

RepHresh Studies

VAGINALE GEL GEL VAGINAL

This document presents abstracts of studies which prove the efficacy of the Vaginal Gel, RepHresh, in relieving feminine itching, irritation and odours and treating and preventing bacterial vaginosis.

Note: The product tested in the studies is called Miphil[®], which is the Italian brand name for RepHresh[®].

Successful treatment of bacterial vaginosis with a polycarboxophil-carbopol acidic vaginal gel: results from a randomised double-blind, placebo-controlled trial.

Fiorilli Angelo, Molteni Bruno, Milani Massimo, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 2005, vol. 120, no2, pp. 202-205.

Objective: We evaluated the efficacy of a mucoadhesive vaginal gel (MVG, Miphil[®]) with acidic-buffering properties in bacterial vaginosis (BV).

Study design: Double-blind, placebo-controlled, 12-week trial. **Subjects:** A total of 45 non-pregnant women with BV were enrolled in the trial. Patients were treated with MVG 2.5 g or the corresponding placebo (P) daily for the first week and then every 3 days for the following 5 weeks (treatment phase) in a 2:1 ratio. All patients were followed for an additional 6 weeks without treatments (follow-up phase). **Clinical cure** was defined as absence of vaginal discharge, vaginal pH <4.5, a negative fish odour test and a Nugent score <7.

Results: At week 6, 28 out of 30 women (93%) in the MVG group were clinically cured in comparison with only 1 out of 15 (6%) in the P group (P = 0.0001). At week 12, 86% of MVG treated women remained cured in comparison with 8% in P group (P = 0.0001). At baseline, the vaginal pH was 6.1 ± 0.7 in the MVG and 5.5 ± 0.7 in the P group. Vaginal pH significantly (P = 0.003) decreased to 4.3 ± 0.3 in the MVG group. In P group non-significant modifications of vaginal pH were observed (5.1 ± 0.5).

Conclusion: Our results demonstrated that this MVG is an effective treatment of BV.

Efficacy of an acidic vaginal gel on vaginal pH and interleukin-6 levels in low-risk pregnant women: a double-blind, randomized placebo-controlled trial.

D. M. Paternoster, L. Tudor, M. Milani, Journal of Maternal-Fetal and Neonatal Medicine, vol. 15, n° 3, March 2004, pp. 198-201(4).

Background: Increased interleukin-6 (IL-6) levels and a vaginal pH of >4.7 are associated with obstetric complications such as preterm delivery and low birth weight. Topical treatments, able to maintain a physiological vaginal pH, could help in the prevention of vaginal infections.

Study aim: In a randomized, double-blind, placebo-controlled trial, we evaluated the effects of an acidic buffering vaginal gel (Miphil[®]) on vaginal pH and IL-6 levels in pregnant women.

Patients and methods: Seventy low-risk women pregnant with a singleton (second trimester) were enrolled in the trial. Thirty-five were randomized to the acidic gel, 2.5 g every 3 days for 12 weeks, and 35 to the corresponding placebo. Vaginal pH and vaginal IL-6 level were measured at baseline and after 12 weeks. Women were then followed until delivery. The main outcome measures were vaginal pH, vaginal pH normalization (pH <4.5) and vaginal IL-6 levels.

Results: Vaginal pH at baseline was 4.6 ± 0.4 and 4.4 ± 0.3 in the acidic gel and the placebo group, respectively. At baseline, a total of 40% (14/35) and 22% (8/35) of women in each group, respectively, had a vaginal pH of . 4.7. At week 12, the vaginal pH was 4.3 ± 0.3 in the acidic gel group and 4.3 ± 0.3 in the placebo group (NS). The acidic gel normalized the vaginal pH in ten out of 14 women (p=0.04) in comparison with only one out of eight women in the placebo group (NS). The acidic gel induced a significant (p<0.02) reduction of vaginal IL-6 from 12.0 ± 7 to 8.9 ± 5 pg/l (.36%). In the placebo group, IL-6 increased from 9.0 ± 5 to 13.5 ± 6.8 pg/l (+50%) (p=0.05). Birth weight was 2978 ± 700 g in the placebo group and 3241 ± 477 g in the acidic gel group (p=0.06).

