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EFFECT OF DILUTING PROPOFOL ON THE INCIDENCE OF PAIN ON INJECTION AND VENOUS SEQUELAE

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SUMMARY

The effect of diluting propofol in 5% dextrose on the incidence of i.v. injection pain was studied in 100 adult patients. Severe injection pain occurred in 32% (16 patients) who received undiluted propofol, compared with 10% (five patients) who received dilute propofol. We concluded that the dilution of propofol significantly reduced the incidence of severe pain during injection without increasing postoperative venous sequelae.

There have been several studies of the incidence of pain during induction with propofol [1–5]. Pain has been reported in up to 45% of administrations, but adverse venous sequelae have been infrequent [1, 6]. Attempts have been made to reduce pain by injection into a large vein [1] or by using local anaesthetics [2, 3].

This study (approved by the local Ethics Committee) investigated injection pain and venous sequelae when propofol diluted with an equal volume of 5% dextrose was injected into a vein on the dorsum of the hand. Dextrose 5% was chosen as the diluent after discussions with the manufacturer.

METHODS AND RESULTS

We studied 100 adult male or female patients (ASA grades I and II) younger than 70 yr who were scheduled to undergo elective or emergency surgery. Patients with existing signs of venous inflammation were excluded, as were those who had received analgesics in the preceeding 24 h. All patients were premedicated with temazepam 20 mg by mouth. None was told that we were either assessing or expecting injection pain.

In the anaesthetic room, a 22-gauge cannula (Venflon, Viggo) was placed in a vein on the dorsum of one hand through an intradermal bleb of 1% lignocaine. Patients were allocated randomly to two groups: in group I anaesthesia was induced with undiluted propofol 10 mg ml^{-1} injected at a rate of approximately 1 ml s^{-1}; in group II, anaesthesia was induced with propofol freshly diluted to 5 mg ml^{-1} with 5% dextrose injected at a rate of approximately 2 ml s^{-1}. The time from the start of injection to loss of verbal contact and the dose of drug administered were recorded.

During the injection the patient was asked: "is this comfortable?". If the response was negative, the patient was asked, "Does it hurt a little or a lot?" An independent assessor (who was unaware of the propofol formulation) recorded the injection as having caused no pain, moderate pain, or severe pain.

Additional drugs used during maintenance of anaesthesia were injected into the contralateral arm. The cannula through which induction agents were administered was removed after 30 min and the injection site dressed with a dental roll and tape.

Inspection of the injection site was carried out immediately after operation and at 24 h. After the 24-h inspection, each patient was given a questionnaire with the questions: "Does the vein feel tender?". "Does it look red?" and "Does it feel hard or ropey?" to be answered at 4, 8 and 12 days after operation. The questionnaires were returned by post.

There were 32 females and 18 males in group I; 44 were ASA I; mean age was 35.4 (SD 14.1) yr and mean weight 66.6 (11.7) kg. Group II comprised 33 females and 17 males; 44 were ASA I;

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TABLE I. *Incidence of injection pain in patients receiving undiluted (group I) and diluted (group II) propofol. Difference between the two groups significant at* $P < 0.02$ *(Chi-squared test)*

Concentration of propofol	No pain on injection	Moderate pain on injection	Severe pain on injection
Undiluted (10 mg ml^{-1})	25	9	16
Diluted (5 mg ml^{-1})	38	7	5

mean age was 41.0 (15.8) yr and mean weight 63.6 (11.2) kg. Mean time from premedication to induction was 89.5 (45.6) min for group I and 108.8 (64.7) min for group II. There was no significant difference between the two groups in any of these variables.

For induction of anaesthesia, group I received a mean (SD) propofol dose of 2.47 (0.36) mg kg^{-1} at 9.8 (1.64) mg s^{-1} and group II received 2.23 (0.31) mg kg^{-1} at 8.2 (1.4) mg s^{-1}. The rates of delivery were significantly different ($P < 0.001$, Student's t test). The mean induction time was 16.9 (3.7) s in group I and 17.8 (5.4) s in group II (ns).

Pain on injection experienced by the patients is shown in table I.

At the 24-h inspection, three patients in group I had a tender vein; in group II one had erythema and two had a tender vein. From the questionnaires (87% were returned), one patient in group I and one in group II reported "hardness" of the vein after 4 and 8 days, respectively, with redness and tenderness. Both these patients had a normal clinical assessment of the injection site at 24 h. They were asymptomatic by 12 days. There were no significant differences in venous sequelae at any time between the two groups (χ^2 test).

COMMENT

The difference in the rate of delivery of propofol may be accounted for by the need to use more than one 20-ml syringe in some of the group II patients. However, there was no significant effect on induction time, which was the period during which the patients were likely to experience any pain.

There was a significant difference between the groups in relation to injection pain (table I). Almost all of this significance resides in the difference in incidence of severe pain: 32% in group I compared with 10% in group II. The genesis of pain after injection of propofol may involve the activation of pain mediators such as kininogens following exposure of the vein wall to the drug [4]. A mechanism such as this may explain both the inter-individual differences observed and attenuation of pain by dilution.

Although this hypothesis may explain partly the reduction in severe pain in group II, it does not account fo the similar incidence of moderate pain in both groups. Our experimental design attempted to match the delivery rate of propofol (mg s^{-1}) in the two groups and this resulted in visible venous distension during induction in some of the patients in group II. This may have contributed to the incidence of moderate pain. It is possible that a slower rate of injection of dilute propofol might be effective in diminishing moderate pain.

REFERENCES

1. Stark RD, Binks JM, O'Connor KM, Arnstein MJA, Glen JB. A review of the safety and tolerance of propofol (Diprivan). *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 152–156.
2. McCulloch MJ, Lees NW. Assessment and modification of pain on induction with propofol (Diprivan). *Anaesthesia* 1985: **40**: 1117–1120.
3. Brooker J, Hull CJ, Stafford M. Effect of lignocaine on pain caused by propofol injection. *Anaesthesia* 1985; **40**: 91–92.
4. Scott RPF, Saunders DA, Norman J. Propofol: clinical strategies for preventing the pain of injection. *Anaesthesia* 1988; **43**: 492–495.
5. Morton NS, Wee M, Christie G, Gray IG, Grant IS. Propofol induction of anaesthesia in children: A comparison with thiopentone and halothane inhalational induction. *Anaesthesia* 1988; **43**: 350–355.
6. Matilla MAK, Koski EMJ. Venous sequelae after intravenous propofol (Diprivan) — a comparison with methohexitone in short anaesthesia. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3); 162–164.