

Study of a Combined Percutaneous Local Anaesthetic and the TDS[®] System for Venepuncture

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INTRODUCTION

The insertion of a needle through the skin such as phlebotomy or vaccination is painful and may induce great fear and anxiety, especially in children. To avoid the pain and anxiety of venipuncture, topical anaesthetics have been in use to provide needleless induction of local anaesthesia. Current topical local anaesthetics such as EMLA[®], Astra Pharmaceuticals Ltd. [1] and AMETOP[®] gel [2], Smith & Nephew Healthcare Ltd., whilst effective, require institutional support. One hour prior application of EMLA[®] [3] and 30 to 45 minutes (AMETOP[®]) [4], limit clinical and patient acceptance. The development of a topical delivery system with faster time of anaesthetic onset would be helpful in emergency cases and for an increasing number of surgical day cases seen, especially in paediatrics. The Transdermal Delivery System (TDS[®]) is a patented process for creating a formulation to deliver drug across skin using a liquid vehicle, measured by unit dose or metered pump spray. The combination of TDS[®] with lidocaine produces the new topical local anaesthetic system.

OBJECTIVE

To evaluate the two TDS[®] local anaesthetic systems (TDS[®]α and TDS[®]β) for their speed of onset of anaesthesia, and drug penetration into the circulation.

METHODS

The study was a double blinded and placebo controlled, with a one week washout period between two phases, involving 100 healthy volunteers. The treatment (active and placebo) were randomly administered via metered pump spray of 1 mL to the area of 4 cm² on the dorsal surface of the hand. Five minutes later, the application areas were routinely cleaned using alcowipes and were then cannulated using a 20G butterfly needle.

Phase 1

TDS[®]α (active) and TDS[®]α (placebo)

Phase 2

TDS[®]β (active) and TDS[®]β (placebo)

Study Materials

Study Materials were supplied by Transdermal Technologies Inc. Florida USA.

- 1 TDS[®]α Anaesthetic System (alcohol based) containing 4% w/v lidocaine and 2% w/v tetracaine.
- 2 TDS[®]β Anaesthetic System (water based) containing 4% w/v lidocaine and 2% w/v tetracaine.
- 3 TDS[®]α and TDS[®]β placebo.

Pain Assessment

1 Verbal Rating Score (VRS)

Volunteer was asked the following question: "How strong was the pain of the procedure?" and provided with a choice of five categories: 1 no pain; 2, minimal sensation; 3, mild pain; 4, moderate pain; 5, severe pain. The volunteer selected one answer for each hand by circling the number.

2 Verbal Analogue Score (VAS)

A 100 mm horizontal line with endpoints that were anchored by descriptors 'no pain' and 'severe pain' was used. Volunteer was asked "What did the procedure feel like?" and then requested to make a vertical line on the horizontal line which represented the intensity or unpleasantness of their pain by the procedure. Values were measured in mm from the left hand edge of the horizontal line.

Blood Sampling

Blood sample was taken to assess the systemic level of lidocaine at two hours after the treatment application. Plasma samples were analysed using validated LC/MS/MS method.

Statistical Analysis

All the data was analysed using GraphPad Prism 4.0 (www.graphpad.com/prism/Prism.htm) and Minitab 14 statistical software (www.minitab.com/). The active treatments were compared to the placebo control using Wilcoxon's Signed Rank test. The lidocaine concentrations at two hours for TDS[®]α and TDS[®]β were compared using Student's paired t test.

RESULTS

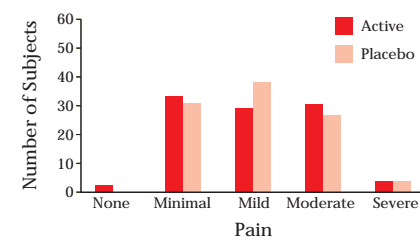


Figure 1 : Verbal Rating Score (VRS) for TDSα. Values are subjects percentage vs. categories; n = 100; p=NS, Wilcoxon's Signed Rank test

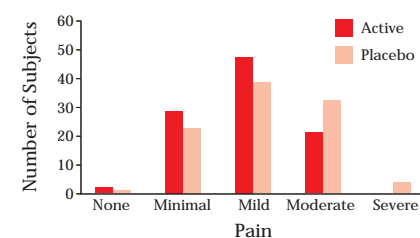


Figure 2 : Verbal Rating Score (VRS) for TDSβ. Values are subjects percentage vs. categories; n = 100; P<0.02, Wilcoxon's Signed Rank test.

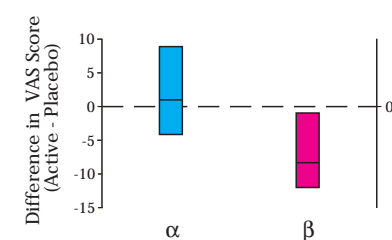


Figure 3 : The median differences in VAS score of active and placebo (α = TDSα and β = TDSβ). Values are median ± 95% CI; n=100; p= NS for TDSα and p< 0.02 for TDSβ, Wilcoxon's Signed Rank test.

DISCUSSION

Between the two TDS[®] systems tested, the water based (TDS[®]β) anaesthetic system was more effective than alcohol based (TDS[®]α). The distribution of scores of the active treatment group in Phase II (TDS[®]β) was generally shifted from the two highest scores (moderate and severe) to the lower level of score (mild), with no subjects on active treatment rating the pain as severe and reducing those who scored moderate by 36.4% (Figure 2). The above result was further supported by the plasma lidocaine concentrations two hours after the active treatment was applied which have shown that the mean plasma level for TDS[®]β was slightly higher than TDS[®]α with the mean ± SD [range] were 3.51 ± 9.31[0-64.5] ng/mL and 2.51 ± 6.8[0-55.9] ng/mL, respectively (p=0.287, NS; paired t test).

CONCLUSION

In conclusion, topical application of the TDS[®] local anaesthetic system was effective in providing skin anaesthesia for dorsal hand vein cannulation in healthy subjects, after 5 minutes of application. TDS[®]β (water based) was found to be more effective than TDS[®]α (alcohol based) and can be used for further development of this system. These findings also indicate the rapid transdermal drug delivery by the TDS[®] system.

ACKNOWLEDGEMENTS

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