Conclusions: The use of the acidic gel in low-risk pregnant women is able to maintain a physiological vaginal ecosystem and prevents the increases of

vaginal pH and vaginal IL-6. Prospective and controlled trials are warranted to evaluate whether this acidic gel can reduce obstetric complications linked to vaginal inflammation during pregnancy.

Efficacy of the combination of 2 g oral tinidazole and acidic buffering vaginal gel in comparison with vaginal clindamycin alone in bacterial vaginosis: a randomized, investigator-blinded, controlled trial.

Milani M, Barcellona E, Agnello A. Eur J Obstet Gynecol Reprod Biol. 2003 Jul 1;109(1):67-71.

Objective: To evaluate the efficacy of tinidazole (T) (Trimonase, Mipharm, Italy) and an acidic vaginal gel (Miphil) (M) in comparison with vaginal clindamycin (CL) (Cleocin Pharmacia Upjohn) in BV.

Design: A multicentre, randomised, investigator-blinded, controlled trial.

Population and Methods: 64 women with BV were enrolled. Thirty-two were allocated to receive oral T 2g, single dose, and 32 were assigned to CL 2% for 7 consecutive days. After week 1, T group were treated with an acidic vaginal gel, 2g every 3 days, for additional 3 weeks, whereas CL group did not received any additional treatment. Patients were evaluated at week 1 and 4. Vaginal pH, the BV-blue test (Gryphus Diagnostics, USA) and the whiff test were performed at baseline and at week 4.

Main outcomes measures: Clinical cure rate; normalisation of vaginal pH (pH <4.5); and laboratory cure rate (defined as a clinical cure rate and a negative results of BV-blue and whiff test). **Results:** At baseline, vaginal pH values were (mean ± S.D.) 5.4 ± 0.7 and 5.3 ± 0.5 in T and CL groups, respectively. Six patients (2 in T group and 4 in CL group) withdrew from the study due to side effects. At week 1, the clinical cure rates were 84% in both T and CL treated group (P=N.S.). At week 4, clinical cure rates were 94% in T+M group and 77% in CL group (P=N.S.). The laboratory cure rates were 81% in T+M group and 59% in CL group (P<0.04). Vaginal pH normalisation (i.e. pH <4.5) was achieved in 78% and in 38% of T+M and CL groups, respectively (P<0.0007).

Conclusions: In the short term, 2g single oral dose tinidazole was at least as effective as 7-day of vaginal clindamycin. The sequential treatment of tinidazole and acidic vaginal gel was superior to vaginal clindamycin in lowering vaginal pH and achieving a higher laboratory tests normalization rate at 1-month follow-up.

Efficacy of Lactobacilli, an acidic vaginal gel (Miphil®), or a combination of both on bacterial vaginosis: a randomized, controlled, clinical trial.

Giovanni Miniello, Massimo Milani, Review of practical gynecological obstetrics and perinatal medicine. Official body of the Association of Italian Hospital Obstetricians and Gynecologists and the European Society of Breast Echography. Quarterly - Vol. 16, no. 1-2001. Translated from Italian.

Background: Bacterial vaginosis (BV) is a very common vaginal infection. Recurrency rate remain high despite proper pharmacological treatment. Several, non controlled, open studies have suggested that use of exogenous lactobacilli or the application of acidic douches could be helpful in BV, but these advices are not evidence-based.

Study aim: in this randomised, controlled, parallel groups, 4-week trial, carried out in women with BV, we evaluated the effects of exogenous lactobacilli (LB) (Normogin, vaginal tablets) in comparison with an acidic vaginal gel (VG), sharing a long lasting buffer activity (Miphil), on vaginal microflora and vaginal pH.

Methods and Patients: vaginal microflora was evaluated using a Gram stained vaginal smear microscopic evaluation and scored according to Nugent's criteria. The vaginal pH was evaluated by means of pH paper test. A total of 24 women (mean age 36 ± 6 years) with a diagnosis of BV, according to Amsel criteria, were randomised to LB or VG or their combination (LB+VG).

