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Use of lidocaine-prilocaine patch for the mantoux test: Influence on pain and reading

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Abstract

A formulation of a eutectic mixture of lidocaine-prilocaine (EMLA®) changes basal skin perfusion. Its use for alleviating pain associated with the Mantoux test may modify the recruitment of sensitised lymphocytes and then the response to tuberculin test. Twenty-four healthy BCG-vaccinated volunteers (26.7 ± 4.1 years) received on each forearm an intradermal injection of 10 IU tuberculin, one of the forearms being randomly pre-treated for 1 h with EMLA-patch®5%. Pain associated with the Mantoux test was evaluated using a visual analogue scale. The transversal diameter of the induration was read at 72 h. Subjects with 6 mm difference between diameters (i.e. twice the usual variation for a Mantoux test) were recorded. Results were compared using a paired *t*-test. When using lidocaine-prilocaine prior to the test, a three-fold decrease in pain was noted ($p < 0.0001$). Reading of the test were not affected by the lidocaine-prilocaine application ($p = 0.26$). Four subjects had 6 mm or more difference between their two tests, two of them having an induration greater than 15 mm with lidocaine-prilocaine. Lidocaine-prilocaine reduces significantly pain associated with the Mantoux test but does not normally affect the test reading. However, when the induration is more than 15 mm, a control without lidocaine-prilocaine has to be considered.

Keywords: Tuberculin skin test; Analgesia; Lidocaine-prilocaine; Tuberculosis

1. Introduction

The Mantoux test is an intradermal tuberculin test expressing a delayed hypersensitivity to tuberculin caused by either BCG vaccination or *Mycobacterium tuberculosis* contact (Small and Fujiwara, 2001). Different tuberculin formulations and doses can be used, and, in France, a purified protein derivative-tuberculin (Mérieux Laboratories, Paris, France) is used at a dose of 10 IU per test. Response to tuberculin depends on the number of sensitized lymphocytes recruited at the injection site, and the higher their number, the higher the obtained induration. Many variables may affect the interpretation and the results of the Mantoux test (e.g. experience and technique in application, subject age, underlying immunosuppresion, etc.) (Menzies, 1999; Stuart et al., 2000). Therefore, despite its limits of sensitivity and specificity, this test remains a key tool both for epidemiological surveys and clinical purposes (Small and Fujiwara, 2001; Menzies, 1999; Stuart et al., 2000).

For a few years, attention has been focused on medically induced pain and its prevention. Thus, diagnostic or therapeutic acts, such as venous punctures, lumbar punctures, radial artery canulation, vaccination, thoracostomy tube removal, circumcision, etc., are most often preceded, both in children and adults, by a cutaneous application of EMLA®, a eutectic mixture of lidocaine and prilocaine cream (AstraZeneca Laboratories, Rueil-Malmaison, France) (Juhlin et al., 1980; Rosdahl et al., 1988; Halperin et al., 1989; Smith et al., 1990; Taddio et al., 1992a,b, 1994, 1997; Valenzuela and Rosen, 1999; Halperin et al., 2000). The depth and duration of skin analgesia after topical application of lidocaine-prilocaine depends on the application time, but usually 2 h of analgesia are obtained with a 1 h-application (Bjerring and Arendt-Nielson, 1990). Temporary blanching or erythema of the skin area after lidocaine-prilocaine application is frequently observed, related to a vasoconstrictive effect after short application time and to a vasodilatation after longer application (Evers et al., 1985). Recent studies demonstrate that the

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number density of physiologically active capillaries is significantly decreased with long application time, but that analgesized skin, when subjected to heat stimuli, responds by increasing skin perfusion (Arildsson et al., 2000a,b). This response does not originate from increased perfusion in superficial capillaries, but rather in the deeper lying vessels (Arildsson et al., 2000a).

Because lidocaine-prilocaine changes basal skin perfusion and its regulation, its use for allievating pain associated with the Mantoux test may interfere with the tuberculin response by modifying the number of recruited sensitized lymphocytes. The aim of this study was to compare in healthy volunteers the induration obtained with a Mantoux test depending on whether a previous lidocaine-prilocaine application is performed on the forearm or not.

