PET500 a newly formulated tetracaine product is effective in reducing penile sensitivity

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Introduction

Premature ejaculation (PE) is one of the most common male sexual disorders affecting 30-40% of sexually active men, with up to 75% of them experiencing at some points in their lives.[1,2]

PE impacts on a man's life by reducing his self-esteem, affecting relationships, causing anxiety, embarrassment and depression.[3,4]

Current acceptable pharmacological treatments that are used to treat PE include topical anaesthetics, tricyclic antidepressants, selective serotonin re-uptake inhibitors (SSRIs) and Chinese traditional herbs.[5,6]

Stud100® is the only licensed product registered in the EU for such treatment (amide [lidocaine] based). Treating PE with local anaesthetics is one of the oldest form of therapy, the rationale being that PE patients suffer from penile hypersensitivity and therefore reducing sensitivity delays ejaculation.

Development of a local topical anaesthetic with a short onset and offset time would provide an ideal treatment profile for managing patents with PE effectively.

Tetracaine is a para-aminobenzoic acid (ester based) that has been shown to ameliorate pain from venous cannulation. It has an advantage in that it is effective within 30-40 minutes after application with a longer acting time of up to 3-4 hours.[7,8]

Aims

The aim of this study was to assess the onset and duration of PET500 (a new formulation of a tetracaine-based product) when applied topically to the glans penis, and to assess its safety and tolerability.

Two controls were used: a matching vehicle as a negative control (placebo) and Stud100® as a positive control.

Methods

Study Design

This was an open-label, placebo- and positive-controlled, randomised, dose-ranging, cross-over, single-centre pilot study. PET500 (containing 0.26mg or 0.65mg or 1.3mg tetracaine) or placebo or Stud100® were applied topically onto the glans penis in liquid spray form.

Local sensitivity and tolerability assessments were performed pre-dose, up to 120 minutes post-dose or until full sensitivity returned (30 minutes).

Von Frey filaments were used to assess the changes in touch sensitivity on the glans penis after IMP application.

Data Analysis and Statistical Methods

The onset and duration of action were recorded categorically by treatment. Efficacy analysis was conducted on both an intent-to-treat (ITT) and a per-protocol (PP) population.

The PP population was the population of primary interest for the efficacy analyses, with the ITT analysis being provided as a safety check.

Safety Assessment

Adverse events (AEs) were recorded from the first dose of study medication until follow-up.

Subject Disposition

49 male volunteers were screened with 20 randomised onto the study. All 20 subjects completed the study and were included in the ITT population, with 18 subjects in the PP population.

For the PP population, 12 were Caucasians, the mean age of 27.5 years (range 20-37 years) and average BMI of 25.73kg/m^2 (range 21.4-33.1kg/m^2) were calculated.

Results

EFFICACY RESULTS

A decrease in sensitivity following administration of placebo, all doses of PET500 (0.1%, 0.25%, 0.5%) and Stud100®.

ONSET OF ACTION

Majority of subjects reported an onset of action within eight minutes of application with the greatest response seen between 0-1 minute (Figure 1).

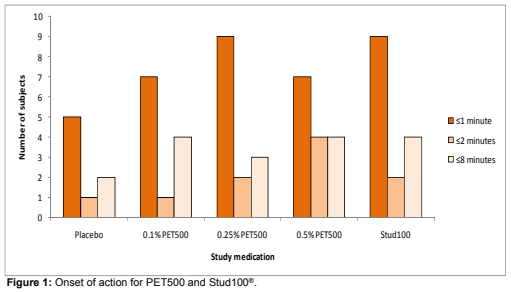

Figure 1: Onset of action for PET500 and Stud100®.

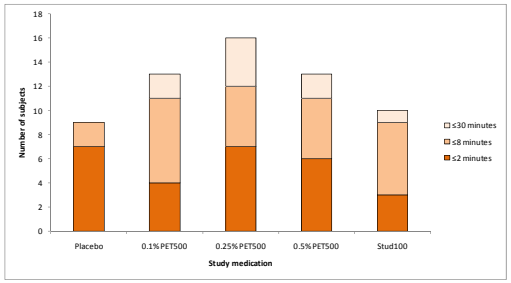

Figure 2: Duration of action for PET500 and Stud100®.

