CASE REPORTS

Treatment of acute hepatic encephalopathy with L-dopa

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Summary
A clinical report of a 30-year-old woman who developed acute hepatic failure in the fifth month of pregnancy is presented. L-dopa administration resulted in marked improvement in both level of consciousness and electroencephalogram. The literature dealing with L-dopa therapy in hepatic encephalopathy is reviewed.

Introduction
Severe hepatic encephalopathy complicating viral hepatitis or drug reactions is associated with a mortality of between 50 and 85% (Lunzer, 1975). Treatment may include exchange transfusions, charcoal haemoperfusion (Gazzard et al., 1974), extracorporeal liver perfusion (Benhamou, Rueff and Sicot, 1972), liver transplantation and total body wash-out (Cline et al., 1973). This variety of regimes reflects the poor understanding of the pathogenesis, and the difficulties in management of hepatic encephalopathy. Fischer and Baldessarini (1971) and Fischer and James (1972) proposed that in hepatic encephalopathy, the accumulation in the central nervous system of ‘false neurotransmitters’ such as octopamine and β-phenylethanolamine, may be responsible for the characteristic neurological derangements. It was proposed that the use of L-dopa in these patients would prompt the restoration of physiological neurotransmitters and reverse the cerebral disturbance. Such a beneficial effect of L-dopa in three patients with hepatic coma had been described first by Parkes, Sharpstone and Williams (1970). The present authors wish to report a dramatic improvement after L-dopa therapy in the level of consciousness and in electroencephalographic tracing in a pregnant patient with fulminant hepatic failure.

Case report
A 30-year-old nurse in the fifth month of pregnancy was admitted to hospital because of jaundice. For 2 months before the onset of her illness she had been in repeated contact with patients suffering from viral hepatitis, during the course of her nursing duties. Two weeks before admission she had developed fatigue, nausea and vomiting, and 2 days before admission a temperature of 39°C had been observed. She had not received injections, dental treatment or medication. On examination she was fully conscious and slightly jaundiced with a temperature of 36°C. A few spider angiomata were visible over the anterior chest wall but the liver and spleen were not palpable. The size of the uterus was compatible with the duration of the pregnancy. Neurological examination was normal and there was no asterixis. Laboratory investigations: prothrombin time <12%; partial thromboplastin time 57 sec (normal <50); platelets, blood fibrinogen levels, bleeding, clotting and euglobulin lysis times were all within normal limits. Haemoglobin 12·7 g/100 ml; WBC 11·7 x 10⁹/l; total bilirubin 99 μmol/l (direct reacting 41 μmol/l); SGOT >7500 μu./ml (normal <50 μu./ml), SGPT 1065 μu./ml (normal less than 30 μu./ml); alkaline phosphatase 125 μu./ml (normal <80 μu./ml), vitamin B₁₂ 12 000 pg/ml (normal 200–800 pg/ml); total protein 60 g/l; albumin 23 g/l, and cholesterol 3·5 mmol/l. Blood urea nitrogen 2·5 mmol/l. HB₄Ag and HB₄Ab were not detected by radio-immunoassay.

Twenty-four hours after admission the patient became confused and developed a flapping tremor. Arterial blood ammonia was 200 μg/100 ml (normal <50 μg/100 ml). An EEG performed a few hours later
revealed slow, irregular activity of delta waves (Fig. 1). The patient received an infusion of 10% glucose, potassium chloride, fresh frozen plasma and neomycin enema. She became progressively apathetic, drowsy and stuporous. On neurological examination, she responded to pain stimuli only by movements of the extremities. The pupillary, corneal and gag reflexes were present and she breathed spontaneously. The legs were rigid and the tendon reflexes exaggerated. Treatment was begun with L-dopa, 1 g every 6 hr by mouth. One hour after the first dose there was a striking and dramatic improvement in her level of consciousness. She became more lucid and was able to speak coherently over the next 24 hr. Within 48 hr she had regained full consciousness and was able to control her activities. Concurrently the EEG tracings returned to normal (Fig. 1). L-dopa treatment was discontinued after 1 week. The only side effect noted was a sinus tachycardia of up to 140/min, which regressed after withdrawal of the drug. Fetal movement and heart sounds were recorded throughout the illness and 4 months later she had a normal delivery of a healthy baby.

