Cyanosis of the hands following the use of alphaprodine in dental anaesthesia

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A case is presented of asymptomatic cyanosis of the hands, seen four hours after dental surgery under intravenous, local and inhalational anaesthesia. Alphaprodine hydrochloride, a synthetic opiate and one of the agents used, may produce dilatation of the venous bed with passive venous pooling. Such a mechanism is thought to have occurred in this case, manifesting as cyanosis. A weakly positive intradermal skin test to alphaprodine suggests immediate type hypersensitivity as a possible underlying cause.

Opiates are used widely in medical practice, both for sedation and anaesthesia. Side effects, particularly respiratory and cardiovascular, are well known, and use of these agents is often modified to minimise such effects. One action, namely dilatation of the venous bed, is sometimes used to advantage to reduce "preload" in patients with acute myocardial infarction, but is at other times an unwanted effect. This clinical report discusses an unusual manifestation of this side effect.

Case report

An 18-year-old girl, previously well, on no medications, and not taking oral contraceptives, underwent extraction of two wisdom teeth. At the start of the procedure 3.6 cc of two per cent lidocaine with 1:100,000 epinephrine was injected locally, and

10 mg alphaprodine injected intravenously. Throughout the 15-minute procedure the patient received nitrous oxide 40 per cent and oxygen 60 per cent, in addition to a constant infusion of methohexitone (total dose 180 mg over 15 mins). During the procedure she was sitting upright with her hands resting freely on her lap, and with her feet dependant. She wore thick woolen socks to her knees.

There were no immediate complications and she recovered in the sitting position over the next 30 minutes. She then returned home feeling well and rested, again largely in the sitting position. Four hours later her father noticed that both her hands were blue, a fact that had not previously been observed by the patient.

When seen in the emergency department shortly thereafter, the patient denied any symptoms whatever, and specifically denied weakness or sensory abnormality of the hands. Physical examination revealed glove distribution of cyanosis in both hands to the wrists. Radial pulses were equal and of good volume, and nailbed capillary filling was prompt. The cyanosis was partly relieved by elevation of the arms. There was no objective sensory deficit, weakness, or oedema of either hand. A healing venupuncture site was observed in the left antecubital fossa. Examination of the legs and feet was unremarkable and a general systemic examination was normal.

Within 36 hours of the anaesthetic the cyanosis had completely resolved, and full examination was normal. The patient remained asymptomatic.

Key words

ANALGESICS: alphaprodine; COMPLICATIONS: cyanosis, hypersensitivity.

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Investigations

The results of tests performed on blood drawn during the emergency department visit were: Hb 138 g·L⁻¹; WCC 12.6 with mild neutrophilia; platelets normal; ESR 4; urinalysis normal; serum

protein electrophoresis normal; rheumatoid factor -ve; ANA -ve; Complement C3 normal; C4 mildly reduced; direct antiglobulin test -ve; atypical antibodies -ve; cold agglutinins -ve; blood cultures (aerobic and anaerobic) -ve.

Intradermal prick skin testing was performed on the right forearm one week after the extractions. Lidocaine two per cent with epinephrine 1:100,000, methohexitone, and alphaprodine were all obtained from the dental surgeon. One ml was taken from each and mixed separately with 1 ml of distilled water in order to provide half-strength samples. In addition, 1 ml samples were taken of each agent to provide full-strength samples. A 1 ml sample of distilled water was taken for use as a control solution.

One drop of each of the control solution and half-strength samples was put on the patient's forearm, and an intradermal prick was made through each drop with a clean stylet, allowing a very small amount of the sample to enter the superficial dermis. Each drop was then carefully wiped off and the test areas were marked. The tests were read at ten minutes and 24 hours and the following results were noted. Alphaprodine gave a 2 mm wheal at ten minutes but was negative at 24 hours. Control, lidocaine, and methohexitone were negative at both readings.

Because of the mild reactions, all the tests were repeated using the full-strength (undiluted) solutions, with control sample and technique as above. Alphaprodine gave a 4 mm wheal at ten minutes but was negative at 24 hours. Control, lidocaine, and methohexitone were again negative at both readings.

Discussion

The results of investigations carried out on this patient make it unlikely that she was suffering from immune complex disease, paraproteinemia, sepsis, or other disease that could cause cyanosis as an expression of such mechanisms as vasculitis or hyperviscosity.

The one abnormal result was the skin test reaction to alphaprodine. However, some controversy exists as to the accuracy of skin testing in diagnosing hypersensitivity to medications. Of the many techniques used, intradermal prick testing (as described above) is thought to be the most reliable.¹ The size of reaction thought necessary for a positive result is

also the subject of discussion, but a consensus would accept a wheal of 3 to 4 mm diameter as the minimum acceptable.¹ Even so, a positive reaction may represent hypersensitivity to (or irritation by) a component of the solution other than the medication itself. Opiates have been known to occasionally induce wheals by non-immunological means,² though usually it represents IgE mediated reactions. In this case there would appear to be reasonable evidence to suggest an immediate type hypersensitivity to alphaprodine although the clinical expression is not typical of an allergic response.

Alphaprodine is an opiate narcotic, closely related to meperidine, and as such the following cardiovascular effects can be expected.³ Relative hypotension when upright, increase in heart rate, reduced peripheral arterial and venous resistance, and increased peripheral blood flow. None of these would be expected to be clinically significant at therapeutic doses, however, especially in the supine position.

Allergic reactions include urticaria and other rashes (both local and generalised), and rarely anaphylaxis.³ A case of severe respiratory depression, coma, and death was reported in a child,⁴ but the dose of alphaprodine was considered high, and adequate treatment was delayed for two hours. Another report of respiratory depression and hypoxic encephalopathy in a young child⁵ was seen with long-term neurological sequelae. However, this was in the setting of multiple pharmacological usage, and the implication of alphaprodine has been questioned.^{6,7}

Alphaprodine is detoxified in the liver, and reduced doses are advisable in the setting of hepatic failure.⁸ Opiates will interact with other medications, particularly phenothiazines, monoamine oxidase inhibitors, and tricyclic antidepressants.^{3,5} Dose reductions are necessary in these situations to prevent respiratory depression, but there is no potentiation of the venodilatory effects.^{3,5} This patient was not receiving any of the above classes of drug and did not display clinical evidence of hepatic dysfunction.

In summary, therefore, it is likely that this girl experienced mild generalised venodilatation secondary to administration of alphaprodine with gravitational venous pooling in the hands. Similar pooling in the feet and lower legs was probably prevented by support from the thick knee length socks that she

was wearing. Whilst the results of skin testing are not conclusive, there is some evidence to suggest an immediate type hypersensitivity to alphaprodine. Such a reaction may have potentiated the venodilatation seen in this patient.

References

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Résumé

On présente le cas d'une cyanose asymptomatique des mains, observé quatre heures après chirurgie dentaire sous anesthésie générale par agents volatiles, anesthésie locale et anesthésie intraveineuse. L'hydrochlorure d'alphaprodine est une opiacée synthétique et l'un des agents utilisés pouvant produire une dilatation veineuse ainsi qu'une stase. Un tel mécanisme a pu survenir dans ce cas se manifestant par une cyanose. Un test cutané légèrement positif à l'alphaprodine suggère une hypersensitivité de type immédiat comme cause possible.