Effects of adrenaline and felypressin (octapressin) on blood flow and sensory nerve activity in the tooth

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The present investigations in cats were designed to study the effects of local anaesthetics containing adrenaline and felypressin (octapressin) on dental pulp function.
Intradental sensory nerve excitability was measured using electrodes placed in dentinal cavities in canine teeth. Changes in pulp blood flow were measured using the disappearance rate of a radioactive tracer placed in the same cavities.
Injections (0.5 ml) of lidocaine (20 mg/ml) – adrenaline (12.5 μg/ml) or prilocaine (30 mg/ml) – octapressin (0.54 μg/ml) were given supraperiosteally in the apical area of the tooth. Adrenaline either alone or with lidocaine caused almost complete inhibition of pulp blood flow within a few minutes. This effect was followed by a total inhibition of the sensory nerve activity. In most cases there was a recovery of both functions after 3 hours. Octapressin, on the other hand, had no inhibitory effects on pulp blood flow or sensory nerve activity. Lidocaine and prilocaine were also without effect.
These findings indicate a different mode of action of the two vasoconstrictors and suggest that octapressin may be preferred in infiltration anaesthesia during treatment of the vital tooth.

Keywords: Hormones; dental pulp, nerve impulses

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Adrenaline is frequently used to delay the absorption of local anaesthetics. However untoward cardiovascular effects and other contraindications to catecholamines have been reasons for introducing other types of vasoconstrictors such as phenylalanine – lysine – vasopressin (octapressin) (*Boissonnas & Guttmann*, 1960). Octapressin has a low toxicity in animals and in humans, with few systematic effects (for references see *Fisher et al.*, 1965). Comparisons of adrenaline and octapressin have shown that both enhance dental plexus anaesthesia (*Berling*, 1966). Octapressin has thus become an acceptable alternative to adrenaline in odontology. However, apart from their general effectiveness in prolonging local anaesthesia, little is known about the influence of these two agents on dental pulp function. The present study in cats was therefore carried out in order to compare the actions of adrenaline and octapressin on blood flow and sensory nerve function in the tooth.

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MATERIAL AND METHODS

Operative procedure

Experiments were performet on 10 adult cats (3.5–4.5 kg) anaesthetized with chloralose (40 mg/kg) and urethane (50 mg/kg). The trachea was cannulated and blood pressure was recorded from the femoral artery. The body temperature was kept constant at about 38 °C by heating lamps. The jaws were immobilized by means of a steel rod and dental acrylic. The general procedures are similar to those of *Edwall & Scott* (1971).

Neurophysiological measurements

Two cavities were prepared in the upper canine teeth leaving a thin layer of intact dentin over the pulp. One cavity was made over the pulp horn and the other close to the gingival margin. The cavities were filled with isotonic saline. Two platinum wire electrodes were inserted in the cavities and differential recordings were made between the two electrodes (Fig. 1). Signals were displayed on a cathode ray tube and fed into a tape recorder and equipment for frequency analysis (*Edwall & Scott*, 1971, *Haegerstam*, 1975 a). The potentials obtained by using this method have been shown to originate from intradental sensory fibres (*Arwill et al.*, 1973). Since no spontaneous activity can be recorded in freshly prepared cavities, aconitine (10^{-4} g/ml) was introduced into the coronal cavity for 3 min after which the cavity was washed with isotonic saline. Aconitine produced a steady discharge in the intradental sensory neurons (*Haegerstam*, 1976 b) which was consistent for more than 3 hours.

Measurements of pulp blood flow

A third cavity was prepared in between the two other cavities (Fig. 1). In this cavity a depot (0.1 µl) of a radioactive tracer solution (I^{131}, 80 µCi/µl) was applied and the cavity was covered with a thin plastic film to prevent evaporation.

