

DISSERTATION FOR FCPS (OBSTETRICS AND GYNECOLOGY) DROTAVERINE FOR ACCELERATION OF LABOUR IN TERMS OF CERVICAL DILATATION

Dr. Rubeena Aslam*

**Department of Obstetrics and Gynecology, DHQ Teaching hospital, Gujranwala*

**Corresponding Author:*

Part I

SUPERVISOR CERTIFICATE

It is hereby certified that this thesis is based on the results of research carried out by Dr. Rubeena Aslam. It has not previously been presented for FCPS(Obstetrics and Gynecology) degree. Dr.Rubeena Aslam has done this research work under my supervision. She has fulfilled all the requirements and is qualified to submit the accompanying thesis for the degree of FCPS in Obstetrics and Gynecology.

Name of Supervisor

DR.TAHIRA AKHTAR

Associate Professor, Department of Obstetrics and Gynecology, DHQ Teaching hospital, Gujranwala

DEDICATED

TO

MY

FATHER & MOTHER

ACKNOWLEDGEMENTS

It is only by the blessings of Almighty Allah, that I was able to complete this tedious task of thesis writing.

I wish to express my sincerest regards to my supervisor ,Dr Tahira Akhtar,associate professor(Obstetrics and Gynecology),DHQ Teaching hospital Gujranawala . Her interest in teaching, experience in the field of research, depth of technical guidance and most of all, his moral support have been an invaluable asset to me.

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LIST OF ABBREVIATIONS

Abbreviations	Complete term
BMI	Body Mass Index
NO	Nitric Oxide
NOS	Nitric Oxide Synthase
SD	Standard Deviation
SPSS	Statistical Package for Social Sciences

Part II

ABSTRACT:

Background: Acceleration of labour is process of stimulating the uterus to increase the frequency, duration and intensity of contractions after the onset of spontaneous labour. Drotaverine is an effective medicine to treat spasm or twitches of the smooth muscles in the stomach and heart.

Objective: To compare the outcome for acceleration of labour in terms of mean duration of 1st stage in laboring patients receiving drotaverine versus control group.

Material & Methods

Study Design: It was randomized control trial

Setting: Department of Obstetrics and Gynecology GMC Teaching hospital Gujranwala

Duration: 6 months after the approval of synopsis i.e. from (.....) to (.....)

Data collection: The patients were divided into two groups. The results were noted in terms of duration of first stage of labour in two groups. All the collected data was entered and analyzed on SPSS version 11.

Results: The mean age of the patients was 27.47±6.66 years. Among of 248 respondents the mean duration of active stage labour in group A was respondents was 2.08±0.82 hours and in group B was 3.10±0.86 hours. Statistically significant difference found between study groups i.e. p-value=0.001.

Conclusion: Drotaverine appear to significantly helpful for acceleration of labour by reducing duration of 1st stage in laboring patients

Keywords: Drotaverine, Control, Duration, Stage, Labour

INTRODUCTION:

Acceleration of labour is process of stimulating the uterus to increase the frequency, duration and intensity of contractions after the onset of spontaneous labour.¹ Prolongation of labour is one such dilemma that every obstetrician tries to avoid because it is likely to increase the work burden, especially in busy labour wards, with consequence inadequacy of obstetric care.²

Labour is a natural physiological process characterized by progressive increase in frequency, intensity and duration of uterine contractions involving leading to cervical ripening, dilatation and finally expulsion of fetus and placenta.³ type 4 phosphodiesterase enzyme is present in increased concentration in IIIrd trimester which contribution in regulation of uterine contractility.²

Drotavrine is structurally related to papaverine is a selective inhibitor of phosphodiesterase and no anticholinergic effects.⁴ it reduces the smooth muscle spasm by maintaining the cAMP level and calcium level on specification sites of cervix, thus facilitates the cervical dilatation.⁴ A recent Cochrane review found low quality evidence that antispasmodic drugs reduces the duration of first stage of labour and increase the cervical dilatation.¹

Drotavrine reduces the duration of labour and prevents prolonged labour⁵ as recommended by the World health organization maternal health and safe motherhood programme 1994, that if the rate of cervical dilatation is less than 1cm/hr then a women should be transferred to high level of care,⁶ and the first stage of labour should not exceed to 12hrs, otherwise quoted prolonged labour,⁶ as prolonged labour is associated with increase burden and poor outcome.² A randomized study conducted in 2014 concluded the results that the mean duration of first stage of labour in primigravida control group was 5 hours 48 minutes+1hour 23 minutes and in multigravida control group was 4hours and 43 minutes+1hour 7minutes while in tramadol group was 4 hours+1hour 28 minutes and 3hour 19minutes +1 hour 5 minutes respectively.⁶

