

# Review Prolong Labour - Role of Antispasmodics and Prostaglandins

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**Abstract**— The purpose of this Review is to discuss about Prolong Labor and its complications. The Review will also discuss the role Of Antispasmodics And Prostaglandins in Active Management of labor.

**Index Terms**— Antispasmodics, Prostaglandins, Prolong Labour, Prolong, partogram, pregnancy, pregnancies.

## 1. DEFINITION

It is difficult to give a clear definition for prolonged labour. In practice, as recommended by the WHO maternal health and safe motherhood programmer (WHO 1994)<sup>1</sup>, a woman should be transferred to a higher level of care if her rate of cervical dilatation (according to the partogram) becomes less than 1 cm/hour, and requires prompt, appropriate management if it is less than 1 cm in four hours.

## 2. PURPOSE

To review the role of antispasmodics and Prostaglandins on labour in term pregnancies.

## 3. DESCRIPTION

Labour is essentially one of the most primitive natural physiological events that has intrigued physiologists to this date, the intricacies remaining an enigma. The most vexing issue faced by obstetrician is the deviation of normal labour. Among others, prolongation of first stage of labour is often due to protracted or arrest of dilatation of cervix. Drug which will hasten cervical dilatation and decrease pain without interfering with uterine contractility and thus effectively shorten duration of labour and still not causing any ill effect to the mother and fetus is an ideal drug.<sup>4-5</sup>

A labour which is unduly prolonged is likely to give rise to one or more of 3 types of distress namely maternal, fetal or obstetrician. Of the three the last may be most dangerous! Ian Donald.<sup>2-3</sup> Prolonged & painful labour presents a picture of mental anguish & physical morbidity. It constitute danger to the survival & subsequent neurological development of infant. Prolonged labour can lead to increased maternal and neonatal mortality and morbidity due to increased risks of maternal exhaustion, postpartum haemorrhage and sepsis,

fetal distress and asphyxia and requires early detection and appropriate clinical response. The causes of prolonged labour relate to maternal age, induction of labour, premature rupture of membranes, early admission to the labour ward, epidural analgesia and high levels of maternal stress hormones, but are unknown in most cases <sup>1</sup>. The risks for complications of prolonged labour are much greater in poor resource settings.

In 1964, Bishop systematically evaluated a group of multiparous women for elective induction and developed a standardized cervical scoring system. The Bishop score helps delineate patients who would be most likely to achieve a successful induction. The duration of labor is inversely correlated with the Bishop score; a score that exceeds 8 describes the patient most likely to achieve a successful vaginal birth. Bishop scores of less than 6 usually require that a cervical ripening method be used before other methods.<sup>2-4</sup>

In addition, a recent review to determine the —slowest-yet-normal|| dilatation rate amongst primigravid women, determined that this dilatation rate approximates 0.5 cm/hour and that expectations of a faster dilatation rate (1 cm/hour) can lead to unnecessary interventions aiming to accelerate labour.

The concept of —active management of labour|| was developed to assure a woman that her labour would not exceed 12 hours. Anything beyond that constituted prolonged labour. This package of care includes accurate and early diagnosis of the first stage of labour, early artificial rupture of membranes, ongoing support of the woman in labour by a professional caregiver and augmentation of labour with oxytocin. Active management of labour versus physiological,

expectant management, has shown to decrease the occurrence of prolonged labour (more than 12 hours). Active management significantly shortened the duration of labour significantly. It also showed a small reduction in the rate of caesarean sections. There was no significant difference in maternal and neonatal morbidity. Early intervention with amniotomy and oxytocin augmentation, as a preventative strategy with mild delays in progress, leads to a reduction of in the duration of labour.

For the mother it provides relief from pain, controls alteration in circulation, ventilation and undue muscular efforts. For the fetus, shorter and less traumatic labor, protection against hypoxia, fetal depression at birth, protection against needless instrumental delivery. To the obstetrician, it provides a better control over events emerging during the course of labor and ensures optimum conditions to prevail at the time of child birth

Various tranquilizers, analgesics and sedatives used to relieve labour pains can lead to fetus. Other commonly used drugs in labour like oxytocin and prostaglandins, although reduce duration of labour, they do not reduce the suffering caused by labour pains.

