THE INFLUENCE OF INJECTED THIOPENTONE ON MUSCLE TISSUE

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SUMMARY
Muscle biopsy was carried out in twelve dogs, 24 hours after the intramuscular injection of 5 per cent thiopentone. The specimens were examined histologically and in seven of the twelve animals foci of muscle necrosis were found. In a further two there were signs of acute inflammation. Control biopsies from the opposite limbs did not reveal any comparable findings. It is suggested that the disadvantages of intramuscular thiopentone outweigh its marginal clinical value.

Since the detailed description of the use of thiopentone by Lundy (1935) it has gained wide acceptance as the intravenous anaesthetic agent par excellence and is used in over 80 per cent of all anaesthetics in Great Britain (Dundee, 1956). It is also administered rectally in an aqueous solution (Weinstein, 1939; McNaught Inglis, 1954), and by suppository (Aladjemoff, Kaplan and Gestesh, 1958).

Keown et al. (1957) described the use of intramuscular injections of 5 per cent thiopentone to provide anaesthesia for cardiac catheterization in infants and children. It was later suggested that intramuscular thiopentone had a wider application in children for basal narcosis prior to inhalation anaesthesia and to control violent epileptiform seizures (Keown and Hitchcock, 1960) and to produce sedation during regional anaesthesia (Keown, 1961). Dhruva (1960) used intramuscular thiopentone to produce basal narcosis as an aid to paediatric anaesthesia in forty-one children and Litarczek et al. (1960) report its use in ninety-four cases for the induction of anaesthesia.

Since aqueous solutions of thiopentone are strongly alkaline and irritant to the tissues, intramuscular injections may produce local damage. We decided, therefore, to carry out histological studies of muscle tissue in dogs following injections of thiopentone.

METHODS AND MATERIALS
Healthy mongrel dogs weighing between 6 and 14 kg were used in the experiments. Each was given a deep intramuscular injection of freshly prepared thiopentone 5 per cent in normal saline into the hind leg. The dose was 10 mg/lb. (4.6 mg/kg) of body weight. An equal volume of normal saline was injected, as a control, into the muscle of the opposite hind leg. All injections were given under sterile conditions and the site of skin puncture was marked with a cross. Twenty-four hours later the dogs were anaesthetized with ether and 5 ml of methylene blue was injected intramuscularly through the previous puncture marks on the right and left hind legs. Muscle biopsies were immediately performed and the central portion of the area stained blue was examined microscopically. In order to localize as accurately as possible the areas of muscle which had been injected with the thiopentone and with the control solution, all injections were made at 90° to the skin using needles of identical size and length. Biopsy material was fixed in 4 per cent formaldehyde solution and paraffin sections were stained by haematoxylin-eosin.

HISTOLOGICAL FINDINGS
In seven of the twelve animals, muscle biopsies taken from the site of the intramuscular injection showed foci of muscle necrosis, involving isolated fibres or small groups of fibres, with an associated inflammatory reaction in the interstitial tissue.
Marked floccular change with loss of cross striations of individual muscle fibre. Interstitial inflammatory reaction. (H.E. × 500)

Fragmentation of necrotic muscle fibres. Marked inflammatory reaction in and around the area of muscle damage. (H.E. × 500)

(figs. 1 and 2). The affected muscle fibres showed increased acidophilia, loss of cross striations, and varying grades of floccular degeneration. The sarcolemmal sheaths of the affected fibres sometimes remained intact, and sometimes solitary fibres showing marked floccular change were seen between apparently normal fibres (fig. 1). The more severely affected fibres, however, showed fragmentation with disruption of their sarcolemmal sheaths, the nuclei of which were shrunken and pyknotic (fig. 2). In all seven cases the damage to the muscle fibres was accompanied by a marked inflammatory reaction in the interstitial tissue. The inflammatory infiltrate was composed of both polymorphonuclear leucocytes and mononuclear cells, and there was evidence of early phagocytosis of necrotic muscle fibres. Proliferation of sarcolemmal nuclei was present and contributed to the cellularity of the interstitial tissues in the areas of muscle damage.

In two additional animals a polymorphonuclear cell infiltration was seen in the interstitial tissues but there was no evidence of muscle necrosis in the biopsy specimen. It is possible that this inflammatory reaction occurred at the periphery of small foci of muscle necrosis which were not included in the sections examined.

In the remaining three animals, no histological changes of note were observed in muscle biopsies taken from the injection site.

In the control biopsies from the opposite limbs, no evidence of muscle necrosis and no comparable interstitial inflammatory exudate were evident in the control biopsies from the opposite limbs. In nine animals the control biopsies were completely negative, one dog showed mild interstitial haemorrhage, and two showed a very mild granulocytic infiltration of the interstitial tissues.

DISCUSSION

In this experimental work the dose of thiopentone and the concentration of the injected solution were those used by the various authors who have reported on the clinical use of intramuscular thiopentone. It is hardly surprising that the in-
Injection of a highly irritant fluid into muscle tissue should lead to acute inflammatory changes and even necrosis in a large percentage of cases. What is surprising is the paucity of clinical reports of local damage after intramuscular thiopentone. This is possibly due to the fact that the method has not been widely adopted, and perhaps to a natural reluctance to publish such complications. Nevertheless two reports have appeared. Dillon and Kavan (1960) describe the occurrence of a crater-like area of necrosis, which developed after injection of thiopentone into the deltoid muscle which required a "postage stamp" skin graft and which eventually healed leaving a depression in the skin. In this case recovery was complete after some months.

There are other disadvantages and dangers associated with intramuscular thiopentone. The injection is painful and in children invariably causes crying. The commonest complication noted by Keown and Hitchcock (1960) was hypoventilation which sometimes progressed to apnoea. There was also occasional respiratory obstruction due to relaxed tongue and jaw or laryngospasm. Cardiovascular depression, usually transitory, was also observed.

The object of intramuscular thiopentone, basal narcosis for the paediatric patient, can be obtained by other, more conventional, methods with less danger and discomfort to the patient. We would suggest, therefore, that the clinical value of intramuscular thiopentone is at best marginal.

REFERENCES

L’INFLUENCE DE LA THIOPENTONE INJECTION DANS LE TISSU MUSCULAIRE


ZUSAMMENFASSUNG