Another randomized study conducted in an Academic tertiary care hospital concluded the results that laboring women who received roloverine had faster cervical dilatation than those assigned to placebo (2.43+1.84 vs 1.85+1.39 cm/hour, p=0.03).²

The rational of my study is to re-evaluate the safety and efficacy of using the antispasmodic, drotavrine to reduce the duration of the active stage of labour among nulliparous and multiparous women being managed by a standard intrapartum protocols in our population. Although literature is available as studies conducted in other population but there is no local study available on this topic in Pakistan. As there are genetic differences from one population to other, the effect of the drug may also vary accordingly and the study results may not be consistent with already existent literature as my hypothesis is that these is increased rate of cervical dilatation in laboring patients (both primigravida and multigravida) with the use of drotavrine so if I find the drotavrine to have a significant effect on acceleration of labour, it will help to decrease the risk of prolonged labour, maternal morbidity, caesarean sections rate, increase of placenta previa and morbidly adherent placenta and will increase the rate of normal vaginal births.

LITERATURE REVIEW:

Pregnancy

Pregnancy, also known as gravidity or gestation, is the time during which one or more offspring develops inside a woman.⁷ A multiple pregnancy involves more than one offspring, such as with twins.⁸ Pregnancy can occur by sexual intercourse or assisted reproductive technology. It usually lasts around 40 weeks from the last menstrual period and ends in childbirth.^{7,9} This is just over nine lunar months, where each month is about 29½ days.^{7,9} When measured from conception it is about 38 weeks. An embryo is the developing offspring during the first eight weeks following conception, after which, the term fetus is used until birth.⁹ Symptoms of early pregnancy may include missed periods, tender breasts, nausea and vomiting, hunger, and frequent urination.¹⁰ Pregnancy may be confirmed with a pregnancy test.¹¹

Pregnancy is typically divided into three trimesters. The first trimester is from week one through 12 and includes conception. Conception is when the sperm fertilizes the egg. The fertilized egg then travels down the fallopian tube and attaches to the inside of the uterus, where it begins to form the fetus and placenta.⁷ The first trimester carries the highest risk of miscarriage (natural death of embryo or fetus).¹² The second trimester is from week 13 through 28. Around the middle of the second trimester, movement of the fetus may be felt. At 28 weeks, more than 90% of babies can survive outside of the uterus if provided high-quality medical care. The third trimester is from 29 weeks through 40 weeks.¹²

Prenatal care improves pregnancy outcomes. Prenatal care may include taking extra folic acid, avoiding drugs and alcohol, regular exercise, blood tests, and regular physical examinations.¹² Complications of pregnancy may include high blood pressure of pregnancy, gestational diabetes, iron-deficiency anemia, and severe nausea and vomiting among others.¹² Term pregnancy is 37 to 41 weeks, with early term being 37 and 38 weeks, full term 39 and 40 weeks, and late term 41 weeks. After 41 weeks, it is known as post term. Babies born before 37 weeks are preterm and are at higher risk of health problems such as cerebral palsy. Delivery before 39 weeks by labor induction or caesarean section is not recommended unless required for other medical reasons.¹³

About 213 million pregnancies occurred in 2012, of which, 190 million were in the developing world and 23 million were in the developed world. The number of pregnancies in women ages 15 to 44 is 133 per 1,000 women. About 10% to 15% of recognized pregnancies end in miscarriage.¹⁴ In 2013, complications of pregnancy resulted in 293,000 deaths, down from 377,000 deaths in 1990. Common causes include maternal bleeding, complications of abortion, high blood

pressure of pregnancy, maternal sepsis, and obstructed labor.¹⁵ Globally, 40% of pregnancies are unplanned. Half of unplanned pregnancies are aborted. Among unintended pregnancies in the United States, 60% of the women used birth control to some extent during the month pregnancy occurred.¹⁵



Fig i: A pregnant woman¹²

Historical development

Otto Rank (1884–1939), one of Sigmund Freud's disciples, wrote that the emotional shock of being born is an individual's first source of anxiety. He believed that a "primal fixation" with the prenatal state is the root of all neuroses and character disorders¹⁶ and developed a process of psychoanalysis based on birth experiences.^{17, 18} Nandor Fodor (1895–1964), one of Rank's patients, was the first to specifically emphasize the significance of prenatal experiences even earlier than childbirth in *The Search for the Beloved: A Clinical Investigation of the Trauma of Birth and Prenatal Condition*,¹⁹ published in 1949.²⁰

