

Vaginal pH Self-Screening as a KISS Regimen in Prevention of Early Preterm Birth

Udo B. Hoyme

Chief Physician, HELIOS Klinikum Erfurt, Germany



Univ.-Prof.Dr.med.habil.
Prof.Dr.h.c. Udo B. Hoyme

Abstract

Self-measurement of vaginal pH is an established screening procedure for prevention of premature birth due to abnormal vaginal flora and bacterial vaginosis. In the Erfurt and Thuringia studies women were instructed to see their physician immediately if their vaginal pH was abnormal (> 4.5) or other risk factors were present, so results could be confirmed and therapy started. Treatment was with *Lactobacillus acidophilus* or, for bacterial vaginosis, antibiotics. In the initial trial, 0.3 % of the neonates with a gestational age $< 32 + 0$ weeks were seen in an intervention group versus 3.3 % ($p < 0.01$) in the control group; in the larger Thuringia study, the figures were 0.94 versus 1.36 % ($p < 0.01$). The rate of newborns < 1.000 g was significantly reduced to 0.38 %, the lowest incidence ever seen in Germany. After discontinuation of the Thuringia trial in 2000, the pre-term birth rates returned to the levels prior to the programme, however, the innovative pH measurement regime described has been introduced in > 20 countries so far.

Disclaimer: Potential conflict of interest: pH-EcoCare was designed and marketed in cooperation with the author.

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Introduction

Abnormal vaginal flora (AVF) as well as bacterial vaginosis (BV) have a significant relative risk for miscarriage or preterm birth. Furthermore, bacterial infectious agents play an important role, also in the etiology of ectopic pregnancy, spontaneous abortion, stillbirth, congenital and perinatal infections and puerperal maternal infections. Since *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and BV have been associated with an increased risk of febrile morbidity especially after surgical abortion, routine screening appears to be indicated prior to the procedure in most populations, but is also considered in general for pregnancy.⁽¹⁻³⁾

Despite all interventional efforts preterm birth rates have remained unchanged for years at about 6 – 8 % throughout Germany. In contrast, both perinatal morbidity and mortality have been reduced significantly over the last years. With the current high standard of neonatal medicine, a further

improvement of those results can only be expected if we succeed in reducing prematurity as the main contributor to perinatal morbidity and mortality.^(1, 3) Because of the preventive character of all measures this requires not only a medical but also a socio-political effort.

AVF and BV, an anaerobic dysbiosis, are found in up to 20 % of pregnancies and represent a relative risk for miscarriage and prematurity of 1.4 – 6.9.^(1, 4-7) An adequate treatment regime, especially in the early stages of pregnancy, can lead to a significant reduction of prematurity.⁽⁶⁻⁸⁾ The efficacy of this concept, in which the pregnant women actively take part, has been investigated in the Erfurt and Thuringia trials.^(3, 11)

Patients and Methods

The objective of these trials was to prove the efficacy of vaginal pH screening as a substitute tool for AVF and BV during pregnancy. Intravaginal pH self-

Table 1. Data from the Thuringia Prematurity Prevention Campaign 1998: delivery (controlled for gestational age) at the Department of Obstetrics, Erfurt. (n = 2,722)

Delivery (gestational age)	Participants (pH self measurement)	Controls A (pH measured by physician)	Controls B (no measurement)
	n = 381	n = 1,001	n = 1,340
≥ 37 + 0	91.9%	90.7%	85.4%
32 + 0 / 36 + 6	7.9%	7.1%	10.4%
< 32 + 0	0.3%	2.2%	4.1%

measurements were carried out twice weekly by the women, as the obstetrician's examinations at 4-week intervals, were not considered to be sufficient. In this study, involving more than 200 local obstetricians, it was impossible and also not intended to investigate specifically the impact of AVF or BV on prematurity, neither to collect new epidemiological data, nor to reassess diagnostic measures and compare different treatment regimes. The aim was rather to estimate the impact on self-measurement of vaginal pH as a sign of a high risk of preterm delivery.⁽³⁾

Each patient was asked to consult her gynecologist immediately when risk indicators or symptoms relevant for prematurity occurred, especially when a pH value of or above 4.6 was obtained. The gynecologist had to decide if the elevated pH was attributable to 1. a physiological condition, 2. pH elevation without evident infection or pathogen present (possibly AVF without BV), 3. BV according to the Amsel criteria, or 4. an indication for hospital admission, e. g. rupture of the membranes or uterine bleeding.

