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Recent Update on Treatment of Preterm Labour

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Summary:

The child is the future asset and hope of any nation. There is global consensus that improving health of the child and mother paves the way for poverty alleviation and development. Preterm birth is 27% of direct cause of neonatal death in developing countries. Even in developed countries premature babies are main concern. So the treatment of preterm labour is given much priority .The goal of prevention and treatment of preterm labour is delivery of a healthy term infant. It is a fact that neonatal outcomes are greatly improved when intrauterine life can be extended until foetal lungs mature. It is therefore suggested that delaying labour for even days can be beneficial. Early and ongoing risk assessment, education of all pregnant women, and psychological intervention regarding smoking, alcohol use, illegal substances use, and domestic violence are important components of primary prevention. "Early diagnosis and early treatment " before advanced cervical changes have positive impact on neonatal morbidity. Screening, motivating, providing health care education and intervention on right time on right way can make a significant contribution to lowering morbidity and mortality from preterm delivery.

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Introdution:

Preterm birth is the highest cause of neonatal death in height mortality countries like Bangladesh. The goal of Bangladesh is committed to achieve MDG4 by reducing infant mortality rate (IMR) by 2/3 with in 2015. Now it is 46/1000 and we have to take IMR to 22/1000 by 2015[1]. Successful reduction of perinatal mortality and morbidity requires implementation of effective prevention of preterm labour. Only a decade is left to reach the target to get the MDG4 so this is high time to know the optimum treatment of (PTL) preterm labour.

13 million PTL occurs worldwide in each year. Though PTL means birth before 37 completed weeks but babies born before 34 weeks, experience most complications. Therefore Prevention and active treatment of PTL is the important means of reducing adverse events for child.[2]

Etiology of PTL is multifactorial but infection is possible cause up to 40% cases[3,4]. Prevention of PTL is very difficult but finding predisposing factors like any infection, and treatment accordingly may reduce its incidence. ACOG recently reported that many of the methods used to stop preterm labour are ineffective. The ACOG announcement confirms NICHD supported research , which found that home uterine monitor were not effective for predicting PTL. Therefore the goal of management of PTL should identifying risks, timing of delivery and prophylactic pharmacology .Also fluid therapy, rest , assurance avoidance of smoking, heavy work and mental stress are important nondrug therapy of PTL. Early warnings signs of PTL may help in timing and route of delivery ,which improves the perinatal outcome[5]. So education to the patients about the symptoms of PTL may bring them to clinician early. At least identifying women at risk of PTL may reduce mortality morbidities and expenses associated with prematurity.[6]

Source:

The materials, for this review was taken mostly from Medscape Reference, medline databases, Cochrane database systemic review. Some other relevant references are taken from journal of American Obs. and Gynecology, journal of Bangladesh College of physician and surgeons, an international journal of obstetrics and gynecology .We searched the articles of the bibliography and different published meta- analysis. We also took information from the book High risk pregnancy and delivery 5th edition by Elizabeth Stepp Gilbert.

Risk of Preterm Labour:

The exact mechanism of PTL is largely unknown but is believed to include decidual haemorrhage (multiple

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gestation, polyhydramnios,abruption), cervical, incompetence, mullerian abnormalities, fibroid uterus. Cervical inflammation, any fever of the patient like urinary tract infection, Asymtomatic bacteruria, Pneumenia predisposes PTL. Risk of domestic violence, stress ,smoking and previous H/O preterm birth are also associated with PTL.

Preconceptual Evaluation:

While the risk for PTL in nulliparous women is hard to determine but past obstetric experience and personal behavior may provide significant insight into future pregnancy outcome in multiparous women, Pre pregnancy measure to reduce PTL may be applicable for genital tract anomalies like some procedures as metroplasty for septated uterus ,cerclage for cervical incompetence (at 12-14 weeks)'. But evidence of randomized trial showed that one woman in 30 cases will benefit from cervical suture. Forceful dilation of cervix should be avoided . Cervical CIN (cervical intraepithelial neoplasia) need to be treated appropriately and care should be taken not to remove too much tissue during LEEP, laser , and cold knife excision. Obstetric laceration of cervix need to be repaired under proper visualization. Midtrimester loss has many etiologies, including syphilis. Antiphospholipid syndrome, diabetes, substance abuse, genetic disorders, congenital mullerian abnormalities so complete workup may be value in selected cases.

Any medical conditions such as diabetes, thyroid disorder and chronic illness should be treated before getting pregnancy.