Pharmacologic agents available for cervical ripening and labor induction include prostaglandins, misoprostol, mifepristone, and relaxin. When the Bishop score is favorable, the preferred pharmacologic agent is oxytocin.

#### **4. PHARMACOLOGIC CERVICAL RIPENING OR LABOR INDUCTION**

##### **4.1 Prostaglandins**

Prostaglandins act on the cervix to enable ripening by a number of different mechanisms. They alter the extracellular ground substance of the cervix, and PGE2 increases the activity of collagenase in the cervix. They cause an increase in elastase, glycosaminoglycan, dermatan sulfate, and hyaluronic acid levels in the cervix. A relaxation of cervical smooth muscle facilitates dilation. Finally, prostaglandins allow for an increase in intracellular calcium levels, causing contraction of myometrial muscle. Risks associated with the use of prostaglandins include uterine hyperstimulation and maternal side effects such as nausea, vomiting, diarrhea, and fever. Currently,

two prostaglandin analogs are available for the purpose of cervical ripening, dinoprostone gel (Prepidil) and dinoprostone inserts (Cervidil). Prepidil contains 0.5 mg of dinoprostone gel, while Cervidil contains 10 mg of dinoprostone in pessary form.<sup>5</sup>

**4.2 Method of Application** -Bring gel to room temperature before application, per manufacturer's instructions. Introduce the gel into the cervix as follows:

If the cervix is uneffaced, use the 20-mm endocervical catheter to introduce the gel into the endocervix just below the level of the internal os.

If the cervix is 50 percent effaced, use the 10-mm endocervical catheter. After application of the gel, the patient should remain recumbent for 30 minutes before being allowed to ambulate. May repeat every six hours, up to three doses in 24 hours.

##### **4.3 Misoprostol**

Misoprostol (Cytotec) is a synthetic PGE1 analog that has been found to be a safe and inexpensive agent for cervical ripening, although it is not labeled by the U.S. Food and Drug Administration for that purpose.<sup>6-7</sup>

Clinical trials indicate that the optimal dose and dosing interval is 25 mcg intravaginally every four to six hours. Higher doses or shorter dosing intervals are associated with a higher incidence of side effects, especially hyper-stimulation syndrome, defined as contractions lasting longer than 90 seconds or more than five contractions in 10 minutes. Risks also include tachysystole, defined as six or more uterine contractions in 10 minutes for two consecutive 10-minute periods, and hypersystole, a single contraction of at least two minutes' duration.

Finally, uterine rupture in women with previous cesarean section is also a possible complication, limiting its use to women who do not have a uterine scar.

**Technique for Intravaginal Application of Misoprostol (Cytotec) Tablets**

Place one fourth of a tablet of misoprostol intravaginally, without the use of any gel (gel may prevent the tablet from dissolving).

##### **4.4 Mifepristone**

Mifepristone (Mifeprex) is an antiprogesterone agent. Progesterone inhibits contractions of the uterus, while mifepristone counteracts this action.

Currently, seven trials are underway involving 594 women using mifepristone for cervical ripening. Results have shown that women treated with mifepristone are more likely to have a favorable cervix within 48 to 96 hours when compared with placebo. In addition, these women were more likely to deliver within 48 to 96 hours and less likely to undergo cesarean section. However, little information is available about fetal outcomes and maternal side effects; thus, there is insufficient information to support the use of mifepristone for cervical ripening.<sup>8</sup>

#### 4.5 Relaxin

The hormone relaxin is thought to promote cervical ripening.