Discussion

The use of L-dopa in acute hepatic encephalopathy has been described by Parkes, Sharpstone and Williams (1970) from two patients with fulminant hepatitis following halothane administration. There was rapid improvement in the level of consciousness as well as in the EEG tracing. Calvi, Cargnel and Davoli (1974) described the beneficial effect of L-dopa in two out of four patients with fulminant hepatitis. Contoyiannis et al. (1975) found benefit for at least 3 days in three out of eleven patients in hepatic coma due to fulminant hepatitis. The improvement in the state of consciousness appeared to be directly related to L-dopa administration. The present patient received L-dopa immediately after lapsing into coma and the effect was rapid with sustained improvement. This case illustrates the possible effectiveness of L-dopa treatment in a case of acute hepatic encephalopathy associated with pregnancy. Parkes et al. (1970), Fischer and Baldes-sarini (1971) and Fischer and James (1972) suggested that failure of the liver to detoxicate various biogenic amines produced from ingested proteins by intestinal bacteria may cause the accumulation in the brain of these substances. Since these amines function as weak transmitters they may interfere with normal synaptic impulse transmission in a manner analogous to that of pharmacological false neurotransmitters.

Case reports

Fig. 1. The right and left occipital tracing from EEG recorded before and during L-dopa therapy.

−1 hr: diffuse, moderate-amplitude delta waves, and triphasic waves before the initiation of L-dopa treatment.

+12 hr: generalized beta and delta waves with some triphasic activity 12 hr after starting L-dopa treatment.

+24 hr: diffuse rhythmic moderate to high amplitude theta waves (6 c/s), after 24 hr.

+48 hr: normal EEG with alpha activity (10 c/s), after 48 hr.
L-dopa may transiently reverse hepatic coma in some patients, presumably by serving as a precursor of the normal neurotransmitters dopamine and noradrenaline, or by displacing the false neurotransmitters from the synaptosomes.

The analysis of published reports describing the effect of L-dopa therapy in patients with hepatic encephalopathy are presented in Table 1. Fischer and Baldessarini (1971) noted improvement in three patients with acute on chronic hepatic encephalopathy but no EEG data were given. Similar results were described by Fischer and James in seven out of eight patients with profound hepatic coma (1971), and in another patient also (1972); by Sarrazin et al. (1971) in four patients; in one patient by Calvi et al. (1974) and in three by Weiss, Pitman and Javdan (1974). Arousal reaction in EEG tracing following marked improvement in the level of consciousness in one patient was reported by Stefanini and Hetherington (1972) and by Abramsky and Goldschmit (1974) in four patients with acute on chronic hepatic encephalopathy. Lanzinger and Kommerell (1974), however, did not find any changes in either clinical or EEG parameters in three patients with acute on chronic hepatic failure.

Lunzer et al. (1974) reported significant improvement after L-dopa therapy in four of six patients with severe chronic hepatic encephalopathy due to cryptogenic cirrhosis, although serial EEG showed no significant changes. Parkes et al. (1970) recorded improvement in consciousness and also in EEG tracing of one patient with end-stage cirrhosis.

Among the adverse reactions to L-dopa therapy are cardiovascular, gastrointestinal, respiratory and neuropsychiatric manifestations. Hypotension, cardiac arrhythmia, gastrointestinal bleeding, nausea and diarrhoea have been described as complications of L-dopa therapy in Parkinson's disease (Boshes, 1972), and may thus in some cases aggravate the already serious clinical state of hepatic failure. Hypotensive reactions have been observed in two patients with hepatic encephalopathy receiving L-dopa (Lanzinger and Kommerell, 1974), prompting a reduction of the administered dose. Nausea, vomiting and diarrhoea occurred in one case reported by Stefanini and Hetherington (1972), but no fatalities have as yet been attributed to the use of the drug.

This experience suggests that the administration of L-dopa may produce a dramatic improvement in some patients with hepatic encephalopathy and supports other similar experience in the literature. Although the response cannot be predicted, it would seem justified to try this treatment in cases of hepatic coma if other conservative measures fail.

Acknowledgment
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References

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* Hepatic encephalopathy is subdivided according to Lunzer (1975).
† n.g. — not given.
Cardiac tamponade and acute renal failure following
Salmonella agona pericarditis

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Summary
A 19-year-old female presented with cardiac tamponade complicated by acute renal failure. Salmonella agona was cultured from pericardial aspirate after repeated pericardiocentesis in several sites. Treatment with ampicillin and intermittent haemodialysis led to complete recovery.

Introduction
Systemic complications of Salmonella infection are well described and are usually the result of bacteraemia (Christie, 1974). Pericarditis associated with typhoid fever and other invasive Salmonella spp. is uncommon although recognized for many years (Levin and Hosier, 1961) and in a few cases bacilli have been cultured from pericardial aspirate. Spontaneous cure has been described (Cohen, Fink and Gray, 1936) but death has occurred despite intensive antimicrobial therapy (Bird, 1969).

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