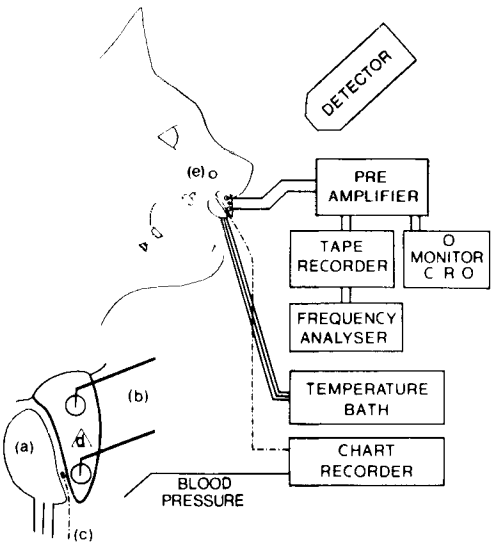

Fig. 1. Drawing showing experimental set up. Inset represents enlargement of tooth, thermode (a), electrodes (b) in cavities, thermocouple circuit (c), and cavity for disappearance measurements (d), (e) shows position of anaesthetic vasoconstrictor depot.

Pulp blood flow was determined according to the methods of *Edwall & Kindlova* (1971) and *Edwall & Scott* (1971).

The disappearance of the tracer depot was monitored by an external scintillation detector. The detector output was fed into a recording channel containing a single channel pulse height analyser and digital printout. The experiments were started 5–10 min after the isotope injection, when the disappearance rate was predominantly monoexponential. Counting periods of 40 sec were used. The disappearance rate was calculated as k-values and changes in the k-values were related to changes in the pulpal blood flow.

Injection of anaesthetic solutions

Supraperiosteal injections (0.5 ml) were made apical to the upper canine teeth. The cannula was inserted into the tissue in the same position as infiltration anaesthesia would be induced clinically. In some cases the exact position of the needle was estimated on two radiographs taken in different projections.

The cannula was left in position to ensure the same site of injection when the result of two consecutive procedures was compared in the same tooth.

The following solutions were tested:

1. Lidocaine 20 mg/ml – adrenaline 12.5 μg/ml.
2. Prilocaine 30 mg/ml – octapressin 0.54 μg/ml.
3. Lidocaine 20 mg/ml (as hydrochloride).
4. Adrenaline 12.5 μg/ml (as bitartrate).
5. Octapressin 0.54, 5.4 μg/ml.

The order of injected solutions was changed in different experiments to avoid systematic errors in the result due to interactions between different agents.

The solutions were obtained from usual commercial sources. When necessary agents were solved in isotonic saline.

RESULTS

Fig. 2 shows the influence of two different local anaesthetics on the intradental sensory nerve activity. Prilocaine (30 mg/ml) – octapressin (0.54 μg/ml) had no effect on the aconitine – induced activity, whereas lidocaine (20 mg/ml) – adrenaline (12.5 μg/ml) which was given 1 hour later, abolished the activity within 3 min. This inhibition was always preceded by a transient increase in activity seen in Fig. 2 and in the following figures. The preparation was then inexcitable for 2 hours, after which the activity gradually returned to a steady state level. Similar results were obtained in 9 teeth.

Fig. 3 illustrates the results when solutions of lidocaine (20 mg/ml) and adrenaline (12.5 μg/ml) were injected separately. Lidocaine did not influence the sensory nerve activity while adrenaline abolished the activity within 3 min. After 2 hours of inexcitability the nerve activity gradually returned to a steady state level seen in the figure. These results (5 procedures) demonstrate that adrenaline was the component of the anaesthetic solution which abolished intradental sensory nerve activity.