Material emerging from sessions of psychedelic psychotherapy using LSD and other hallucinogenic drugs was the foundation for research into the enduring effects of pre- and perinatal experiences in adult life conducted by Frank Lake, Athanasios Kafkalides (1919-1989) and Stanislav Grof. Grof went on to formulate an extensive theoretical framework for the analysis of pre- and perinatal experiences, based on the four constructs he called Basic Perinatal Matrices. Lake and Grof independently developed breathing techniques, following Wilhelm Reich (1897-1957) as an alternative to the use of psychedelic drugs, which was subject to considerable legal difficulty from the mid-1960s onwards. A related technique called Rebirthing was developed by Leonard Orr (born 1937); and Core process psychotherapy trainees relive presumed birth trauma as part of their training.²¹

Public attention was drawn to the importance of prenatal experiences by the 1981 book, *The Secret Life of the Unborn Child*, by Thomas R. Verny (born 1936), who founded the Association for Pre- & Perinatal Psychology and Health. David Barnes Chamberlain (1928-2014), who was president of the Association for Pre- & Perinatal Psychology and Health from 1991 to 1999, published a popular book entitled, *Babies Remember Birth* (1988), outlining new experimental research that supports the existence of pre-natal memories. Further evidence was presented by Ludwig Janus (born 1939) in *The Enduring Effects of Prenatal Experience* (1997).²¹

Perhaps the first book to effectively convey the importance of trauma-free childbirth to the wider public was *Birth Without Violence* (1975), by French obstetrician Dr. Frederick Leboyer (born 1918),²² which helped popularize the practice of placing newly-born infants in a tub of warm water, known as a "Leboyer bath" to simulate the familiar pre-natal environment of warm amniotic fluid. Following on from Leboyer, another French obstetrician, Michel Odent (born 1930), pioneered the practice of low intervention labour and took the "Leboyer bath" one step further, developing the use of warm-water pools for a water birth.²²

In 2004, Wendy Anne McCarty,^{23, 24} co-founder of the Prenatal and Perinatal Psychology MA and PhD Programs at Santa Barbara Graduate Institute, reviewed the 30 years of clinical research in prenatal and perinatal psychology and current mainstream early development models. In her book *Welcoming Consciousness*, she introduced the Integrated Model of early development that was reflective of the prenatal and perinatal psychology clinical findings. The transcendental and human aspects of awareness documented from the beginning of life became the core thread in this holonomic holographic model.^{23, 24}

Epidemiology of pregnancy

About 213 million pregnancies occurred in 2012 of which 190 million were in the developing world and 23 million were in the developed world. This is about 133 pregnancies per 1,000 women between the ages of 15 and 44.¹⁴ About

10% to 15% of recognized pregnancies end in miscarriage. Globally 40% of pregnancies are unplanned. Half of unplanned pregnancies are aborted.¹⁴

Of pregnancies in 2012 120 million occurred in Asia, 54 million in Africa, 19 million in Europe, 18 million in Latin America and the Caribbean, 7 million in North America, and 1 million in Oceania. Pregnancy rates are 140 per 1000 women of childbearing age in the developing world and 94 per 1000 in the developed world.¹⁴

The rate of pregnancy, as well as the ages at which it occurs, differ by country and region. It is influenced by a number of factors, such as cultural, social and religious norms; access to contraception; and rates of education. The total fertility rate in 2013 was estimated to be highest in Niger (7.03 children/woman) and lowest in Singapore (0.79 children/woman).²⁵

In Europe, the average childbearing age has been rising continuously for some time. In Western, Northern, and Southern Europe, first-time mothers are on average 26 to 29 years old, up from 23 to 25 years at the start of the 1970s. In a number of European countries (Spain), the mean age of women at first childbirth has crossed the 30-year threshold.²⁵

This process is not restricted to Europe. Asia, Japan and the United States are all seeing average age at first birth on the rise, and increasingly the process is spreading to countries in the developing world like China, Turkey and Iran. In the US, the age of first childbirth was 25.4 in 2010.²⁶

In the United States and United Kingdom, 40% of pregnancies are unplanned, and between a quarter and half of those unplanned pregnancies were unwanted pregnancies.²⁷

Globally, an estimated 270,000 women die from pregnancy-related complications each year.²⁸

Timing of childbirth

In the ideal childbirth labor begins on its own when a woman is "at term". Pregnancy is considered at term when gestation has lasted between 37 and 42 weeks²⁹.

