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Phenylpropanolamine´s decongestive effect on the nasalmucosa of pregnant women with nasal stuffiness*

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SUMMARY

Pregnancy rhinitis is common and very troublesome for many women. Today, no safe and effective treatment is available for this condition. The aim of this placebo-controlled double-blind study was to evaluate the decongestive effect of phenylpropanolamine (PPA 50 mg) twice daily for seven days in 38 women with pregnancy rhinitis. In the morning, before starting the course of treatment, and two to three hours after taking the last dose of the study-medicine in the morning on the eighth day, recordings of the position of the nasal mucosal surface were made with rhinostereometry. Every evening, the women filled in a questionnaire about their symptoms on a scale from 0-9 (0=no symptoms, 9=extremely severe symptoms). The effects of the drug on their blood pressure and other side-effects were also determined. The patients used a newly-evaluated telephone method to assess their daily symptoms.

PPA 50 mg had a decongestive effect on the nasal mucosa, as measured with symptom scores and rhinostereometry. In the placebo group, this effect was found with rhinostereometry, but not on nasal stuffiness as judged by the symptom scores. The reason why the placebo group also experienced a decongestive effect after treatment may have been due to stress because the patients were in a hurry and such stress may have a decongestive effect on the nasal mucosa. No effects on the blood pressure or other side-effects were detected.

In conclusion, this study shows that PPA 50 mg twice daily may be an effective and safe treatment in pregnancy rhinitis.

Key-words: pregnancy rhinitis, phenylpropanolamine, rhinostereometry, nasal stuffiness, telephone method

INTRODUCTION

Nasal congestion during pregnancy, a common condition, is thought to affect 18-30 % of pregnant women [1]. This type of rhinitis may develop at any time during pregnancy and the nasal stuffiness usually disappears shortly after delivery. The cause of nasal blockage is not known and it may be due to hormonal factors [2-4]. The condition is troublesome and can cause disturbed sleep, daytime tiredness and dryness of the mouth [5]. No satisfactory treatment is available. Although local nasal decongestion temporarily relieves pregnancy rhinitis, this treatment cannot be given for more than a few days since it may result in rhinitis medicamentosa, which is characterized by tolerance, rebound swelling and nasal hyperreactivity [6, 7]. In clinical practise, nasal stuffiness during pregnancy is usually treated with topical steroids because they are effective in the treatment of most types of rhinitis [8]. It has been assumed that this treatment is also suitable in pregnancy rhinitis. However, a recent study showed that topical steroids had no effect on pregnancy rhinitis [9].

Phenylpropanolamine (PPA), a beta-phenylethylamine derivate, is widely used as a nasal decongestant for oral administration in sustained-release preparations. It is commonly given to relieve nasal blockage in viral infections of the upper respiratory tract or allergic rhinitis and is available over-the-counter in most countries [10, 11]. PPA has no known negative effects on the foetus. In a recent extensive study, no teratogenic effect of PPA was found [12]. The action of PPA may be mediated directly by activation of post-junctional adrenoreceptors, indirectly by affecting the release and/or re-uptake of noradrenalin or by both mechanisms [13].

PPA in double the recommended dose has a significant decongestive effect on the nasal mucosa in healthy subjects [14]. The aims of this placebo-controlled double-blind study were to evaluate the decongestive effect of PPA 50 mg twice daily in women with pregnancy rhinitis by using rhinostereometry and the subjective assessment of symptoms of nasal stuffiness as well as to study the effect of this drug on the systolic and diastolic blood pressures.

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MATERIAL AND METHODS

Patients

Forty pregnant women with a mean age of 33.4 [25-42] years and in mean gestational week 29 [24-35] were included in the trial. They had all complained of persistent nasal obstruction for at least two weeks and were patients in Munkbrons Antenatal Clinic in Stockholm.

It was designed as a parallel randomized, double-blind trial, with 20 women in each group. All of them were healthy Caucasians and not on any medication. Vitamin and/or mineral supplements were allowed. Before entering the trial, a medical history was taken and a medical examination done, which consisted of blood pressure, auscultation of the lungs and heart and an ear, nose and throat examination. The blood pressure was also recorded at the end of the trial. They had used no topical vasoconstrictors and had not had a common cold or sinusitis during the last two weeks before entering the trial. They had no history of allergy or other rhinological disease, high blood pressure or toxaemia in a previous pregnancy. They have no family history of high blood pressure. The patients were divided into two groups who were randomly selected for treatment with PPA, 50 mg twice daily or placebo for seven days. The study drugs were manufactured and supplied by Recip AB, Stockholm, Sweden.

