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Review Article

PREDICTION OF PRETERM LABOR (PTL) AND SUPPLEMENTARY PROBLEMS: A REVIEW

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ABSTRACT

Previous history of preterm labor is one of the important risk factor (risk of PTL in subsequent pregnancies are 15.3% and 21% after one and two preterm births Preterm labor (PTL) is one of the foremost causes of perinatal morbidity and mortality. It is one of the major public health problems, especially with reference to mortality, disability and health care expenses. The overall incidence of PTL is around 10-19%. Out of all PTL 55 % occur spontaneously, 25% following preterm pre-labor rupture of membranes (PPROM) and another 20% iatrogenic.. Others include multiple pregnancy, uterine over distension, uterine anomalies, cervical incompetence, bacterial vaginosis, bleeding in early pregnancy, poor socioeconomic status, elderly and adolescent age group and tobacco use. Cervical length assessment by USG, fetal fibronectin, vaginal pH is being used. Progesterone and clindamycin (abnormal vaginal flora) antibiotic is being used with reasonable evidence. Corticosteroids and antibiotics help in reducing neonatal morbidity and mortality and tocolytics (nifedepine and atosiban are recommended) helps in allowing the steroids to act. New predictors like higher vaginal pH (> 4.5) and Gram stain score of 9 to 10 with Nugent criteria in early pregnancy is increasingly associated with preterm labor. Search for selective and safe tocolytic is also under consideration, specially the prostaglandin synthetase inhibitors and the role of potassium channels in myometrium. Successful prediction, prevention and treatment of preterm labor have significant influence on the perinatal outcome, health care expenditure and quality of life. As the cause for preterm labor is still an enigma, it is difficult to predict, prevent and treat PTL successfully. At present the treatment of PTL is mainly antibiotics, tocolytics and corticosteroids with varied success.

KEYWORDS: *Preterm birth, Fetal Fibronectin, Preterm labor, Predictors of PTL, Tocolytics.*

INTRODUCTION

Unfortunately there is very miniature change in the incidence of PTL in the last half century. This problem in a country like India has different magnitude, as the cost involved in caring these pre- term babies is enormous, which is not within the reach of the poor. Real preventive and therapeutic measures are still not available because of the persistence of suspicions of measures to prevent preterm labor. Preterm labor (PTL) is one of the leading causes of perinatal morbidity and mortality. It is one of the major public health problems, especially with reference to mortality, disability and health care expenses [1]. Effective strategy for both prevention and management can definitely improve the perinatal outcome. This review is an effort to provide an update onpreterm labor condition.

Meaning:

Incidence of regular uterine contractions (four or more in 20 minutes or eight or more in 1 hour) and cervical changes (effacement equal to or greater than 1 cm) in women with intact fetal membranes and gestational age less than 37 weeks [2].

The Problem Thoughtful?

The overall incidence of PTL is around 10-15% (6-15% Range) [3]. Out of all PTL 50% occur spontaneously, 25% following preterm pre-labor rupture of membranes (PPROM) and another 25% iatrogenic risks. It is leading cause of neonatal death and disability especially cerebral palsy, deafness, blindness and chronic lung disease. The care of the preterm babies is highly expensive and not within the reach of the poor, this is one of the main reasons for increased mortality in developing countries.

Can we predict the Problem of Preterm Labor?

The answer of this question is a large no, but there have been some attempts though by which prediction of preterm labor taking into consideration by following factors.

1. Risk factors.
2. Fetal fibronectin(FFN).
3. Bacterial vaginosis.
4. Length assessment in cervical by USG.

Risk Factors:

Previous history of preterm labor is one of the important predictor as it is estimated that the recurrence risk of PTL in subsequent pregnancies is 14.3% after one preterm birth and it is almost double with two preterm births (28%) [4-6].

The other risk factors are:

1. Multiple pregnancies.
2. Uterine over distension (polyhydramnios, macrosomia and fibroids).
3. Uterine anomalies.
4. Cervical incompetence.
5. Bacterial vaginosis.
6. Bleeding in earlypregnancy.
7. Poor socioeconomic status.
8. Elderly and adolescent age group.
9. Tobacco use (smoking and smokeless).