Events before completion of 37 weeks are considered preterm. Preterm birth is associated with a range of complications and should be avoided if possible²⁹.

Sometimes if a woman's water breaks or she has contractions before 39 weeks, birth is unavoidable. However, spontaneous birth after 37 weeks is considered term and is not associated with the same risks of a pre-term birth. Planned birth before 39 weeks by Caesarean section or labor induction, although "at term", results in an increased risk of complications. This is from factors including underdeveloped lungs of newborns, infection due to underdeveloped immune system, feeding problems due to underdeveloped brain, and jaundice from underdeveloped liver²⁹.

Babies born between 39 and 41 weeks gestation have better outcomes than babies born either before or after this range. This special time period is called "full term". Whenever possible, waiting for labor to begin on its own in this time period is best for the health of the mother and baby. The decision to perform an induction must be made after weighing the risks and benefits, but is safer after 39 weeks²⁹.

Events after 42 weeks are considered postterm. When a pregnancy exceeds 42 weeks, the risk of complications for both the woman and the fetus increases significantly. Therefore, in an otherwise uncomplicated pregnancy, obstetricians usually prefer to induce labour at some stage between 41 and 42 weeks²⁹.

Childbirth

Childbirth, also known as labour and delivery, is the ending of a pregnancy by one or more babies leaving a woman's uterus.³⁰ In 2015 there were about 135 million births globally. About 15 million were born before 37 weeks of gestation, while between 3 and 12% were born after 42 weeks. In the developed world most deliveries occur in hospital, while in the developing world most births take place at home with the support of a traditional birth attendant.³¹⁻³⁴

The most common way of childbirth is a vaginal delivery.³⁵ It involves three stages of labour: the shortening and opening of the cervix, descent and birth of the baby, and the pushing out of the placenta. The first stage typically lasts twelve to nineteen hours, the second stage twenty minutes to two hours, and the third stage five to thirty minutes. The first stage begins with crampy abdominal or back pains that last around half a minute and occur every ten to thirty minutes. The crampy pains become stronger and closer together over time. During the second stage pushing with contractions may occur. In the third stage delayed clamping of the umbilical cord is generally recommended. A number of methods can help with pain such as relaxation techniques, opioids, and spinal blocks.³⁶

Most babies are born head first; however about 4% are born feet or buttock first, known as breech. During labour a woman can generally eat and move around as she likes, pushing is not recommended during the first stage or during delivery of the head, and enemas are not recommended. While making a cut to the opening of the vagina, known as an episiotomy, is common it is generally not needed. In 2012, about 23 million deliveries occurred by a surgical procedure known as Caesarean section. Caesarean sections may be recommended for twins, signs of distress in the baby, or breech position. This method of delivery can take longer to heal from.^{37, 38}

Each year complications from pregnancy and childbirth result in about 500,000 maternal deaths, 7 million women have serious long term problems, and 50 million women have health negative outcomes following delivery. Most of these occur in the developing world. Specific complications include obstructed labour, postpartum bleeding, eclampsia, and postpartum infection. Complications in the baby include birth asphyxia.³⁹

Signs and symptoms of childbirth

The most prominent sign of labour is strong repetitive uterine contractions. The distress levels reported by labouring women vary widely. They appear to be influenced by fear and anxiety levels, experience with prior childbirth, cultural ideas of childbirth and pain,⁴⁰ mobility during labour, and the support received during labour. Personal expectations, the amount of support from caregivers, quality of the caregiver-patient relationship, and involvement in decision-making are more important in women's overall satisfaction with the experience of childbirth than are other factors such as age, socioeconomic status, ethnicity, preparation, physical environment, pain, immobility, or medical interventions.⁴¹

Descriptions

Pain in contractions has been described as feeling similar to very strong menstrual cramps. Women are often encouraged to refrain from screaming, but moaning and grunting may be encouraged to help lessen pain. Crowning may be experienced as an intense stretching and burning. Even women who show little reaction to labour pains, in comparison to other women, show a substantially severe reaction to crowning³¹. Back labour is a term for specific pain occurring in the lower back, just above the tailbone, during childbirth³¹.