Rhinostereometry

The swelling of the nasal mucosa was recorded with rhinostereometry. This optical, direct, non-invasive method first described in 1982 [15], was designed to measure nasal mucosal swelling with a high degree of accuracy. It enables topographic measurements in the nose without manipulation of the nasal structures. Such measurements require a defined fixed point to which the position of any object studied can be related. The origin of a three-dimensional co-ordinate system is used as the fixed point. The apparatus consists of a surgical microscope placed on a micrometre table fixed to a frame. The microscope can be moved in three angular directions to establish the co-ordinate system. Measurements can be made only if the nasal cavity is placed in the co-ordinate system in such a way that it resumes the same position with a high degree of precision on repeated measurements. This is achieved by immobilizing the subject´s head and attaching it to the frame by an individually-made tooth-splint. The objective and eyepiece of the microscope are chosen to give the microscope a short depth of focus. The eyepiece is equiped with a horizontal mm-scale, which is used to measure the position of the nasal mucosa- i.e., mucosal swelling. Since the microscope has a short depth of focus, the mucosal surface position can be recorded in the plane of focus along the mm-scale. Thus, the mucosal area studied during the measurements is restricted to almost a line. With this method, the area of measurement can be re-identified with a high degree of accuracy in the same individual several times with the subject as her own control. In recordings of positional changes, the accuracy of the method is 0.2mm.

Trial

When the study began and before the treatment with PPA or placebo, the baseline position of the nasal mucosa was determined in the morning. This was done by making repeated recordings of the inferior concha in both nasal cavities, after an acclimatization period of 30 min [16]. Throughout the week, the effect of the treatment was assessed by recording the symptoms of nasal stuffiness on a scale from 0-9 (0= no symptoms, 1= extremely mild, 2= very mild, 3= mild, 4= mild to moderate, 5= moderate, 6=moderate to severe, 7= severe, 8= very severe, 9= extremely severe). The symptoms were assessed at baseline and on the evening of day 1 just before treatment and on the evening of day 1 to day 7, at about 2 h after intake of the drug [17]. All subjects used the telephone method in which they estimated their nasal stuffiness. This consists of calling a computer and being given stepwise instructions about how to choose one of the alternatives (symptom score 0-9) by pressing a key on the telephone. They also had to state whether they had any side-effects. The results and the time of the calls were recorded by the computer. We have used this method in a previous study and it has been objectively evaluated [18]. They also filled in a diary card for purposes of comparison. The patients then began to take PPA 50 mg or placebo twice daily. Their last dose was on the morning of day 8. Two to five hours later, we measured mucosal baseline positions again with rhinostereometry.

Statistics

The Student t-test was used to evaluate the rhinostereometric measurements from both nostrils which were added, and the Wilcoxon sign-ranked test to analyse the symptom scores.

RESULTS

Two subjects were excluded from the study: one developed sinusitis after five days, and another tonsillitis after four days. They belonged to the placebo group. On the last day, two subjects complained of abdominal pain, one of whom had acute lumbago and one was hospitalised because of a vaginal bleeding (placenta praeviae). They belonged to the PPA group. Both of them completed the treatment and filled in their symptom score diaries but they were not seen on the last study visit. Therefore, no rhinostereometry recordings of the nasal mucosa were made on day 8. The rhinostereometry and blood pressure measurements were available in 34 subjects, 18 in the PPA group and 16 in the placebo group, while the symptom scores were available in 38 subjects, 20 in the PPA group and 18 in the placebo group.

Rhinostereometry

The decongestive effect after treatment was 1,6 (SD 1.8) mm ($p < 0.01$) in the PPA group versus 1.7 (SD 1.5) mm ($p < 0.01$) in the placebo group. We found no statistically significant difference between the decongestive effect of PPA and placebo using rhinostereometry.

