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Development of Tolerance to Ketamine in an Infant Undergoing Repeated Anesthesia

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Ketamine is useful for sedation of children undergoing repeated radiation treatments. The development of tolerance after multiple administrations of ketamine has been observed in animals, in children 6 months to 16 years of age, and in adults. The present report describes the development of tolerance during multiple administrations of ketamine to an 11-week-old infant undergoing radiation treatment of an orbital tumor.

REPORT OF A CASE

An 11-week-old, 6.4-kg male infant began a series of radiation treatments for retinoblastomas of the right eye. At that time the child was receiving no medications. Outpatient treatment was three times/week for 4 weeks. No premedication was administered. Ketamine was selected as the anesthetic.

An insulin syringe was used to measure the 10 per cent ketamine, which was injected into the quadriceps muscle of the thigh. Injection sites were alternated from thigh to thigh. For the first three treatments a dose of 30 mg of ketamine (4.72 mg/kg) was adequate. However, a total dose of 145 mg, in divided doses, was given over 2 hours on the first day because of a delay in carrying out the simulated treatment before the actual treatment (fig. 1). At the fourth and fifth treatments, ketamine, 35 mg, was inadequate to prevent movements that interfered with proper positioning. Supplementary injections of 15 and 35 mg, respectively, were necessary. At the sixth treatment a single dose of 50 mg was satisfactory. By the seventh and eighth treatments, this dose was inadequate, so the single dose for the ninth and tenth treatments was increased to 75 mg. The dose selected for the 11th treatment was 85 mg, because some significant movement had occurred during the tenth treatment session. The 12th and 13th (final) treatments were carried out with a dose of 105 mg.

Preliminary positioning for treatment was done during the 5 to 7 min required for the anesthetic to become effective. When the infant became quiet, with only slight movements of the extremities that did not jeopardize proper positioning of the head, final positioning was done. Persistence of vigorous movements of extremities for longer than 10 min after injection was accepted as an indication for a supplemental injection of ketamine.

Respirations and oscillations of the peripheral pulse monitor were observed via closed-circuit television during the brief radiation exposure. At no time was interruption of treatment necessary because of movement of the head during the treatment session. There was no problem with increased salivation. After treatment the child was quietly observed in the recovery room until ready for dismissal.

DISCUSSION

The development of tolerance to ketamine has been described in animals. In rats a decrease in sleep time was noted during a schedule of daily doses over 10 consecutive days.[1] In another study[2] a 26 per cent decrease in sleep time was noted in rats between the first and second daily doses of ketamine. Similarly, the duration of anesthesia has been noted to decrease in monkeys undergoing successive ketamine anesthesia.[3] However, in none of these studies was there a determination of the increase in dose required to produce the same results.

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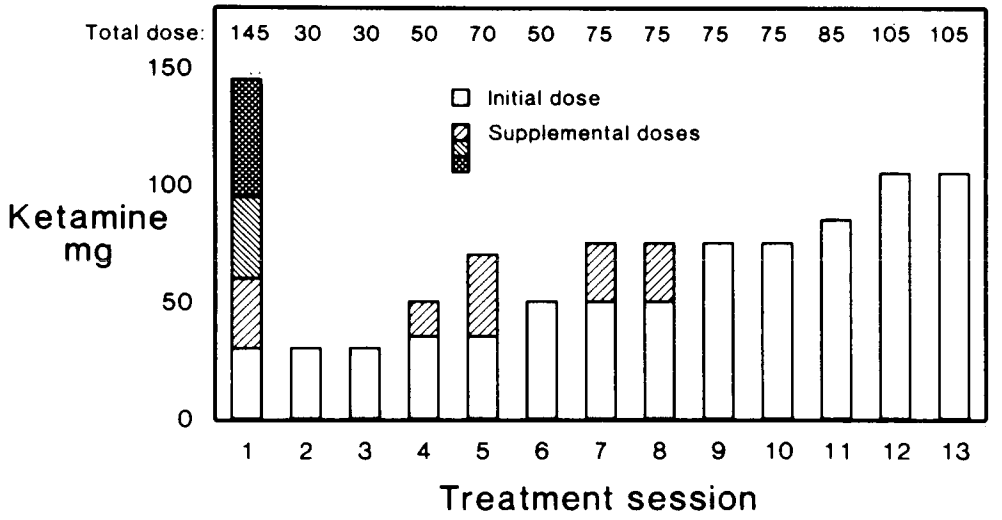

FIG. 1. Tolerance to ketamine developed after repeated administrations to 11-week-old infant for sedation before radiation treatment sessions.

Compared with results in laboratory animals, the tolerance to ketamine in humans appears to develop more slowly and with a lower incidence. Bjarnesen and Corssen[4] noted that tolerance to ketamine developed in patients who received the drug more than eight times. The mg/kg dose was similar to that shown to produce tolerance in animals. In contrast to the present case, an increase in successive doses of 33 per cent was sufficient to provide satisfactory anesthesia.

Bennett and Bullimore[5] noted that tolerance to ketamine, as evidenced by the shortening of the period of sedation, apparently developed in 7 of 10 children receiving radiotherapy daily. The treatment times involved apparently lasted from 5 to 25 min and the dose used was 5 mg/kg body weight. When a shortening of the duration of adequate sedation was noted, a 25 per cent increase in the dose was found to be satisfactory at subsequent treatment sessions.

Cronin *et al.*[6] described the use of ketamine for sedation in 17 children, whose ages ranged from 6 months to 3.5 years. An increase in dose requirement was observed in some of the children. A 6-month-old child required ketamine in the dose range of 12.5–22.3 mg/kg during 10 radiotherapy treatments.

Our criterion for adequate sedation, namely avoidance of movement of extremities sufficient to interfere with positioning of the head, may be different from the criteria of other investigators, who observed length of sleeping time, sedation, and adequacy of analgesia for treatment of burns. One of the features of ketamine is the persistence of movement of extremities, and our goal was to achieve a dose at which these movements would be minimal. We did not observe any perceptible trend in length of awakening time; the longest time from injection of ketamine to dismissal from the hospital was 97 min.

We conclude that ketamine is a safe, satisfactory, and predictable agent for providing adequate sedation for children undergoing radiation treatments. When using ketamine for repeated procedures, tolerance to the anesthetic may develop.

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