Effect of dexamethasone on experimental cerebral infarction in the gerbil

M. J. G. HARRISON AND R. W. ROSS RUSSELL

From the National Hospital, Queen Square, London

SUMMARY Cerebral infarction was produced in the gerbil by ligation of one common carotid artery. The mortality from the lesion was significantly reduced by the daily administration of dexamethasone in the first 48 hours after surgery.

The beneficial action of steroids in the prevention and treatment of cerebral oedema in patients with brain tumours is accepted (Rasmussen and Gulati, 1962; French and Galicich, 1964; Garde, 1965; King, Moon, and Brown, 1965). In the case of cerebral infarction, another situation where oedema often occurs and is thought to contribute to mortality, the clinical evidence is conflicting. Thus two controlled trials showed no benefit (Dyken and White, 1956; Hetzel, Lander, and Robson, 1957), but other early reports (Russek, Russek, and Zohman, 1955; Rubinstein, 1965), and a recent double-blind study have suggested that cortisone or dexamethasone can improve the prognosis for patients with cerebral ischaemic 'strokes' (Patten, Mandel, Bruun, Curtin, and Carter, 1971).

Experimentally, steroids have been shown to reduce cerebral oedema from various causes—for example, exposure of the brain to air (Prados, Strowger, and Feindel, 1945), stab wounds (Foley, Chambers, and Adams, 1953), the injection of sesame oil (Hatanaka, Sano, Kitamura, Kamano, and Masuzawa, 1963), or triethyl tin (Taylor, Levy, McCoy, and Scheinberg, 1964). Plum, Alvord, and Posner (1963), however, found that dexamethasone failed to influence the mortality of rats exposed to anoxia after unilateral carotid artery ligation.

Adult Mongolian gerbils (*Meriones unguiculatus*) develop cerebral infarction after unilateral ligation of the common carotid artery (Levine and Sohn, 1969), apparently due to the presence of an incomplete circle of Willis. Approximately two-thirds of animals develop a cerebral infarct and in 90% of these the lesion proves fatal in one to three days (Levine and Sohn, 1969; Khan, Lawrence, and Pranzarone, 1971). This

preparation seemed a useful one in which to assess the effect of dexamethasone on the course of cerebral infarction. Kahn *et al.* (1971) have recently reported that intravenous dextran 40 significantly reduced the mortality from cerebral infarction in the gerbil using this same technique.

METHOD

Adult gerbils of either sex, weighing 32 to 160 g were anaesthetized with intraperitoneal pentobarbitone sodium (Nembutal) (60 mg/kg). A ventral midline cervical incision was made. The right common carotid artery was exposed, separated from adjacent tissues, and doubly ligated with silk sutures. The skin was sutured with silk.

In a control group of animals (average weight 71 g) the artery was exposed but not ligated.

Dexamethasone (Decadron—Merck, Sharp, and Dohme) was given at the end of the operation, and once daily for 48 hours postoperatively by intraperitoneal injection (5 mg/kg/day) in another group (average weight 86 g). Untreated animals (average weight 96 g) received normal saline by intraperitoneal injection or no injection.

Survival was recorded at eight, 16, and 24 hours and daily thereafter for six days postoperatively and at one week. The brain was removed after death or when killed at one week. Results of histological examination will be reported later.

RESULTS

CONTROLS Sixteen animals had a mock operation in which the carotid artery was exposed but not ligated. All survived the procedure. One animal died five days later, the others surviving until they were killed at one week.

UNTREATED Twenty six animals underwent ligation of the common carotid artery, and received

no steroid. All the animals recovered from the immediate effects of the anaesthetic and surgery. There were 10 deaths between eight and 24 hours, and seven further deaths between one and five days. The total mortality was thus 17 out of 26 (65%) (Table).

TREATED Sixteen animals received dexamethasone after ligation of the common carotid artery. There were no immediate deaths. One animal died between eight and 24 hours postoperatively and two others between one and five days. The total mortality was thus three out of 16 (19%) (Table 1).

TABLE

MORTALITY IN RELATION TO NATURE OF TREATMENT

Deaths	Controls (n = 16)	Untreated (n = 26)	Steroid (n = 16)
8 to 24 hours	0	10	1
1 to 3 days	0	6	1
3 to 7 days	1	1	1
Total mortality	1/16	17/26	3/16

Thus all the animals survived the immediate effects of anaesthesia and surgery. The mortality from unilateral carotid ligation (65%) parallels that reported by others (Levine and Sohn, 1969; Khan *et al.*, 1971). The administration of dexamethasone in this study reduced the mortality from cerebral infarction from 65% to 19%. This difference is significant at the 1% level ($\chi^2 = 6.9$; $P < 0.01$).

DISCUSSION

A significant reduction in mortality from experimental cerebral infarction in the gerbil has been shown to result from the daily administration of dexamethasone in the 48 hours immediately after vascular occlusion. The dosage schedule is high (5 mg/kg) but not higher than that used in the negative study of Plum *et al.* (1963). Differences in species and in experimental technique presumably account for the variation in results.

A recent double-blind clinical study has suggested that dexamethasone may improve the

morbidity from acute cerebral ischaemia (Patton *et al.*, 1971). The results of the present study provide experimental support for further such clinical trials.

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