Management of PTL:

Diagnosis:

Contraction of sufficient frequency and intensity to effective progressive effacement and dilation of the cervix at 24 –37 weeks gestation are indicative of active PTL.

Criteria for tocolysis include more than 6 contractions per hour resulting in a demonstrated cervical dilation >2 cm. If contractions present without cervical changes treatment is only continued observation or theraputic sleep and assurance.

CBC , urine analysis, cervical specimen for group B streptococcus, Chlamydia and gonorrhea should be sent. Wet mount for bacterial vaginosis and trichomonas and USG can be done.

If genital tract infection is suspected from previous PTL antenatally, it seems reasonable to take HVS electively at 29-24 weeks of gestations.[7]

Sonographic evaluation of precocious cervical ripening from 24 weeks of gestation has varying support for many years ,it can be done in risk group. Normally cervical length is 35 – 40 mm in 22 weeks, 35mm in 24 –28 weeks, 30 mm in > 32 weeks. Biochemical markers of PTL by estimating fetal fibronectin is better option to predict PTL and this is a very promising method.[8] But again Cervical cerclage, prophylactic bed rest and empirical use of tocolytics is not proved to be very effective but is reasonable to offer once diagnosis is made. Progesteron injection administered weekly between 16 -20 weeks have been shown to decrease the chance of PTL in current pregnancy by 33% (Petrini and others, 2005) but the same results have not been shown to be effective for a multiple gestation (Thorp, Mercer, Sorokin and others, 2009).

Tocolytics:

Tocolytics are the drugs which suppress the uterine contraction and hypothetically it seems to stop the uterine contraction Many research is going on to see the effectiveness of these drugs particularly for the stopping of preterm labour. Still there is no clear evidence that these drugs improve the outcomes following PTL and it is reasonable not to use them randomly. However tocolytics drugs should be considered for few days while completion of the course of steroid or in utero transfer of the fetus to a tertiary center. A wide variety of tocolytis agents have been advocated to suppress the uterine contraction, these are B-agonist like solbutamol, terbutalin, ritordine , calcium channel blockers as nifidipine, Indomethacin, prostaglandin synthetase inhibitor and magnesium sulphate. Others are Nitric oxide donar and oxytocin receptor antagonist- 'Atosiban'. Metanalysis of studies showed that use of tocolytics reduces the Preterm birth ocuring up to seven days of treatment but it can not halt the process[9]. Nevertheless it is very helpful as it allows some time by which steroid administration can be done which prevents respiratory distress syndrome of premature neonates . Ritodrine is no longer being used

as its severe adverse effects are associated with palpitation, tachycardia, dyspnoea and chest pain[10]. Moreover rarely they may produce pulmonary oedema, myocardial ishcaemia and arrhythmia. Indomethacin is a effective tocolytic but it is associated with premature closer of ductus arteriosus, renal, cerebral vasculities and necrotizing colitis in neonates[11]. Regarding magso4, it is also very effective in suppression of uterine contraction but Peter S and et al of Motefiore medical centre of Newyork showed that it is associated with maternal side effects-like nausea headache, drowsiness and flushes and respiratory and motor depression in neonates[12]. Magso4 is considered before 34 weeks .The usual dose is 1 to 2gm iv/hour for 24 hours. Serum level should be 4 to 8 gm /dl .It is very effective and is helpful for the premature neonates but should not be used more than 7 days. Epidemiologic evidences also indicates a connection between maternal hypocalcemia and skeletal abnormalities in neonates.[13, 14 ,15]

Atosiban is very popular drug it has good safety profile for mothers but not devoid of fetal adverse effects .In comparison to other tocolytics, Atosiban seems to be superior but similar to nifedipin in efficacy. Nifedipine is very effective tocolytics with high safety profile. Global consensus is that Atosiban and nifedipine are preferable drugs for tocolytics. Nifedipine does not cause hypotension in normotensive laboring women, it may produce slight headache in mother. The most added benefit of nifedipine is that it reduces the incidence of respiratory distress syndrome, necrotizing colitis, intraventricular haemorrage [16].

