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EDITORIAL

Prevention and not merely prediction of preterm labor and delivery

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Abstract

Different methods have been proposed to screen for preterm labor and delivery; most of these aim to predict the risk that preterm delivery is going to take place. However, interesting though this knowledge might be, knowing the future is of no use when no changes can be made. Recent publications have suggested new and exciting modalities to actually diminish the frequency of preterm birth in patients selected by transvaginal cervical length measurement; these modalities include vaginal progesterone and vaginal pessaries. Although promising, many questions remain to be answered; not least about the long term outcome for both neonates and mothers, but also on the eventual introduction of such strategies to the general obstetric population. One of the main problems that urgently needs clarification is how we are going to offer this best of medicine to those needing it most: deprived and socially isolated women who have the highest risk for preterm labor and delivery, probably not due to any congenital cervical problems, but to a combination of environmental, microbiological and social factors, including transgenerational poverty and deprivation.

Spontaneous preterm delivery is the major factor contributing to neonatal mortality and morbidity and can result in life long lasting health problems for the early born child. Optimizing neonatal care, preparing the fetus with corticosteroids and/or magnesium sulfate and trying to postpone delivery with tocolytics are all considered a form of "palliative" care once the disaster of spontaneous preterm delivery seems inevitable, but actually the success rate of these interventions is moderate at the best[1]. Over the years, a multitude of publications have been produced on methods to predict preterm delivery; from a patient's history (a previous preterm birth is a strong predictor but are we really interested in this as the majority of preterm deliveries in the western world are in primiparous women), to uterine contraction monitoring, different serum markers in maternal blood and/or saliva and, most popular, transvaginal cervical length measurement and both qualitative and quantitative detection of fetal fibronectin in cervicovaginal fluid. Logically, this is now resulting in ongoing studies to determine whether screening in low risk women is worthwhile[2]. Even then, cervical shortening and the appearance of fetal fibronectin are most probably late signs of an inflammatory response and real prevention ought to act before the inflammation is initiated. Romero coined the term "fetal inflammatory response syndrome" or FIRS[3] but

it is more probably not primarily a fetal but a maternal inflammatory response at the beginning of the chain of events resulting in preterm labor and delivery. As we still do not completely understand what is happening in normal term labor, it is hard to discover the pathological changes that lead to preterm labor. Cervical ripening and myometrial contraction also occur in term labor, accompanied by inflammatory changes, and actually, during the whole of normal pregnancy, any parameter used to express "inflammation" seems to be activated. Modulating inflammation and immune activation promises to be one of the ways to really prevent preterm labor[4] but unluckily, the most straightforward method for this, using anti-inflammatory drugs such as indomethacin, were quite successful in postponing delivery but at the expense of major fetal/neonatal side effects. It was hoped that simple interventions such as screening for asymptomatic bacteriuria and periodontal disease would significantly lower the incidence of preterm delivery. These promises have not been kept: data on the effect of treatment for asymptomatic bacteriuria are scarce and more recent findings seem to find minimal, if any, effect[5]; a meta-analysis on treating periodontal disease did not find a reduction in preterm delivery[6]. Much work has been done on bacterial vaginosis and abnormal vaginal flora (whatever that may be) and treatment in early pregnancy (treating after 20 wk is too late as the inevitable chain of events has already begun) and clindamycin seems to reduce the risk of spontaneous preterm birth at less than 37 wk but not at less than 33 wk; once again, a moderate effect at best[7]. If one tries to look at the clinical picture in a more global way, these poor results from our intervention should not be surprising: not only are we treating blindly without really understanding what we are shooting at, but all these interventions have let us lose sight of the pregnant woman as a whole in her environment. Just imagine the patient with periodontal disease: in most cases you will find that it is not just a few million bacteria in the periodontal space but it is a lack of dental and personal hygiene, often associated with smoking, unhealthy food habits and lack of access to good dental (and general health) care. Treating teeth, or urine or vaginal flora, will never compensate for social deprivation, an insecure financial situation and a health system failing to provide care to the poorest. No wonder that dedicated antenatal clinics for women with a high risk for preterm birth are not a success when we do not know what we are treating and when you do not reach the real high risk group (unplanned pregnancies in "inflammatory", meaning untreated, women), no change can be expected[8]. The real care, as with all primary prevention in medicine, should not be at a central, far away, highly specialized clinic but at the local level.

The history of the search for the prevention of preterm labor is full of promising and finally failing interventions, such as calcium and magnesium supplementation[9]. We do have a few little successes, such as abdominal cerclage in those with no or a minimal cervix[10], although the dispute about (vaginal) cerclage will probably continue for decades.

What is considered a "major advance" at the moment is the story of vaginal progesterone in the prevention of preterm labor. Vaginal progesterone can be administered in vaginal capsules, in most studies, 200 mg was used (but probably 100 mg is enough), or in a vaginal gel, in most studies 90 mg was used. Progesterone is better absorbed after application with a vaginal gel than using capsules. It has been demonstrated in a review by Rode *et al*[11] that the use of vaginal progesterone in patients with a previous preterm birth resulted in significant lowering of the percentage of women delivering before 32 wk. Once more, as with simple history taking, most preterm births occur in women giving birth for the first time.

Recently, a very well designed prospective randomized trial clearly demonstrated that screening women with transvaginal ultrasound and measuring cervical length at 19 to 23 wk, followed by vaginal progesterone gel if the cervix is between 10 and 20 mm, results in almost halving the number of preterm births[12], which confirms previous data using vaginal progesterone tablets in women with a cervix less than 15 mm[13]. This is really good news but leaves us with some questions too: Does it improve the neonatal outcome in the long term? What if the cervix is less than 10 mm? Why does it work in only half of cases and, most importantly, how will we reach those deprived high risk women and offer them a vaginal ultrasound at 19 to 23 wk, realizing that preterm delivery is more frequent in late bookings?

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