Effect of percutaneous local anaesthetics on pain reduction during pulse dye laser treatment of portwine stains

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Summary

We have used EMLA, 4% amethocaine gel and placebo for facial portwine stains, for a period of 1 h, in a double-blind study. After removal of the preparations from the skin surface, each area was treated with six pulses of the laser, each 5 mm in diameter. Any pain noted immediately after treatment was recorded using both visual analogue (VAS) and verbal rating (VRS) scores. Twenty nine patients completed the study and statistical analysis of the results indicated that both EMLA and 4% amethocaine gel were superior to placebo (P<0.001). However, when EMLA and 4% amethocaine gel were compared, the amethocaine preparation was significantly better (P<0.05, VAS; P<0.005 VRS) than EMLA in reducing pain caused by the laser treatment. (Br. J. Anaesth. 1997; 78: 286–289).

Key words

Anaesthetics local, amethocaine. Anaesthetics local, EMLA. Complications, portwine stains.

Portwine stains (PWS) are benign, disfiguring vascular birthmarks consisting of ectatic dermal capillaries. They are relatively common with an incidence of approximately 0.3% in the general population. The former are caused by malformed blood vessels close to the skin surface. As approximately 80% of portwine stains are found on the face or neck this disfigurement can lead to various psychosocial problems. Current treatment of these lesions involves the use of a pulse dye laser which emits a pulsed coherent light of wavelength 585 nm which is absorbed selectively by oxyhaemoglobin in capillaries. The pulse duration of 450 μs is less than the thermal relaxation time of the dermal capillaries which enables the incident laser light to photo-coagulate the capillaries while minimizing thermal diffusion into surrounding tissue. As a result, the possibility of scarring is reduced. The pulse dye laser has proved to be both effective and safe and is currently considered the treatment of choice for portwine stain birthmarks.

However, this treatment can be painful, especially if large areas are involved. Young children often require general anaesthesia before this procedure and older patients some type of local anaesthesia. It has been reported that EMLA cream, when applied for a period of 1–2 h before treatment, can reduce the pain associated with this procedure.1 In our experience, however, when applied for 2 h or more before treatment, EMLA provided only partial pain relief.

An amethocaine-based preparation has been shown to provide more effective percutaneous local anaesthesia than EMLA.2 Therefore, the purpose of this double-blind study was to compare the efficacy of the two formulations with placebo for prevention of pain during treatment of portwine stains by pulse dye laser.

Patients and methods

Formulations

EMLA was obtained from Astra, UK, and amethocaine gel 4% w/w was prepared as described previously.2 A placebo gel was also prepared to match the two active formulations. All three formulation were packaged into standard lacquered aluminium tubes, using standard pharmaceutical methods. Each tube was then assigned a randomized number.

Patient selection

Ethics Committee approval was obtained for the study and of the 30 patients enrolled, 29 completed the treatment. Inclusion criteria were age more than 12 yr of age, a portwine stain of at least 3×3 cm and no adverse response after 12 weeks to a test treatment with the pulse dye laser at a fluence of 6.25–6.5 J cm⁻².

Study design

The design of the study was organized so that each patient could act as their own control. In order to facilitate this, hollow adhesive templates (0.1 cm thick) were made with internal dimensions of 3×1 cm. Three of these were then attached to the...
portwine stain area as shown in figure 1. Thereafter, 1 g of each formulation was applied, in a random manner, to the interior of each template. All three templates were then covered with an occlusive dressing and left for 1 h. At the end of this period all three formulations were removed from the portwine stain and the area wiped clean. Six pulses of the laser were then given within each treated area and the pain response noted immediately by the patient using visual analogue (VAS) and verbal rating (VRS) scores.

PAIN ASSESSMENT

We used both VAS and VRS scores for assessment of pain. With the former, patients were asked to mark a point on a 10-cm horizontal line that corresponded to the degree of pain they felt immediately after each treatment. One end of the line represented no pain while the other was designated as very painful. Four categories of VRS pain scoring were used; 1 = no pain, that is complete anaesthesia; 2 = very slight pain (almost complete anaesthesia); 3 = moderate pain (some anaesthesia has occurred); 4 = very painful (no apparent anaesthesia). For statistical purposes scores 1 and 2 were considered clinically acceptable whereas a score of 3 or 4 implied that the treatment had been unsuccessful. VAS data were analysed by ANOVA and detailed comparisons were undertaken by the Scheffé test. In contrast, VRS results were analysed using the chi-square method in the form of a 2 × 3 contingency table.

