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Prolonged Cutaneous Sequelae After Intra-Arterial Injection of Propofol

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ABSTRACT

Propofol is a popular drug for the induction of anaesthesia and sedation in the intensive care. Previous cases of inadvertent intra-arterial injection propofol injection have had no more than a few hours of hyperaemia. However in this case, residual cutaneous hyperaemia for 12 days were found after intra-arterial injection. This report also highlights the presence of an aberrant radial artery at a site that is used commonly for intravenous cannulation. Early suspicion should be aroused if the patient complains of pain on injection that is not abolished by lignocaine and if blanching of the hand is seen on injection. A useful precaution is establishing a running intravenous line before the administration of drugs. The literature concerning prevention and treatment of inadvertent intra-arterial injection is discussed.

Keywords: aberrant artery, pain on injection

CASE REPORT

A previously healthy 16-year-old boy was scheduled for elective tonsillectomy. An 18G venous cannula (Venflon) was inserted into a superficial vessel on the radial side of the left forearm near the wrist. Flash back was obtained with a single attempt and the venula was threaded with ease. It was then plugged with a rubber stopper, while digital pressure was applied.

A mixture of 14 mLs of 1% propofol and 2 mLs of 1% lignocaine was then administered. The patient complained of pain in the hand. It was assumed to be venous pain and additional 2 mLs of 1% lignocaine was given, followed by the rest of the induction dose. However, the patient still complained of pain in the hand but loss consciousness quickly. A total of 140 mg of propofol was given over 30 seconds . Blanching of the skin was noticed at the site distal to the venula. This was transient and within 5 seconds, was replaced by hyperaemia of the hand. Intra-arterial injection was then suspected; the stopper was removed and connected to a primed infusion set and arterial pulsatile flow was noted to back-flow up the tubing, confirming our suspicion. The hand was inspected and showed good capillary return and the radial pulse was strong. Loss of consciousness was rapid within 20 seconds and there was no noticeable delay. Intra-arterial heparinised saline (30 units in 3 mLs) and 3 mLs of 1% lignocaine was injected through the venula, while a separate running venous line was established. Atracurium 40 mg was given intravenously and the patient was intubated.

The tonsillectomy proceeded uneventfully under balanced anaesthesia with isofluorane, atracurium and nitrous oxide and oxygen. The pulse oximeter probe on the affected hand read 100% throughout the operation. The hand was carefully observed. There was mild hyperaemia and oedema of the whole hand. Capillary return was normal.

In the recovery area, the patient had no complaints of pain, motor or sensory loss in the hand. There was an oval area of 10 cm by 5 cm of skin proximal to the injection site on the forearm that was hyperaemic. The forearm and hand was oedematous. Papaverine 40 mg was injected around the artery at the site of puncture and an ipsilateral brachial plexus block with 10 mLs of 0.125% bupivacaine was given via the interscalene route for pain relief and to achieve sympathetic blockade for vasodilatation. The patient was brought back to the ward and a referral was made to the orthopaedic surgeon. The patient's hand was monitored hourly for presence of radial pulse and speed of capillary return in the nail bed after pressure.

Six hours after the incident, the patient had no complaints of pain, sensory or motor loss to the affected hand. Circulation of the hand was assessed to be adequate, the radial pulse was strong, colour was pink in the fingers and capillary return was normal. Twenty-four hours from the time of the incident, the area of hyperaemia and oedema of the forearm was still present and similar in severity.

The area was hyperaesthetic but otherwise, the motor and sensory functions of the hand were normal. The patient was seen by an orthopaedic surgeon who confirmed the presence of a superficial aberrant radial artery at the site of injection by doppler flow studies. There was no corresponding artery found in the other arm.

The patient was given a memo that advised against intravenous cannulation in that arm. He was otherwise well and discharged with a follow-up appointment with the orthopaedic surgeon. Three days after the incident, in a telephone conversation with the patient, the patient said that the hyperaemic patch was very faint and he was otherwise well.

On follow-up 12 days after the incident, the colour of the skin was normal and he had no objective sensory loss to touch or motor loss.

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DISCUSSION

There are a number of interesting points in this case that are in contrast with other reported cases and also brings to attention, means of prevention and early detection. In the forearm, the aberrant radial artery may be superficial to the extensor muscles and superficial to the deep fascia at the wrist[1]. At this point, it would lie at a favoured site of venous cannulation.

In two case reports, intra-arterial propofol was given via the radial artery[2,3]. In three other cases, propofol was given at the antecubital fossa via the brachial artery[4-6].

In all previous reports of inadvertent intra-arterial injection of 1 to 11 mLs of 1% propofol, there was no prolonged sequelae beyond 4 hours[6].

Lack of pulsation because of the presence of a tourniquet or application of digital pressure while applying a stopper can prevent detection. Unrecognised arterial cannulation and administration of drugs are apt to occur when there is an anomalous artery or when arterial pulsations are diminished such as when blood pressure is low or a tourniquet is present. Blood may not spurt back through the venula when the gauge of the venula is small or the venula bevel is only partly through the wall[7]. A test dose for the presence of severe pain may seem a useful suggestion but may have false negatives if given slowly. Furthermore, in the case of a less innocuous drug such as thiopentone 5% to 10%, 1 to 2mLs can cause considerable arterial damage[7]. The best precautionary measure seems to be establishing a running intravenous drip[7] prior to any injection.