DURATION OF ACTION

The number of subjects on PET500 reporting onset was similar to that of Stud100® (17 subjects). Overall, the majority of subjects had duration of action less than eight minutes following treatment (Figure 2).

END OF ACTION

Comparing PET500 dose levels, 7 and 5 subjects on 0.1% and 0.5% PET500 respectively reported an end of action between 2-8 minutes while 6 subjects on 0.25% PET500 reported action between 8-30 minutes.

CHANGE FROM PRE-DOSE TARGET FORCE

PET500 demonstrated almost immediate onset within the first ten minutes as did Stud100®, which displayed an initial weaker effect and a delayed more pronounced effect after approximately ten minutes (Figure 3). In terms of mean target force, all doses of PET500 and Stud100® had a similar initial extent (depth) of effect (Figure 3). There was no difference between the PET500 concentrations which had an anaesthetic effect between placebo and Stud100® within the first 10 minutes (Figure 4).

Stud100® was found to have a biphasic effect with much greater desensitising effect after ten minutes which lasted for 20 minutes (Figure 3). This observed amplification effect raises the question whether anaesthesia over 30 minutes is of any benefit for PE when clinical studies have shown an effect in minutes. One subject had a high sensitivity threshold of 18 (100g) after Stud100® application, which skewed the summary statistics at 15 minutes.

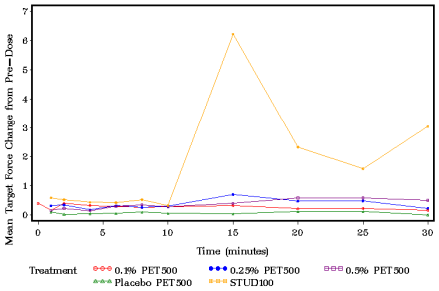

Figure 3: Mean target force change from pre-dose – PP population.

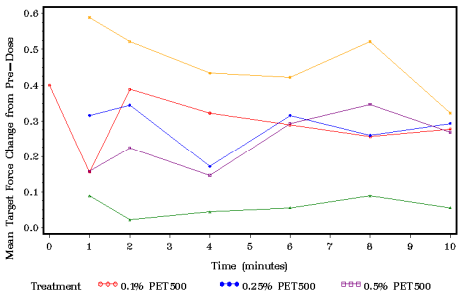

Figure 4: Mean target force change from pre-dose – PP population (0-10 minutes)

LOCAL TOLERABILITY

Only two observations other than '0' were noted.

- One subject reported drying of the penis after receiving placebo
- One subject reported erythema on glans penis after receiving Stud100®
- No observations for subjects dosed with active PET500

Safety Results

Safety and Tolerability

All test products were well-tolerated. There were no serious adverse events and no subjects were withdrawn from the study due to an AE.

Three AEs were reported which were considered mild in intensity (two were captured by local tolerability assessments). No AEs were reported by subjects dosed with active PET500 doses.

Conclusions

The application of PET500 to the glans penis desensitised touch sensitivity as demonstrated by an increase in mean target force compared to placebo.

PET500 had an immediate desensitising effect on the glans penis which for the first ten minutes is comparable to Stud100®.

- Two studies with 1380 and 500 men have shown that the mean IVELT was approximately 7.3 and 5.4 minutes, respectively[9,10]
- The observed change in sensitivity threshold was 0.2-5.4g for PET500 which places PET500 between Stud100® and placebo in terms of anaesthetic effect
- If the observed change in sensitivity threshold was sufficient to prolong IVELT to the reported average value of around 7.5 minutes, PET500 would be effective in treating PE
- Dapoxetine is the only drug with regulatory approval for PE in several EU countries and has been shown to improve IVELT by up to 3 minutes [11, 12]

In terms of safety and tolerability, PET500 was well-tolerated with no AEs reported on any of the active doses of PET500.

Overall, this study demonstrates that PET500 has the potential to be developed as the first tetracaine-based product for the effective treatment of premature ejaculation.

References

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