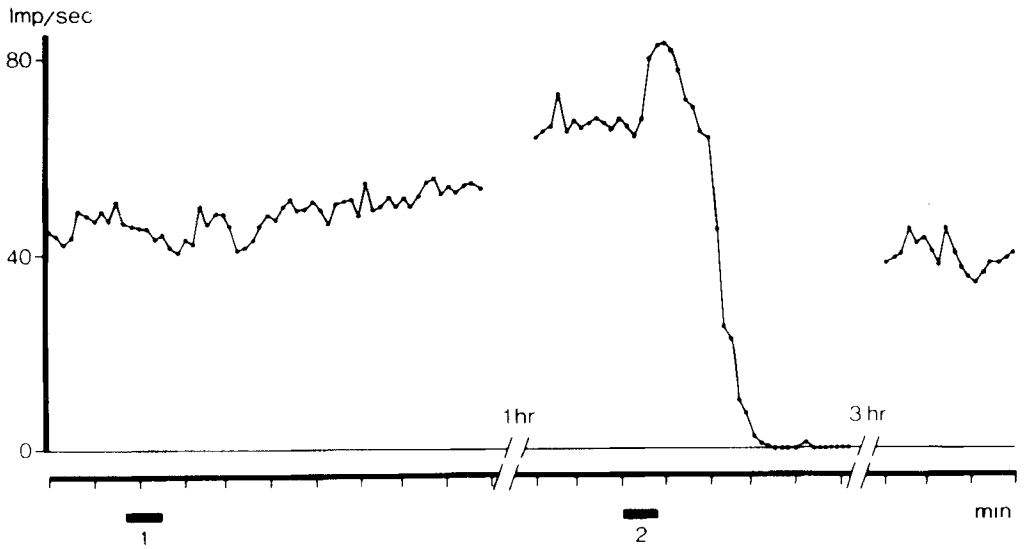

Fig. 2. Effect of injections of local anaesthetic solutions on impulse frequency.

1. Prilocaine 30 mg/ml – octapressin 0.54 μg/ml.
2. Lidocaine 20 mg/ml – adrenaline 12.5 μg/ml.

To further investigate this effect of adrenaline, simultaneous measurements of pulp blood flow and intradental sensory nerve excitability were carried out. Fig. 4 illustrates the nerve impulse frequency and the disappearance rate during injections of octapressin (0.54 μg/ml) and adrenaline (12.5 μg/ml). Octapressin had no effekt on these two parameters. However, when adrenaline was injected 30 min later in the same experiment, the k-values were markedly reduced within 3 min. This was followed by a total reduction of the nerve impulse activity. During the following 2 hours the disappearance of the tracer showed a complete standstill and the sensory neurons were inexcitable. After this period, k-values increased irregularly and nerve activity started some minutes later. Three hours after the injection, both functions were normal compared to control (not shown in the figure). These results represent the typical findings obtained in 6 teeth, in two of which octapressin was used in a tenfold higher concentration (5.4 μg/ml).

In 5 out of 20 teeth there was no effect of adrenaline on pulp blood flow or sensory nerve activity within 15 min of the injection. By changing the position of the needle, however, it was always possible to obtain typical effects as shown in the figures. The absence of responses to octapressin was always followed by clear-cut responses to adrenaline.

DISCUSSION

The present study shows that injections of adrenaline either alone or with lidocaine reduce pulp blood flow and abolish experimentally induced intradental sensory nerve activity. Octapressin had no such action. Lidocaine and prilocaine were also without effect.

The reduction of blood flow after injection of adrenaline was always followed by a