Psychological

Childbirth can be an intense event and strong emotions, both positive and negative, can be brought to the surface. Abnormal and persistent fear of childbirth is known as tokophobia³¹. During the later stages of gestation there is an increase in abundance of oxytocin, a hormone that is known to evoke feelings of contentment, reductions in anxiety, and feelings of calmness and security around the mate⁴². Oxytocin is further released during labour when the fetus stimulates the cervix and vagina, and it is believed that it plays a major role in the bonding of a mother to her infant and in the establishment of maternal behavior. The act of nursing a child also causes a release of oxytocin.

Between 70% and 80% of mothers in the United States report some feelings of sadness or "baby blues" after giving birth. The symptoms normally occur for a few minutes up to few hours each day and they should lessen and disappear within two weeks after delivery. Postpartum depression may develop in some women; about 10% of mothers in the United States are diagnosed with this condition^{35, 36}. Preventive group therapy has proven effective as a prophylactic treatment for postpartum depression.^{43, 44}

Cervical dilation

Cervical dilation (or cervical dilatation) is the opening of the cervix, the entrance to the uterus, during childbirth, miscarriage, induced abortion, or gynecological surgery. Cervical dilation may occur naturally, or may be induced by surgical or medical means.⁴⁵

Induced dilation in childbirth

Prostaglandins contribute to cervical ripening and dilation. The body produces these hormones naturally. Sometimes prostaglandins in synthesized forms are applied directly to the cervix to induce labor. In women who have had a previous cesarean section, the American College of Obstetricians and Gynecologists issued a bulletin that misoprostol never be used for this purpose. American College of Obstetricians and Gynecologists's findings conclude that the collagen softening properties of misoprostol could be absorbed through the cervix and vaginal vault up into the low transverse scar of a typical cesarean section, and significantly increase the risk of uterine rupture. Prostaglandins are also present in human semen, and sexual intercourse is commonly recommended for promoting the onset of labor, although the limited data available makes the effectiveness of this method uncertain.⁴⁵

Other means of natural cervical ripening include nipple stimulation, which produces oxytocin, an organic hormone which is necessary for uterine contractions. Nipple stimulation can be performed manually, by use of a breast pump, or by suckling. Henci Goer, in her comprehensive book, *The Thinking Woman's Guide to a Better Birth*, details how this practice was researched in two separate studies of 100 and 200 women in the mid nineteen-eighties. Women were assigned randomly to two groups. In one group, nipples were stimulated for one-hour sessions, three times per day. In the other group, women were to avoid any form of nipple stimulation or sexual intercourse. The researchers concluded in both studies that nipple stimulation could indeed ripen the cervix and in some cases induce uterine contractions. Goer further notes that in the smaller study, an external fetal monitor was used, and no uterine hyperstimulation was noted.⁴⁵

Cervical dilation may be induced mechanically by placing devices inside the cervix that will expand while in place. A balloon catheter may be used. Other products include laminaria (made of dried seaweed) or synthetic hygroscopic materials, which expand when placed in a moist environment.⁴⁵

Uterine Characteristics

The human uterus is composed of 2 basic parts, the fundus and the cervix. The fundus is composed of 2 layers: the myometrium and endometrium. The myometrium, which is predominantly smooth muscle cells, comprises the wall of the uterus and is the thickest layer. The endometrium, which lines the endometrial cavity, undergoes dramatic changes during the menstrual cycle.⁴⁶

In the absence of pregnancy, it sheds down to the basal layer at the end of the cycle during menses. The normal pregnant cervix is 3.5 cm or longer and is composed predominantly of connective tissue, mainly collagen. In contrast to the fundus, it has only 10-15% smooth muscle. It changes little during the menstrual cycle and pregnancy until the onset of cervical ripening.⁴⁶

The human cervix consists mainly of extracellular connective tissue. The predominant molecules of this extracellular matrix are type 1 and type 3 collagen, with a small amount of type 4 collagen at the basement membrane. Intercalated among the collagen molecules are glycosaminoglycans and proteoglycans, predominantly dermatan sulfate, hyaluronic acid, and heparin sulfate.⁴⁶

Fibronectin and elastin also run among the collagen fibers. The highest ratio of elastin to collagen is at the internal os. Both elastin and smooth muscle decrease from the internal to the external os of the cervix.⁴⁶

Ripening of the Cervix

Cervical ripening refers to the softening of the cervix that typically begins prior to the onset of labor contractions and is necessary for cervical dilation and the passage of the fetus. Cervical ripening results from a series of complex biochemical processes that ends with rearrangement and realignment of the collagen molecules. The cervix thins, softens, relaxes and dilates in response to uterine contractions, allowing the cervix to easily pass over the presenting fetal part during labor.⁴⁶