2. Material and methods

This pilot, open, randomised study, approved by the Ethics Committee of Marseille 2 (No 00/28), was conducted in 24 healthy adult volunteers recruited among medical students. They were regularly followed up by the university medical service and were all vaccinated with BCG. Subjects having a tuberculin skin test in the previous 3 months, subjects with possible contrindication to lidocaine-prilocaine (porphyria, methaemoglobinemia, allergy to one of the constituents) and pregnant women were excluded.

After written informed consent, each subject had two intradermal injections of tuberculin on the volar aspect of each forearm. Prior to injection, lidocaine-prilocaine (EMLA-patch® 5% with 25 mg lignocaine and 25 mg prilocaine for 1 g of emulsion) was applied for 1 h in a random order on only 1 of the 2 forearms. The colour of the skin where lidocaine-prilocaine was applied was noted. Then, 10 IU of tuberculin Mérieux was administered intradermally by a single physician (L.M.) on each forearm. Necessary precautions were taken to avoid any bias due to quality, quantity or method of administration. Pain induced by the Mantoux test was evaluated for each intradermal injection by a visual analogue scale (score from 0 – absence of pain – to 100 extremely painful).

Skin tests were read at the 72nd hour by another physician (J.C.D.), blind of the first part of the study. Reading always started with the right forearm and then the left one repeated once for determining the intra reader concordance. Induration was measured by the pen method in the transversal axe with a medium ballpoint pen (Pouchot et al., 1997; Bouros et al., 1991). A line was draw from a point 5–10 mm away from the margin of the skin induration towards its centre, until resistance was felt to further movement. When the diameter of induration was equal to or higher than 15 mm, a chest radiography was done and an individual visit with a specialist physician was offered.

Results were expressed as the mean, range, with 95% confidence interval. Comparisons of pain score and transversal diameter were made by a paired *t*-test between lidocaine-prilocaine treated forearms and controls. Because biological variation in response to tuberculin and differences in administration and reading result in an overall standard deviation of less than 3 mm (Menzies, 1999), we have noted the number of subjects having a difference between their two tests corresponding to twice the standard deviation, i.e. 6 mm or more.

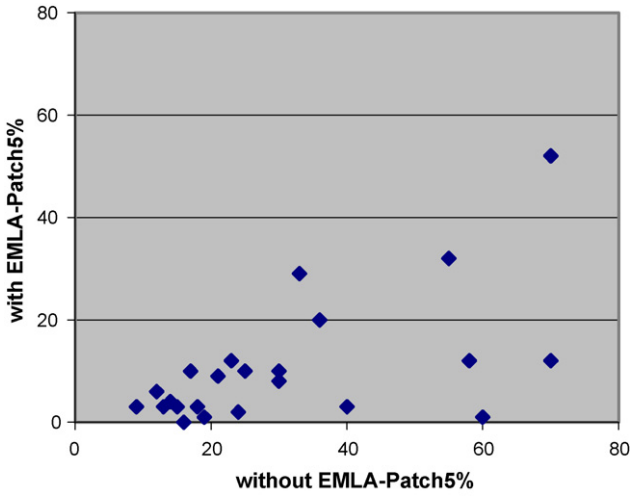

Fig. 1. Effect of lidocaine-prilocaine patch on pain (measured by a visual analogue scale graduated from 0 to 100) associated with Mantoux test in 24 healthy volunteers receiving intradermal injection of 10 IU tuberculin on each of their forearms.

3. Results

The mean age of the 24 volunteers (16 women) was 26.7 ± 4.1 years (range from 23 to 39 years). Eight of them were mild active smokers.

Pain was significantly decreased when lidocaine-prilocaine was used (Fig. 1), with a mean pain score of 32.1 (9–70; 24–40 95% CI) without lidocaine-prilocaine versus 11.1 (0–52; 6–16 95% CI) with lidocaine-prilocaine ($p < 0.0001$).