LASER TREATMENT

All patients were treated using a Photogenica V pulse dye laser (Cynosure). Test treatments consisting of a few pulses with the 5 mm spot at fluences of 6.25–6.5 J cm⁻² were undertaken and the patient reviewed at 12 weeks. If no adverse effects had occurred after this period then the patient received 6 pulses at a consistent fluence of 6.25–6.5 J cm⁻² applied to the centre of each template.

Results

VAS data from the 29 patients are shown in figure 2. Details of the VRS results, showing the distribution of all pain scores, are illustrated in figure 3. In contrast, grouping of pain scores 1 and 2, and 3 and 4 are shown in figure 4. Statistical analysis of the data represented by figure 2, using ANOVA, indicated that there was a significant difference between the formulations (P < 0.001). More detailed analysis, using the Scheffé multi-comparison method, indicated that both amethocaine and EMLA were
significantly better than placebo in producing percutaneous local anaesthesia (P<0.001). This test also demonstrated that the amethocaine-based formulation was more effective than EMLA in reducing pain (P<0.05).

The results illustrated in figure 4 are presented in the form of a 2×3 contingency table (table 1). Statistical analyses of these data using the chi-square method indicated that the formulations tested were not equivalent (P<0.001). More detailed examination showed that both active preparations were better than placebo (P<0.001) and that 4% amethocaine was significantly better than EMLA (P<0.005).

### Discussion

The purpose of the present study was to evaluate pain reduction associated with the use of the pulse dye laser when treating portwine stains. However, pain is a subjective phenomenon and although sensory thresholds for pain vary little between individuals, the tolerance level varies considerably between cultures, individuals and even in the same person at different times. This occurs because the subjective intensity of pain depends not only on the extent of the stimulus but also on the degree to which it occupies the subject. Redirection of attention can weaken the sensation and, in extreme conditions such as the stress of an accident or hypnosis, can abolish it. Because of the difficulties in assessing pain, we used two different types of pain measurement—VAS and VRS. The results shown in figure 2 demonstrated typically the variety of responses obtained from VAS assessment. However, it can be seen that the highest individual score for either of the active preparations was 6 while almost 50% of the placebo responses exceeded this. One patient had a maximum painful score (10) for placebo. At the other end of the scale we observed that the amethocaine-based formulation gave more 0 scores than EMLA. It is clear from the statistical analyses of the data that not only were both active preparations better than placebo but that the amethocaine-based formulation was superior to EMLA.

Analyses of the verbal descriptor score showed a similar trend. A particular advantage in using this technique was that it allowed distinction between clinically acceptable (pain scores 1 and 2) or unacceptable (pain scores 3 and 4) topical anaesthesia. Amethocaine accounted for most patients in the pain score 1 category (15) (fig. 3); less than 25% of EMLA-treated patients were in this category. Approximately the same number of patients had a pain score of 2 when either amethocaine or EMLA was used. However, although only one individual had a pain score of 3 for the amethocaine formulation, 10 EMLA-treated patients had this score. No individual scored 4 for either active preparation. Although none of the placebo-treated patients had a pain score of 1, six scored 2 (i.e. clinically acceptable anaesthesia) and approximately 33% scored 3. These results indicated a placebo response but both active formulations were significantly better than placebo. Previous experience has shown that there is almost no placebo response when trained volunteers are used, that is individuals are pretreated with the active formulations so that they can assess the sensation of percutaneous local anaesthesia before taking part in the formal clinical study. Although both the VAS and VRS methods gave the same results (after statistical analyses) the VRS data were more highly significant.

In a previous study, Ashinoff and Geronemus examined the effects of EMLA on the efficacy of pulse dye laser treatment of portwine stains. The application time for EMLA was the same as in this study and although they claimed that adequate anaesthesia was attained, no quantitative data were reported to substantiate these claims. However, they concluded that the use of this formulation did not appear to adversely influence the efficacy of the pulse dye treatment.

It has been reported previously that 4% amethocaine was more effective than EMLA in reducing the pain of venepuncture. This was, perhaps, not surprising considering the in vitro penetration characteristics of both preparations. It has been reported that approximately the same amount of amethocaine penetrated human skin from a 4% amethocaine formulation as did prilocaine and lignocaine from EMLA. If this occurred in vivo then it would be expected that the amethocaine-based formulation would be more effective as the drug is approximately four times more potent than either prilocaine or lignocaine.

The results of this study indicated clearly that even using the recommended application period of 1 h for EMLA did not appear to be sufficiently long to provide clinically acceptable percutaneous topical local anaesthesia in approximately 33% of patients (fig. 4). In contrast, 4% amethocaine provided satisfactory anaesthesia in all but one patient. A logical progression of the research would be to examine the effects of shorter application times for the amethocaine formulation as it has been demonstrated previously that a 30–40-min contact period was suitable for venepuncture.

### References


Local anaesthesia and removal of portwine stains