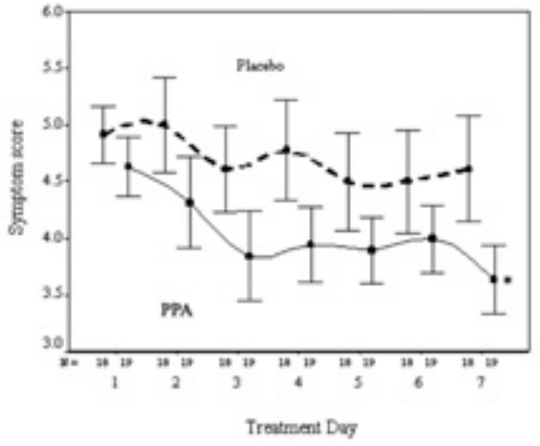

Figure 1. The mean symtom score of nasal stuffiness (0= no stuffiness; 9=severe stuffiness) every evening in 38 women with pregnancy rhinitis during treatment with either PPA 50mg twice daily or placebo. Date are presented as Mean ± SEM *$p < 0{,}01$.

Subjective assessment of symptoms

Nasal stuffiness improved significantly at the end of the study in the PPA group ($p < 0.01$), but not in the placebo group ($p < 0.07$). However no significant difference was noted between the PPA and placebo groups at the end of the study (Figure 1).

Blood pressure

The systolic and diastolic blood pressures showed no significant changes during the study – i.e., on the baseline day, the mean systolic blood pressure was 106 mg Hg and the mean diastolic blood pressure 64 mm Hg, while at the end of the study, the mean systolic blood pressure was 107 mm Hg and the mean diastolic blood pressure 66 mm Hg.

Other adverse effects

No other side effects were reported during the study.

DISCUSSION

This study shows that in a group of women with pregnancy rhinitis, PPA 50 mg twice daily has a decongestive effect on nasal stuffiness, as measured by symptom score and rhinostereometry. In the placebo group, treatment for seven days also had a decongestive effect on rhinostereometry. However, their symptom scores showed no effect on nasal stuffiness. We found no significant change in blood pressure in either group.

It may be surprising that the rhinostereometric measurements also showed a decongestive effect on the nasal mucosa after seven days of treatment in the placebo group. However, such measurements require an acclimatization period of about 30 minutes before the nasal mucosa reaches a baseline position, which is not affected by physical stress, temperature, etc. On the first day, we took a medical history and did a physical examination before determining the nasal mucosal baseline. Therefore, all subjects had at least 30 minutes for acclimatization. However, on the second examination, we recorded only the blood pressure and made the rhinostereometric measurements in the morning two to five hours after the intake of the study medication. Since some of the women were in a hurry, their acclimatization times may have been less than 30 minutes. In this case, higher concentrations of adrenaline and noradrenaline may have a decongestive effect on the nasal mucosa, which has been shown in other studies [16].

No patient who complained of severe stuffiness (symptom score 8-9) was included in this study because they were all using various amounts of topical decongestants [7]. The patients in our study had moderate nasal stuffiness (symptom score about 6-7), especially in the evenings. Therefore we determined the symptom scores in the evenings. The symptom score method, which the patients report their symptoms on the telephone, is reliable and has been evaluated in another study [18]. Most patients seem to find it easier to assess their symptoms on the telephone. However its main advantage is that a computer records the time when the estimate is made and one can detect inaccuracies afterwards and exclude them. PPA had a decongestive effect on the symptom scores, as determined by the telephone method, which must be regarded as objective. It would have been of value to use the rhinostereometer also in the evenings to record nasal stuffiness, but these women were unwilling to make an additional visit to the clinic in the evening.

Pregnancy rhinitis is a difficult condition to treat and it has been objectively shown that topical steroids have no effect [9]. Oral steroids should also be avoided in pregnant women. Topical decongestives are effective, but cannot be recommended because many such patients develop rhinitis medicamentosa [7]. Since there is no effective treatment for pregnancy rhinitis, the results of this study must be regarded as interesting and useful. We have previously shown that PPA 100mg had a decongestive effect similar to that of oxymetazoline nasal spray 0.5mg/ml in healthy volunteers, as measured by rhinostereometry [14]. In that placebo-controlled study, PPA 100mg had a better decongestive effect than PPA 50mg. However, the higher dose, but not the lower one, significantly affected the systolic and diastolic blood pressures. Therefore, PPA 100mg could not be recommended for any type of rhinitis.

In summary, this study shows that PPA 50mg twice daily relieves nasal stuffiness in pregnancy rhinitis and has no effect on blood pressure. Since it is widely used to treat all kinds of rhinitis and has no negative effects on the foetus, it may also be used as a symptom relief in such patients.

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