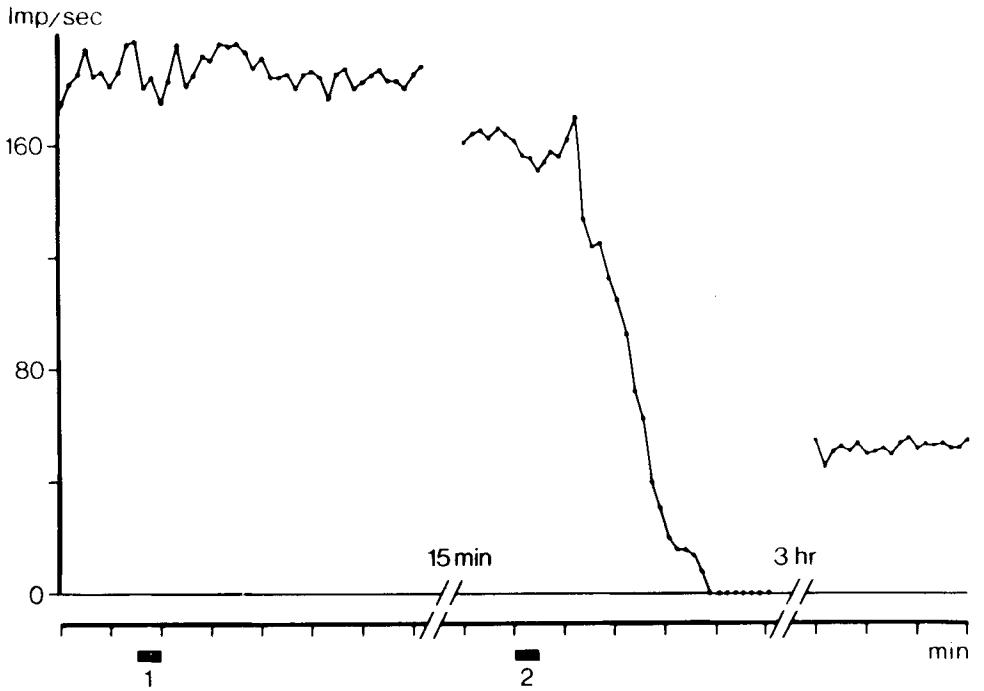

Fig. 3. Influence of injected lidocaine and adrenaline on impulse frequency.

1. Lidocaine 20 mg/ml.
2. Adrenaline 12.5 μg/ml.

depression of nerve activity. This finding is in agreement with previous observations by *Edwall & Scott* (1971) who found similar concomitant reductions in blood flow and sensory nerve excitability in the cat pulp following vasoconstrictor nerve activation. They concluded that the excitability of sensory neurons in the tooth is strongly modulated by changes in blood flow. Thus, in the present study the primary action of adrenaline is a reduction of blood supply to the pulp which secondarily influences the sensory nerve function. This effect was probably not an action of adrenaline on vessels within the pulp, but was rather due to constriction of arterioles proximal to the tooth and close to the injected depot. Support for this view may be found in the experiment where lidocaine (20 mg/ml) was injected alone without any effect on the intradental sensory nerve activity. In previous experiments (unpublished) where a low dose (0.1 mg/ml) of lidocaine was given i.a. or by local application to exposed dentin, the intradental nerve activity was rapidly abolished. It may therefore be suggested that agents such as lidocaine and adrenaline which are easily diffusable and absorbed in tissue are not distributed into the pulp tissue from the submucosal depot.

The lack of effect of octapressin on pulp flow and on nerve activity even in high concentrations suggests different modes of action of adrenaline and of octapressin.