Moreover as nifidipine is cheap, easily adminstrable, safe, effective and beneficial to neonates it can be used as 1st line drug of choice for treatment of PTL. Nifedipine is said to have less side effects than beta mimetics and MgS04.[17]. The dose is 20mg orally followed by 20mg orally after 30 min, if contractions persists 20gm dose can be administered every 8 hours for 48 to 72 hours with maximum dose of 160mg /day. Data of systemic review provide that there is of no benefit of using repeated doses rather there is insufficient evidence of any maintenance therapy that will prevent PTL. Tocolytics are not to be used beyond 34 weeks but clinicians are advised not to deliver the babies at this gestation without any indication because of high risk of neonatal morbidities in infants born at 34-36 weeks gestation compared with deliveries at 37-40 weeks gestation.[18] Contraindication must be known to all ,Cardiac diseases, significant pulmonary diseases, chorioamnities, foetal distress are important contraindications of tocolytic therapy.

Antibiotics:

Spontaneous PTL is associated with infection and there is good evidence that antibiotics used in women with PROM can delay delivery and reduce feto maternal infectious morbidity. In absence of infection, Antibiotics has little to do. Preview meta analysis found that antibiotics increased the duration of pregnancy at least by7 days[19].

However majority of women will deliver in this time regardless of antibiotics therapy and only 15 % of women likely to get benefit from antibiotics. The earlier gestation and having the abnormal genital flora are most likely to benefits from antibiotics. Bacterial vaginosis (BV) needs prophylactic antibiotics. It is important predisposing factor of PTL so women having threaten PTL needs to be screened and antibiotic treatment which delays labour and infection morbidities. For prophylaxis, combination of parentral and oral antibiotics may be necessary on the other hand for therapeutic use - intravenous antibiotics are most likely to be of greatest benefit. Finally antibiotics should be used only for those women with evidence of infection, Since only in these women are antibiotics likely to be of benefit.

Nevertheless prophylactic antibiotics in suspected cases or in group of high risks of PTL has strong role rather than in established PTL. So screening of occult infection by high vaginal swab is one of the important preventive role of PTL.GBS prophylaxis is must only in culture positive women. Based on the information in two large multicenter clinical trials (20)ACOG recommends a 48 hour course of ampicillin and erythromycin followed by 5 days of this regimen during expectant management of PTL. The use of ampicillin clavulanic acid is not recommended. For premature rupture of membrane erythromycin 250 mg orally every 6 hours for 10 days is recommended by the guidelines of Royal college of Obstetrician and Gynaecologists.[21]

Corticosteroid:

Original work by LIGGINS AND HOWIE showed the benefits of single course of Corticosteroids, between 28-34 weeks of gestation on respiratory maturation with

serious side effect. Others have done research that consolidated the work. The timing of therapy in PTL is crucial. The best neonatal results can be obtained after a complete course of two doses of betamethason 12mg at 12hrs apart or 4 doses of dexamethason 6mg 4 hrs apart. Delivery 3-7 days after this completed course is ideal. Before 24 weeks and after 34 weeks there is little value of steroid. However caution should be used in women who present with membranes ruptured for over 24 hrs, here the risks of infection are much higher. Some study showed that antenatal steroid administration is contraindicated in chorioamnities but the scientific basis for this recommendation remains obscured (22 ,23).Recent meta-analysis and systemic review showed that antenatal steroid is safe and effective in improving perinatal outcome even in chorioamnionities (24). But all obstetrician should be very careful about steroid administration in pregnancy with diabetes and multiple pregnancy. For GDM (gestational diabetes) patient , fine tuning of diabetic control with insulin may be necessary. Tuberculosis in Bangladesh is very common so it may render the use of steroid as it may flare up the disease condition. Balance against the risks of flare up and the benefit of neonatal respiratory distress should be considered. No doubt steroid administration reduces Respiratory Distress Syndrome, Intraventricular haemorrage ,necrotizing colitis, in babies born to PTL but it can not stop the process of PTL. Again steroid administration reduces the long term neurological morbidities[25].

Long term side effect of single dose is minimum . The same can not be said for repeated doses where a body of observational data is developing which shows no increase in protection but detriment to fetal growth and development. Therefore repeat doses need to be individualized and should not be used as routine.

Conclusion:

Prematurity in the newborn continues to account for 75 %—80% of neonatal morbidity and mortality (Hamilton and others, 2007).Preventing preterm labour remains one of the great challenge in modern medicine.(26). Proper timing and appropriate route of delivery of preterm baby in sophisticated neonatal backup service, involving senior obstetrician, experienced neonatologist and expert nurses , bring the desired success and thereby reduce the neonatal morbidities and mortalities. To reach MDG and to reduce IMR without losing time we need to give special attention to the management of preterm labour. Nobel laureate Gabeirela Mistral rightiy said "We cannot wait for tomorrow for our children , it is today" .

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