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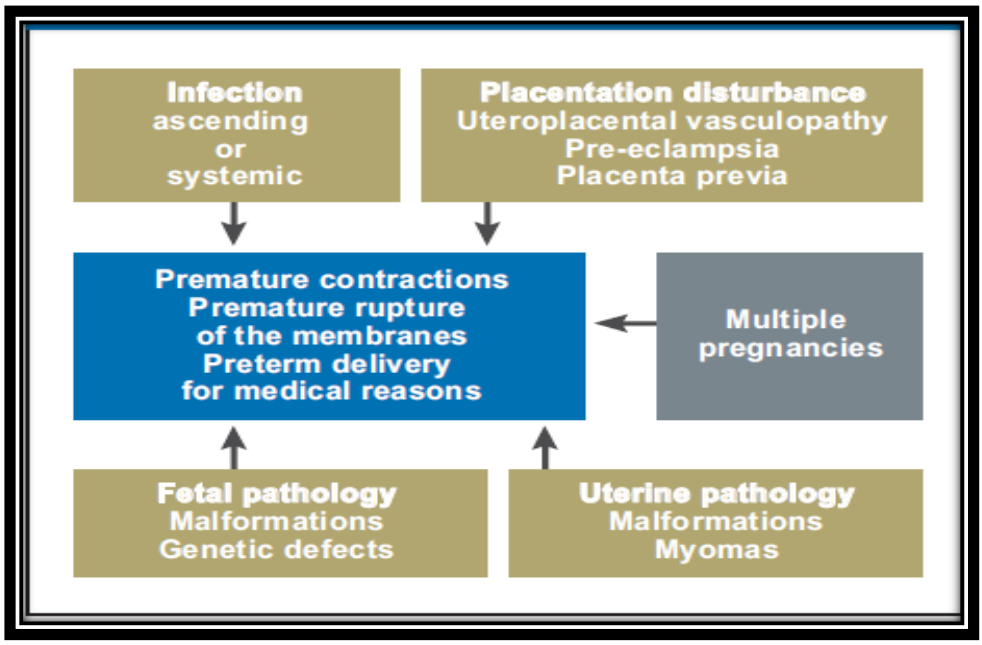

Fig. 1: Risk Factors

Pre-Clude PTL?

Expectation of PTL even in high-risk women is difficult hence a measure to prevent PTL has been attempted with tocolytics, antibiotics and progesterone.

Antibiotics: Studies have shown that use of antibiotics in the presence of abnormal vaginal flora or BV in early pregnancy has reduced the incidence of PTL but however other studies have conflicting reports. There is a wide variation in antibiotic selection and results are conflicting. However a randomized controlled trial with clindamycin as a single drug in early second trimester in cases with abnormal bacterial vaginal flora and BV had beneficial results [9]. However use of antibiotics in PPROM has reduced the incidence of neonatal morbidity but not preterm birth [10].

Progesterone: Prophylactic use of 17 hydroxy caproate has significantly reduced the incidence of PTL but not useful in established PTL (From early pregnancy till 34 weeks) [11]. Vaginal natural micronized progesterone is used for prophylaxis of PTL in women with short cervix with reasonable success [12].

Cervical Cerclage: There is no clear evidence to support prophylactic cervical cerclage routinely. There may be beneficial effects with cerclage in women with short cervix. Role of emergency cervical cerclage is controversial; some have shown benefits of median prolongation of pregnancy by 4-5 weeks (1-18 weeks range) and survival rates upto 89% [13, 14]. Use of emergency cerclage, indomethacin, antibiotics and bed rest have reduced PTL compared to antibiotics and bed rest alone [15]. However at present elective cerclage for prevention of PTL as routine is not recommended and before performing the emergency cerclage one should counsel with regard to the benefits and risks of the procedure (iatrogenic rupture of membranes and infection) [7].

Treatment or Management:

The accurate cause behind PTL, prediction and prevention measures for PTL are met with little or no success. The treatment of PTL puts the obstetrician in clinical dilemma to use the measures with low success rate, lack of specific effects, some serious side effects (Betamimetics) and weak evidence of support for their use.