#### 4.6 Oxytocin

As pregnancy progresses, the number of oxytocin receptors in the uterus increases (by 100-fold at 32 weeks and by 300-fold at the onset of labor). Oxytocin activates the phospholipase C-inositol pathway and increases intracellular calcium levels, stimulating contractions in myometrial smooth muscle. Oxytocin is the preferred pharmacologic agent for inducing labor when the cervix is favorable or ripe. Numerous randomized, placebo-controlled studies have focused on the use of oxytocin in labor induction. It has been found that low-dose (physiologic) and high-dose (pharmacologic) oxytocin regimens are equally effective in establishing adequate labor patterns.<sup>9</sup> The widespread use of antispasmodics help to ensure steady progress of labor reduces the risk of dysfunctional labor and enables early identification of emerging obstetric problems.<sup>10</sup>

#### 4.7 Tramadol Hydrochloride

Tramadol hydrochloride is centrally acting analgesic which has got both opioid and non-opioid mechanism of action. It also causes cervical dilatation. It also causes cervical dilatation. It activates only 30% of opioid receptors ( $\kappa$  and  $\mu$ ). It inhibits noradrenergic uptake and stimulates serotonin release. These are no adverse effect on GIT, respiratory, cardiovascular and central nervous system. Drotin is musclotropic drug acting directly on smooth muscle cells. It has no central action. It produces smooth muscles cell relaxation.<sup>10</sup>

Tramadol hydrochloride is a novel analgesic agent with a dual mechanism of action and is indicated for the management of moderate to moderately

severe pain in adults Tramadol is a non-selective  $\mu$ -opioid receptor agonist that also potentiates the activity of serotonin and norepinephrine, primarily by inhibition of reuptake. In combination with acetaminophen, tramadol is effective in the treatment of moderate to severe postoperative pain with fewer adverse events than traditional opioids. Tramadol is subject to an analgesic ceiling effect. Tramadol is available in both short- and long-acting formulations (to be discussed later). Adverse events commonly associated with tramadol are similar to those seen with other opioid receptor agonists (e.g. constipation, nausea, somnolence and pruritus). Tramadol appears to produce less constipation and dependence than equianalgesic doses of strong opioids. It has been suggested for use in obstetrics because of its rapid and profound analgesia. It does not arrest labor and has wide margin of safety.<sup>11-12</sup>

Intramuscular tramadol 100mg, but not 50mg, provided pain relief equivalent to that with pethidine 75mg. With pethidine, adverse effects were more frequent and respiratory function of the neonates was significantly lower. Tramadol is having less cardiovascular and respiratory depressant. Therefore, the present study has been undertaken to assess the safety and efficacy of tramadol hydrochloride intra muscular (I.M) injections as analgesia for labor.<sup>13-14</sup>

Tramadol has been found to be an effective analgesia in labor without having a deleterious effect on the mother and the fetus. The incorporation of partogram into the protocol helped to eliminate the ill effects of prolonged labors, prompted earlier recognition of dystocia and implementation of measures at the same time. Drug Assisted Labour leads to shorter labors; analgesia is quite effective and side effects of drugs are minimal and safe for the fetus as well; labor is cherished with pleasure and childbirth becomes a joyous event for the mother.

#### 4.8 Drotin ( Drotaverine Hydrochloride)

Drotaverine (INN, also known as drotaverin) is an antispasmodic drug, used to enhance cervical dilation during childbirth.

It is structurally related to papaverine, is a selective inhibitor of phosphodiesterase 4, and has no anticholinergic effects. It is available in Asian and Eastern European countries under several brand names,

Drotaverine is an isoquinoline derivative which binds to the surface of smooth muscles and changes their membrane potential and permeability. It inhibits phosphodiesterase IV enzyme which breaks cAMP and cGMP which

play an important role in regulation of smooth muscle tone. It acts specifically on spastic sites and corrects the cAMP and calcium imbalance relieving smooth muscle spasm.15-16

## 5. REFERENCES

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## 6. CONCLUSIONS

Prolonged Labor,causes a couple of risks-low oxygen levels for the baby,abnormal heart rhythm in the baby ,abnormal substances in the amniotic fluid ,uterine infection 17.Prolonged labor increases the chances of C-section.Labor that takes too long can be dangerous to the baby. It may cause:fetal distress .

The aim of this review was to throw light on drugs used to ease labor stress in virtue of prolong labor.Judicious selection of antispasmodics and cervical dilators significantly reduces maternal and fetal morbidity and mortality.