Results: in comparison with baseline values, no statistical significant modifications of vaginal microflora or vaginal pH were observed at the end of study period in LB treated group. In VG-treated group, vaginal pH and Nugent score decreased from 6.0 ± 0.4 to 4.6 ± 0.5 ($p < 0.001$) and from 7.2 ± 1 to 2.3 ± 2.4 , ($p < 0.001$), respectively. In the combination group (LB+VG), at the end of the study period, the greatest vaginal pH (4.5 ± 0.6) and Nugent score (1.2 ± 29) reductions were observed.

Conclusions: in women with BV, normalization of vaginal pH is associated with an improvement of vaginal microflora. Acidification of vaginal mucous in BV women seems to promote adhesion and

colonisation of exogenous Lactobacilli. In women with BV, the use of LB only is not associated with an improvement of vaginal pH and microflora.

Effect on vaginal pH of a polycarbophil vaginal gel compared with an acidic douche in women with suspected bacterial vaginosis: a randomized, controlled study.

Milani Massimo, Molteni Bruno, Silvani Ilaria, Current Therapeutic Research, 2000, vol. 61, no11, pp. 781-788.

Background: Vaginal pH is a key factor in maintaining a healthy vaginal ecosystem. An increase in vaginal pH is commonly observed during bacterial vaginosis.

Objective: This study was undertaken to compare the effects of polycarbophil, a new bioadhesive polymer in gel form, with those of an acidic vaginal douche on restoration of physiologic vaginal pH in women with a vaginal $\text{pH} \geq 4.5$ and suspected bacterial vaginosis. We also assessed the pH-lowering effect of a single application of polycarbophil compared with that of a single application of acidic vaginal douche in an additional group of women.

Methods: In this controlled, randomized, investigator-blinded study, women aged between 18 and 60 years with a vaginal $\text{pH} \geq 4.5$ and suspected bacterial vaginosis who were attending a gynecologic outpatient clinic for a routine visit were randomly allocated to receive polycarbophil gel 2.5 g or an acidic vaginal douche twice a week for 6 weeks. We determined vaginal pH by means of a pH meter and the presence of a fishy vaginal odor using a potassium hydroxide (whiff) test at baseline and after each treatment. Vaginal pH was measured in the lateral vaginal fornix at baseline and at weeks 3 and 6 by an investigator who was blinded to treatment. In an additional group of women with a baseline vaginal $\text{pH} > 5.0$, we assessed the effect of treatment after a single application of polycarbophil or douche on vaginal pH at baseline and at 8, 32, 56, and 80 hours.

Results: Of 45 women screened, 30 women, 2 of whom were pregnant, participated. All completed the study. An additional 8 postmenopausal women (mean age 56 ± 5 years) received a single application of polycarbophil ($n = 4$) or vaginal douche ($n = 4$). Polycarbophil significantly ($P < 0.001$) reduced vaginal pH from 5.4 to 4.7 ± 0.6 at week 3 and 4.6 ± 0.7 at week 6 compared with baseline and with the vaginal douche group (5.4 ± 0.5 at week 3 and 5.3 ± 0.8 at week 6; not statistically significant). At the end of the study, vaginal pH was significantly ($P < 0.04$) lower in the polycarbophil group than

in the vaginal douche group (4.6 ± 0.7 vs 5.3 ± 0.8 , respectively). Physical and microbiologic signs of bacterial vaginosis were also improved in the polycarbophil group. Both treatments were well tolerated, with no adverse events as determined by the primary investigator. The pH-lowering effect of a single application of polycarbophil gel lasted significantly ($P < 0.01$) longer than that of vaginal douche, decreasing from 5.5 at baseline to 4.5 after 80 hours.

Conclusions: Our findings show that polycarbophil vaginal gel appears to reduce elevated vaginal pH to physiologic levels for 80 hours compared with acidic vaginal douche and to reduce vaginal pH in women with suspected bacterial vaginosis. Such reduction may help prevent the clinical complications associated with an altered vaginal pH. Randomized, controlled, clinical trials are needed to assess the role of polycarbophil vaginal gel in the long-term treatment of acute and recurrent bacterial vaginosis.

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