Concerning the reading of the Mantoux test, the intra reader concordance was less than the recommended 2 mm (1.3 ± 0.2 mm) (Menzies, 1999). Compared in a same subject, reading was not disturbed by the use of lidocaine-prilocaine ($p = 0.26$), with an excellent concordance between the two tuberculin tests (Fig. 2). However, four subjects among 24 had 6 mm or more difference between their two Mantoux tests. Two of them had a decreased transversal diameter when the lidocaine-prilocaine was used (from 12 to 6 mm in the first case, and from 12.5 to 6.5 mm in the other one). Two of them had an increased transversal diameter when the lidocaine-prilocaine was used, with a higher difference in diameters than in case of decrease (from 8 to 19 and 9.5 to 15.5 mm). Any relation was noted between these results and the colour of the skin after lidocaine-prilocaine application. Any subject, pre-treated or not with lidocaine-prilocaine, and having an induration equal or superior to 15 mm, had tuberculosis.

4. Discussion

Our results show that EMLA-patch® 5% reduces significantly the pain associated with the Mantoux test in adults. To our knowledge, this is the first study to quantify the pain associated with a Mantoux test that, from our results, can be considered as rel-

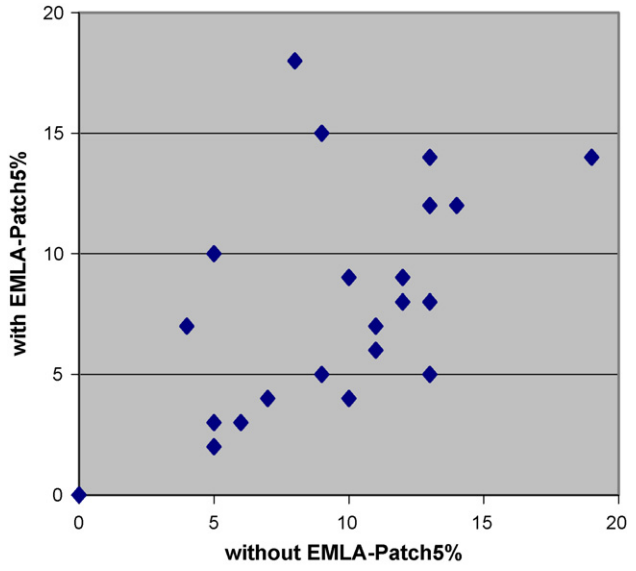

Fig. 2. Effect of lidocaine-prilocaine patch on Mantoux test reading (i.e. transversal diameter measured in mm by the pen method) in 24 healthy volunteers receiving intradermal injection of 10 IU tuberculin on each of their forearms.

atively painful. Usually there is no real complaint from adults concerning tuberculin tests, therefore the mean pain score without previous application of lidocaine-prilocaine is about 32, with a maximum reaching 70 (maximum of 100). The Mantoux test appears to be more painful in adults than intramuscular puncture or injection of influenza vaccine (mean pain score of 15 and 19, respectively, Taddio et al., 1992a). In our study, the use of lidocaine-prilocaine induces a three-fold decrease in score pain and from this point of view it might be recommended in clinical practice for the Mantoux test.

Moreover, readings were not affected by the lidocaine-prilocaine, despite its possible role on the recruitment of sensitized lymphocytes. However, four subjects among 24 had a true difference, i.e. twice the standard deviation due to biologic variation in response and differences in administration and reading (Menzies, 1999) between their two tuberculin tests. Consequences of a such difference are not negligible for half of these subjects who have a response to Mantoux test considered as normal without lidocaine-prilocaine, but who become tuberculosis suspect when lidocaine-prilocaine is applied before the test because of an induration higher than 15 mm (Small and Fujiwara, 2001). These two subjects were considered tuberculosis-free after chest radiography and consultation with a specialist physician.

5. Conclusion

In conclusion, lidocaine-prilocaine reduces significantly pain associated with Mantoux test in adults and does not affect the test reading. However, when the diameter of induration is more than 15 mm, a control without lidocaine-prilocaine has to be considered.

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