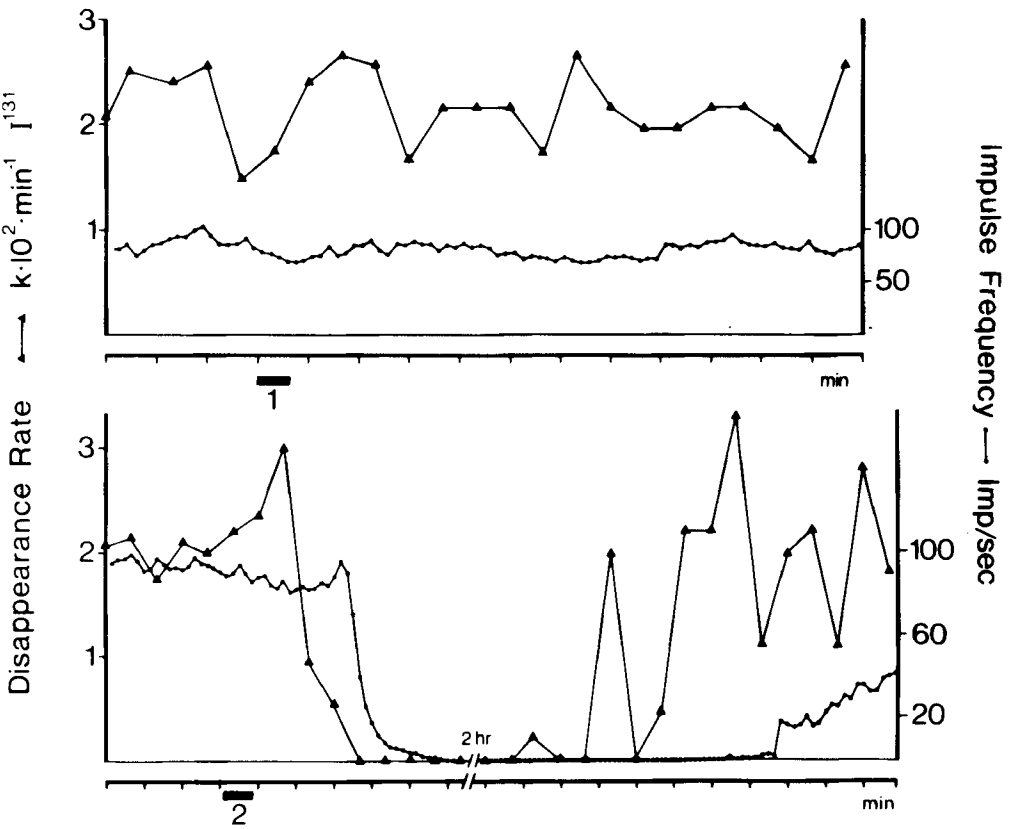

Fig. 4. Effects of injections of vasoconstrictors on tracer disappearance rate ▲—▲ and on impulse frequency ●—●.

1. Octapressin 0.54 μg/ml.
2. Adrenaline 12.5 μg/ml given 30 min later with cannula in the same position.

Previous studies by *Cerletti et al.* (1963) and *Altura et al.* (1965) indicated that adrenaline and octapressin act on different sections of the vascular bed. Thus catecholamines have been shown to constrict precapillary resistance vessels as well as post-capillary capacitance vessels, while octapressin has only a weak constrictor effect on the pre-capillary vessels with a stronger effect on post-capillaries. Thus adrenaline is a more powerful constrictor of pre-capillary vessels than octapressin. This could explain the present results.

On the other hand, it is well established from human and animal studies that both adrenaline and octapressin have a similar effect in delaying the absorption of local anaesthetics (*Berde et al.*, 1961, *Åkerman*, 1966, *Berling*, 1966). These findings suggest that, at least in the injected depot, adrenaline and octapressin have similar constrictor effects on the pre-capillary section thus reducing the number of open capillaries. In view of these conflicting findings, other differences between adrenaline and octapressin must be considered in order to interpret the present results. For example, diffusion limits may be greater for the large polypeptide octapressin than for adrenaline. If this is the case, adrenaline may reach the intraosseos vessels which supply the dental pulp more easily than octapressin. However, further studies are needed to elucidate the proposed differences in the vasoconstrictor actions of catecholamines and octapressin.

In most of the present experiments adrenaline caused a long-lasting and complete standstill of the tracer disappearance. This could indicate a total terardation of pulpal blood flow. However, such a quantitative comparison may not be justified. It was recently demonstrated by *Bolme & Edwall* (1971) in dog skeletal muscle that vasoconstriction induced by maximal nerve stimulation reduced the rate of tracer disappearance more than blood flow. Such dissociation between changes in blood flow and changes in disappearance rate may also be found in the dental pulp (*Edwall*, 1971). It can, however, be stated that the alteration in pulp blood circulation following adrenaline injection was serious enough to produce a total long term abolition of sensory nerve function, provided that the site of injection was in close relation to the apex of the tooth.

In all experiments the changes of pulp function caused by adrenaline appeared to return to control values after a period of 3–4 hours. We have no information as to whether there may be other consequences of the adrenaline-induced ishemia in the pulp which may occur late.

It should be stressed that the present investigation was carried out on healthy pulps which had not suffered from dentinal decay or from insults of thermal trauma during preparation of dentin and impression procedures. In the clinical situation, when such insults are present, infiltration anaesthesia with adrenaline may result in irreversible alterations of pulp functions. This suggestion is supported by previous studies in rat incisors by *Pohto & Scheinin* (1960). Using direct observations of pulp blood flow, they found that additional irritation by heat to exposed dentin caused a higher incidence of irreversible changes of pulpal circulation when blood flow was retarded by mandibular block injections of adrenaline compared to controls without adrenaline.

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