Tocolytics:

These are drugs that relax the myometrium to inhibit uterine contractions. These agents act by different mechanisms and result in non-availability of intracellular ionic calcium leading to inhibition of formation of actin-myosin complex. Though, the usefulness of these agents is questioned. These produce serious maternal and fetal side effects. RCOG (2002) does not recommend their use as it is not supported with evidence. However, these agents are of help to gain few days which will be beneficial, especially for the corticosteroids to act and also for *in utero* transfer to higher Centre for better care. The use of these agents after 34 weeks is not recommended and the lower gestational age limit is not clear.

These agents include:

1. β - sympathomimetics.
2. Calcium channelblockers.
3. Oxytocin receptor antagonists.
4. Prostaglandin synthetase inhibitors.
5. Magnesium sulphate.
6. Nitric oxidedonors.

Use of β – Sympathomimetics:

These include Isosuxprine hydrochloride, ritodrine, terbutaline and salbutamol. The use of these agents is associated with serious side effects like, arrhythmia (including tachycardia), hypotension, pulmonary edema, myocardial ischemia, and death. Other less serious side effects are hyperglycemia and hypokalemia. These normally do not warrant any treatment unless the woman is diabetic or immediate surgery is contemplated. Some tocolytics have specific side effects like, ritodrine may induce vasculitis in women with autoimmune disease, terbutaline may cause increased sensitivity (in babies who are exposed *in utero*) for abnormal neural effects to organo- phosphorous compounds if exposed in later life [16, 17]. These drugs are no more recommended as their efficacy is inferior to calcium channel blockers and atosiban.

Use of Calcium Channel Blockers:

These (Nifedipine and nicardipine) are the first choice agents for tocolysis. These drugs can be used even in women with twin pregnancy, diabetes mellitus, heart disease including cardiomyopathy, where other agents are contraindicated. These agents do not have significant effects on hemodyanamic and metabolic changes [18, 19]. These agents are superior to atosiban (an oxytocin receptor antagonist) in effectiveness and are much cheaper than it [20]. Side effects like myocardial infarction and deaths have been noted rarely with use of nifedipine especially in woman with cardiovascular diseases [21, 22].

Use of Atosiban:

An oxytocin receptor antagonist useful in preterm labor. However it is less effective and costlier compared to calcium channel blockers, but with fewer side effects like chest pain, palpitations, tachycardia, hypotension, nausea, vomiting and headache [20, 23].

Use of Prostaglandin Synthetase Inhibitors:

Drugs like indomethacin are being used in the treatment of PTL. The use of these agents is associated with potential fetal risks like premature closure of ductus arteriosus, persistent pulmonary hypertension, renal and cerebral vasoconstriction and necrotizing enterocolitis and prolonged renal insufficiency in the preterm infant specially in higher doses (>200 mg /day and for > 48 hours) [24, 25]. Other agents like selective cyclo-oxygenase 2 inhibitors are under trial.

Use of Magnesium Sulphate:

Magnesium sulphate as a tocolytic is no more recommended as its use has been associated with increased mortality for the newborn and its ineffectiveness to prevent/delay the preterm birth [26].

Use of Nitric Oxide Donors:

There is insufficient evidence to support the use of nitric oxide donors (nitroglycerine) in preterm labor [27]. Maintenance of tocolytic therapy is attempted with varying success with no improvement in the recurrence episodes of PTL and perinatal outcome [28].

Use of Corticosteroids:

Use of antenatal (24-34 weeks) corticosteroids is associated with reduction of respiratory distress syndrome, neonatal death, intraventricular hemorrhage and necrotizing enterocolitis (betamethasone) [29]. Single course of therapy is recommended [29].

Newer developments: Research is underway in identifying the cause for preterm labor with special reference to infection with various agents that leads to separation of membranes as a consequence of infection.

CONCLUSION

As the cause for preterm labor is still an enigma, it is difficult to predict, prevent an treat PTL successfully. Successful prediction, prevention and treatment of preterm labor has significant influence on the perinatal outcome, health care expenditure and quality of life. At present the treatment of PTL is mainly antibiotics, tocolytics and corticosteroids with varied success. The goal of treatment of preterm labor should be to improve perinatal outcome and reduce morbidity and mortality. Search for selective and safe tocolytic is also under consideration, specially the prostaglandin synthetase inhibitors and the role of potassium channels in myometrium.

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