 2			Group 3
	During MT	No treatment	p Value	During MT	Other androgen treatment	p Value	Testosterone only
Abnormal liver function	6/6	0/6	0.032	13/18	0/18	0.0002	0/18
Abnormal scan	4/6	1*/6	0.25	10/18	1*/18	0.004	4*/18

*Patients had enlarged spleens with increased uptake of colloid.