Pain on injection was certainly not abolished by the addition of lignocaine which is a common practice. Hence the addition of lignocaine to propofol may continue to be employed as a useful technique for reducing venous pain without the fear that it may mask signs of arterial injection. Pain on injection that is not abolished with lignocaine should be carefully checked to exclude intra-arterial injection. The dose of lignocaine used with propofol is usually small (10 to 20 mg). However, it is not known if a large amount would abolish arterial pain. Blanching and hyperaemia that occurred have been reported in as little as 1mL of intra-arterial propofol[3] and not reported in as large a dose as 8 mLs[2]. Lignocaine is a vasodilator and it was suggested that flushing with lignocaine may prevent blanching of the skin[8]. Lignocaine was used at several points in this case and in other cases[4-6] but did not prevent blanching, hyperaemia and flushing[5,6]. The appearance of blanching and hyperaemia on injection must not be dismissed as local histamine release reaction or due to extravasation of drug. In one report, extravasation of a large volume of propofol did not lead to pain or serious complication[9]. Intra-arterial propofol does not lead to a clinically obvious delay in loss of consciousness; hence this would not alert the anaesthetist to the problem.

The persistence of hyperaemia up to 4 hours has been reported[6] but there is no other report of persistence for a period of days as in this case, or the presence of swelling of the hand. As this is the largest dose reported (140 mg), this is likely to be a dose-related phenomena.

In one study, 200 mg of propofol was injected over 120s into an isolated artery of a rabbit ear in-vitro. Propofol was found not to be toxic to the endothelium and may possess vasodilating properties[8]. However the article wisely points out that in vivo, vascular supply can still be compromised by physical interaction of the drug with blood components or by particulate embolisation[8]. Indeed these factors could perhaps account for the blanching and the presence of swelling of the hand after the incident.

Therapy may not have altered the prognosis in this case although the sequelae was prolonged compared to other anecdotal accounts. Most previous reports of the treatment of intra-arterial injections involved thiopentone. However, the general principles probably apply in inadvertent arterial injection of drugs with the potential for arterial thrombosis. In the case of thiopentone, the main pathology has been found to be chemical arteritis and arterial thrombosis, and not arterial spasm[7]. A study into the modes of therapy in the treatment of intra-arterial thiopentone found that intra-arterial injection of vasodilators such as tolazoline, papaverine and procaine only produce transient vasodilation in the femoral artery of the rabbit[10]. Intra-arterial procaine 4%, which is often advocated for the treatment of intra-arterial thiopentone was not found to reduce the area of gangrene in the pinnae of rabbits injected with intra-arterial thiopentone[10]. Sympathetic denervation block probably acts by increasing circulation and has been found to reduce the size of the affected area[10]. Full heparinisation with heparin 2,500 units/kg in rabbits was found to reduce the affected area in the pinnae of rabbit ears. The first dose was injected into the central artery of the pinnae of the ear and subsequent doses via the intramuscular route. However, a high dose for several days was required and a few animals were lost to haemorrhage, usually at the intra-muscular injection site[10]. Thrombosis can be delayed for up to 2 weeks after the intra-arterial injection[7]. Thrombosis and embolectomy have been unsuccessful in establishing perfusion below the wrist[7]. Pain in the arm should be treated with brachial plexus block. The affected part should be elevated to prevent circulatory stasis[7]. The concentration of the solution is an important factor. There has not been a single case of gangrene when the concentration of thiopentone was 2.5% or less[7].

Physician as well as patient education and awareness play a very important part in the prevention of recurrence of such an incident if an aberrant radial attery is present. All physicians who assume the responsibility of intravenous administration of drugs must assume the responsibility to ensure that intravenous drugs are injected into well-identified veins. It is arguable in the case of propofol whether any measure was necessary. Based on the case reports published, permanent sequelae is unlikely with or without therapy[2-6]. In the case of a less innocuous

drug, for example thiopentone, immediate measures that may be helpful would be limb elevation, sympathetic blockade and full heparinisation for a week . This incident is a good reminder to all physicians who are involved with parenteral injection, of the dangers of accidental intra-arterial injection which is an avoidable complication with potentially disasterous complications.

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Reclassification of Preparations Containing Phenolphthalein from GSL to POM

1. Phenolpthalein-containing laxatives have been approved for general sales in Singapore. However, new toxicology data have recently become available, neccessitating a review of the safety of preparations containing phenolpthalein. Data from genotoxicity and carcinogenicity studies in mice have identified a genotoxic and carcinogenic risk. The relevance to humans of these findings has not yet been established. The Medicines Advisory Committee has therefore decided to restrict the use of phenolpthalein by bringing it under prescription control.
2. With effect from 1st April 98, suppliers of preparations containing phenolphthalein would be informed to limit sales of these products to doctors and registered pharmacies only. By 1st July 98, suppliers of such products are expected to complete withdrawal of their products from all retail outlets, except registered pharmacies and doctors' clinics.
3. The CPMP position paper on the genotoxic and carcinogenic potential of phenolphthalein and a list of registered preparations containing phenolphthalein are available from:
   The Pharmaceutical Department, MOH, Tel 325 5606, Fax 222 6797.