In late pregnancy, hyaluronic acid content increases in the cervix. This leads to an increase in water molecules that intercalate among the collagen fibers. The amount of dermatan sulfate decreases, leading to reduced bridging among the collagen fibers and a corresponding decrease in cervical firmness. Chondroitin sulfate also decreases.⁴⁶

Cervical ripening is associated with decreased collagen fiber alignment, decreased collagen fiber strength and diminished tensile strength of the extracellular cervical matrix. An associated change with the cervical ripening process is an increase in cervical decorin (dermatan sulfate proteoglycan 2), leading to collagen fiber separation. Together, these changes lead to softening of the cervix (ie, ripening).⁴⁶

With uterine contractions, the ripened cervix dilates as the presenting fetal part descends, leading to reorientation of the tissue fibers in the cervix in the direction of the stress. Under the effect of myometrial contractions, the cervix passively dilates and is pulled over the presenting fetal part. Evidence also indicates that the elastin component of the cervix behaves in a ratchetlike manner so that dilation is maintained following the contraction.⁴⁶

In summary, cervical ripening is the result of realignment of collagen, degradation of collagen cross-linking due to proteolytic enzymes. Cervical dilation results from these processes plus uterine contractions. This is a complicated series of events in which many changes occur both simultaneously and sequentially. Research in this area is challenging due to both the difficulties inherent in human subjects research and the many differences existing between species.⁴⁶

Role of Various Hormones in the Process of Cervical Ripening

A complex series of interactions occurs whereby various hormones stimulate the chemical reactions critical for cervical ripening. Associated with cervical ripening is an increase in the enzyme cyclooxygenase-2, leading to a local increase of prostaglandin E2 in the cervix. The increase in local Prostaglandins E2 leads to a series of important changes associated with cervical ripening, including the following:

Dilation of small vessels in the cervix

Increase in collagen degradation

Increase in hyaluronic acid

Increase in chemotaxis for leukocytes, which causes increased collagen⁴⁶ degradation

Increase in stimulation of interleukin (IL)-8 release

Prostaglandin F2-alpha is also involved in the process via its ability to stimulate an increase in glycosaminoglycans.⁴⁶

Cervical ripening is associated with increased activity of matrix metalloproteinases 2 and 9, enzymes that degrade extracellular matrix proteins. Cervical collagenase (also called matrix metalloproteinase 1) and elastase also increase. Near term, collagen turnover increases and degradation of newly synthesized collagen increases, leading to decreased collagen content in the cervix.⁴⁶

In animal studies, sex steroids have been demonstrated to be involved in cervical ripening. In the rat cervix, increasing estrogen leads to increased collagenase activity, cervical cell apoptosis, and eosinophil infiltration. Animal models also exhibit a decrease in receptor-mediated progesterone activity, but whether this is involved in cervical ripening is unclear.⁴⁶

The role of inflammatory agents in cervical ripening has also been studied. IL-8 can lead to neutrophil chemotaxis, which is associated with collagenase activity and cervical ripening. These inflammatory agents may be particularly important as mediators of cervical ripening associated with preterm labor.⁴⁶

Recent study has focused on the nitric oxide synthase (NOS) / nitric oxide (NO) system. The NOS/NO system has been postulated to have a regulatory role in the myometrium and cervix during pregnancy and parturition. In rat studies, NO and increased NOS activity are associated with uterine quiescence. NOS activity is higher prior to labor and decreases during labor, thereby playing a role in the onset of uterine contractions associated with labor. In rat studies, NO levels and NOS activity behave in an opposite fashion in the cervix. Prior to cervical ripening, NOS activity is low and then increases at the time of labor, associated with cervical ripening. NOS activity leading to NO production is the final pathway in inducing chemical changes associated with cervical ripening. In the human cervix, ripening is associated with an increase in induced NOS and brain NOS expression in the cervix.⁴⁶

Resident and migrating inflammatory cells can cause the increase in induced NOS activity. Indeed, in the primate, cervical ripening has many aspects of an inflammatory process—tissue remodeling and breakage of chemical bridges between collagen fibers. Inflammatory agents such as IL-1, tumor necrosis factor-alpha, and IL-8 seem to be involved in cervical ripening.⁴⁶