At the obstetrician's discretion, the patient was assigned to receive either no therapy, a 6- or 12-day course of intravaginal probiotic therapy (Gynoflor®, Nourypharma, Oberschleissheim, Germany), 5 days of vaginal clindamycin cream (Sobelin-Creme®, Pharmacia & Upjohn, Erlangen, Germany) or admission to the hospital for specific treatment according to the diagnosis.

Results

In December 1998, 381 women of a total of 2,722 delivering women in that period in Erfurt maternity were included in the pilot trial (14 %). The 2,341 women not participating in the trial served as a control group. Preterm birth rate before the end of 32 gestational weeks was only 0.3 % among the

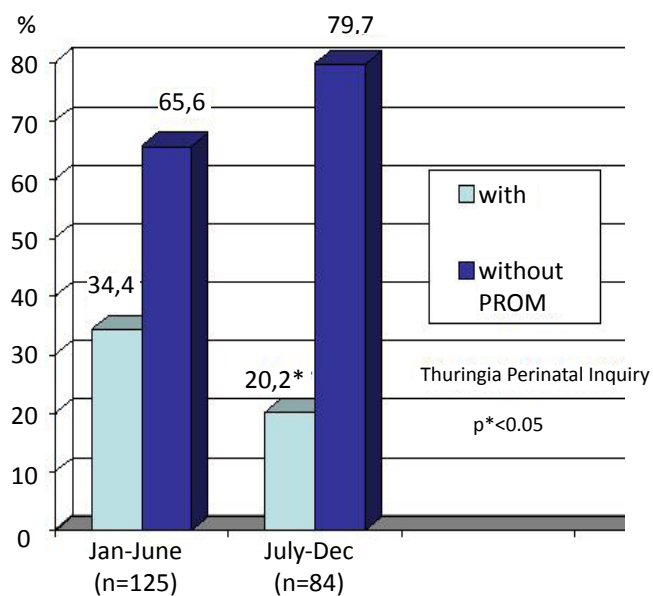
study patients, compared with 2.2 % of patients seen every 4 weeks by physicians, being informed about the trial, but not involved in self-sampling and 4.1 % in a group of pregnant women who received only conventional prenatal care (Table 1). The majority of women appreciated the privacy and preferred the self-care, rather than the feeling of an "object" being looked after, a clear paradigm shift.

Also the evaluation of the perinatal data of 16,276 deliveries during the year 2000 in Thuringia showed similar trends: the total number of preterm births before the end of 32 weeks was significantly less in the 6-month period of self-test compared to the previous 6 months without self-test, also in the different birthweight groups (Table 2). Women doing self-sampling during the study period and reporting back (607 self-sampling women of 8,406 in total, 8 %) had a reduced risk of preterm birth at < 32 + 0 weeks (0.3 vs. 1.58 %; p < 0.05) and at < 37 + 0 weeks (5.3 vs. 8.5 %; p < 0.01) versus controls (first 6 months of year 2000, n = 7,870). Similar results were obtained when comparing the birth weights < 2,500 g (3.45 vs. 6.92 %; p < 0.001). Moreover, more than 1/3 of early premature births were connected with early rupture of membranes in the 1st half of the year; this was only the case in 1/5 in the 2nd half (Fig.1).

Discussion

Abnormal vaginal flora and bacterial vaginosis is a known risk factor for preterm birth. The VIP trial in which enrolment was after 20 weeks of pregnancy found a relative rate of preterm birth of 1.6 for women with BV, comparable for the risk of harbouring *C. trachomatis* or trichomoniasis.⁽⁴⁾ Aerobic types of colpitis with an increase of the pH value⁽⁶⁻⁸⁾ as well as intra- and extra-amniotic infections with enteropharyngeal pathogens are also demonstrated to contribute towards prematurity.⁽⁹⁾

Figure 1. Thuringia Prematurity Prevention Campaign 2000: Share of Premature Rupture of Membranes for Early Preterm Birth (< 32 + 0 weeks)



Dennemark et al.⁽¹⁰⁾ were able to show that by early intervention either with lactobacillus preparations or with intravaginal Clindamycin treatment, a distinct reduction of prematurity could be obtained. In principle, lactobacillus preparations cannot yet be considered a scientifically proven causal therapy in women with an abnormal vaginal flora in pregnancy, but the main objective of treatment in both the Denmark and the Erfurt/Thuringia investigations was the prolongation of pregnancy.

The Erfurt and Thuringia programmes represent a prospective observational study. The main benefit is that because of the active involvement of the pregnant women pH changes could be recognized early in pregnancy and as a consequence most abnormalities

relevant for late miscarriage or premature birth could be addressed with an immediate therapy. The results confirm the positive consequences of the applied measures.

However, the study also has disadvantages.⁽¹¹⁾ Firstly, it is not known what the pathophysiological correlate of an increased pH is. Other signs of imminent preterm birth may be involved in women with increased pH: cervicitis, frequent and recent sexual contact, uterine bleeding, etc. Secondly, we have no detailed information of the medication and actions prescribed, neither do we know how good the compliance of patients was with the treatment. Thirdly, once the patients are alarmed by an abnormal test, other measures to prevent preterm birth may have been introduced besides taking treatment. Fourthly, the major benefit in prevention was not seen for all prematurely born but only for those in the group of early prematurity (< 32 + 0 weeks, e. g. < 1000 g) and therefore highest perinatal morbidity and mortality. A disadvantage, as discussed by opponents of the method? Rather an unique advantage!

Nevertheless, the broad implication in a whole federal state has led to the positive experience with respect to availability and practicability of a broader approach to prevent preterm birth. Whatever the exact mechanism, the results achieved in the study region Thuringia in 2000 are the best ever seen in any of the German states in the past! Indeed, after discontinuation of the campaign due to financial limitations, the prematurity rates in Thuringia immediately rose again to previous levels remaining at the same level in the subsequent years (Table 2).

Table 2. Distribution of Birthweights (%) State of Thuringia 1999-2005. *p < 0.05, **p < 0.01, *p < 0.001**

Year	1999	I/2000	II/2000	2001	2002	2003	2004	2005
N	16233	8162	8458	16408	15995	15436	16058	15633
< 1000g	0.54	0.61*	0.38	0.46	0.63***	0.62**	0.60**	0.56**
< 1500g	1.22**	1.29*	0.97	1.09	1.32**	1.17*	1.15*	1.30**
< 2000g	2.67***	2.67*	2.03	2.36**	2.62***	2.74***	2.34**	2.60***
< 2500g	6.76***	6.91**	5.99	6.64***	6.72***	6.80***	6.35**	6.88***
<1000g Perinatal Center Erfurt		1.5	1.0	1.5	1.6	1.5	1.4	1.7

Outlook

Prevention of preterm birth by screening, diagnosis and antimicrobial therapy of genital infections should be implicated as a necessary step for optimizing and rationalizing health care systems in general.

A controlled, prospectively randomised study addressing pH self-measurement and diagnosis as well as subsequent and adequate treatment is still required but almost impossible to perform. On the other hand, since less is more, further progress can also be expected by applying the KISS (Keep it simple, stupid) principle: pH-measuring devices have to become cheaper to produce, more comfortable and simpler to use and to be completely biodegradable before they become an ubiquitous and successful application in developed and underdeveloped countries (Fig.2).

In addition, in another prospective and controlled pH-screening trial of four insurance companies in five German states between 2004 and 2006 odds ratios for early prematurity < 32 + 0 weeks of 0.85 (0.72 – 1.02) and birth weight < 1500 g of 0.79 (0.66 – 0.95) were seen on the basis of 149,082 deliveries monitored.⁽¹²⁾

Figure 2. Paper-cotton pH-EcoCare™ Comfort Swab (Merete Medical) for pH Self-measurement and Simultaneous Set-up of Wet Mount Microscopic Slide by the Gynecologist



Furthermore, the concept of pH self-measurement in particular seems to result in an efficient reduction of prematurity.^(3,6,8,10) The chance to reduce the extremely costly complications associated with preterm birth with minimal expense comes with the fact that the immeasurable extraordinary strain on all parties involved can be reduced in a beneficial way. Can we as physicians, health care providers and politicians take the liberty to ignore these encouraging prospects?

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