NO also appears to play a role in this process because animal studies show that increased cervical NO leads to an increase in metalloproteinase activity, cellular apoptosis in the cervix, and glycosaminoglycan synthesis in the cervix. All of these changes are associated with the cervical ripening process.⁴⁶

NO also could play a role in premature cervical ripening associated with preterm labor, particularly in preterm labor triggered by infection. Inflammatory cells are rich in induced NOS activity, leading to a dramatic increase in NO in the cervix, which stimulates the chemical changes associated with cervical ripening and leads to preterm labor and delivery. Human and animal studies support a role for NO in the process of cervical ripening. NO donors, when applied to the cervix, induce cervical ripening.⁴⁶

To stop preterm labor successfully, both uterine contractions and cervical ripening must be halted. Speculating that this requires blockage of prostaglandin synthesis in the uterine fundus and cervix (and local NO synthesis in the cervix) is tempting. The role that inflammatory agents play in the cervical ripening process could explain the explosive nature of the cervical changes that occur in preterm labor, particularly when associated with uterine infections.⁴⁶

Vaginal birth

Humans are bipedal with an erect stance. The erect posture causes the weight of the abdominal contents to thrust on the pelvic floor, a complex structure which must not only support this weight but allow, in women, three channels to pass through it: the urethra, the vagina and the rectum. The infant's head and shoulders must go through a specific sequence of maneuvers in order to pass through the ring of the mother's pelvis.⁴⁷

Six phases of a typical vertex (head-first presentation) delivery:

- Engagement of the fetal head in the transverse position. The baby's head is facing across the pelvis at one or other of the mother's hips.
- Descent and flexion of the fetal head.
- Internal rotation. The fetal head rotates 90 degrees to the occipito-anterior position so that the baby's face is towards the mother's rectum.
- Delivery by extension. The fetal head passes out of the birth canal. Its head is tilted forwards so that the crown of its head leads the way through the vagina.
- Restitution. The fetal head turns through 45 degrees to restore its normal relationship with the shoulders, which are still at an angle.
- External rotation. The shoulders repeat the corkscrew movements of the head, which can be seen in the final movements of the fetal head.⁴⁷

Station refers to the relationship of the fetal presenting part to the level of the ischial spines. When the presenting part is at the ischial spines the station is 0 (synonymous with engagement). If the presenting fetal part is above the spines, the distance is measured and described as minus stations, which range from -1 to -4 cm. If the presenting part is below the ischial spines, the distance is stated as plus stations (+1 to +4 cm). At +3 and +4 the presenting part is at the perineum and can be seen.⁴⁸

The fetal head may temporarily change shape substantially (becoming more elongated) as it moves through the birth canal. This change in the shape of the fetal head is called molding and is much more prominent in women having their first vaginal delivery.⁴⁷

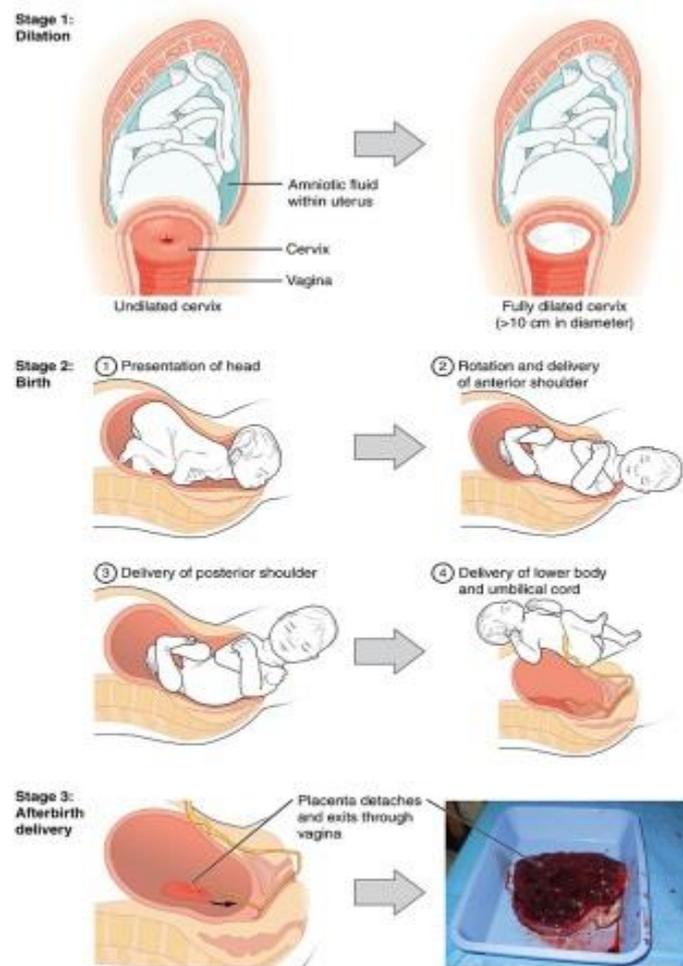


Fig ii: Sequence of images showing the stages of ordinary childbirth⁴⁷

Onset of labour

There are various definitions of the onset of labour, including:

Regular uterine contractions at least every six minutes with evidence of change in cervical dilation or cervical effacement between consecutive digital examinations.⁴⁹

Regular contractions occurring less than 10 min apart and progressive cervical dilation or cervical effacement.⁵⁰

At least 3 painful regular uterine contractions during a 10-minute period, each lasting more than 45 seconds.⁵¹

In order to avail for more uniform terminology, the first stage of labour is divided into "latent" and "active" phases, where the latent phase is sometimes included in the definition of labour, and sometimes not.^{52, 53}

Some reports note that the onset of term labour more commonly takes place in the late night and early morning hours. This may be a result of a synergism between the nocturnal increase in melatonin and oxytocin.⁵⁴

First stage: latent phase

The latent phase of labour is also called the quiescent phase, prodromal labour, or pre-labour. It is a subclassification of the first stage.⁴⁷

The latent phase is generally defined as beginning at the point at which the woman perceives regular uterine contractions. In contrast, Braxton Hicks contractions, which are contractions that may start around 26 weeks gestation and are sometimes called "false labour", should be infrequent, irregular, and involve only mild cramping. The signaling mechanisms responsible for uterine coordination are complex. Electrical propagation is the primary mechanism used for signaling up to several centimeters. Over longer distances, however, signaling may involve a mechanical mechanism.⁴⁷

Cervical effacement, which is the thinning and stretching of the cervix, and cervical dilation occur during the closing weeks of pregnancy and is usually complete or near complete, by the end of the latent phase. The degree of cervical effacement may be felt during a vaginal examination. A 'long' cervix implies that effacement has not yet occurred. Latent phase ends with the onset of active first stage, and this transition is defined retrospectively.⁴⁷

First stage: active phase

The active stage of labour (or "active phase of first stage" if the previous phase is termed "latent phase of first stage") has geographically differing definitions. In the US, the definition of active labour was changed from 3 to 4 cm, to 5 cm of cervical dilation for multiparous women, mothers who had given birth previously, and at 6 cm for nulliparous women, those who had not given birth before. This has been done in an effort to increase the rates of vaginal delivery.⁴⁷

A definition of active labour in a British journal was having contractions more frequent than every 5 minutes, in addition to either a cervical dilation of 3 cm or more or a cervical effacement of 80% or more.⁴⁷ In Sweden, the onset of the active phase of labour is defined as when two of the following criteria are met:⁴⁷

- three to four contractions every ten minutes
- rupture of membranes
- cervical dilation of 3 to 4 cm

Health care providers may assess a labouring mother's progress in labour by performing a cervical exam to evaluate the cervical dilation, effacement, and station. These factors form the Bishop score. The Bishop score can also be used as a means to predict the success of an induction of labour.⁴⁷ During effacement, the cervix becomes incorporated into the lower segment of the uterus. During a contraction, uterine muscles contract causing shortening of the upper segment and drawing upwards of the lower segment, in a gradual expulsive motion.[citation needed] The presenting fetal part then is permitted to descend. Full dilation is reached when the cervix has widened enough to allow passage of the baby's head, around 10 cm dilation for a term baby.⁴⁷

The duration of labour varies widely, but the active phase averages some 8 hours for women giving birth to their first child ("primiparae") and shorter for women who have already given birth ("multiparae"). Active phase prolongation is defined as in a primigravid woman as the failure of the cervix to dilate at a rate of 1.2 cm/h over a period of at least two hours. This definition is based on Friedman's Curve, which plots the typical rate of cervical dilation and fetal descent during active labour. Some practitioners may diagnose "Failure to Progress", and consequently, propose interventions to optimize chances for healthy outcome.⁴⁷

Second stage: fetal expulsion

The expulsion stage (stimulated by prostaglandins and oxytocin) begins when the cervix is fully dilated, and ends when the baby is born. As pressure on the cervix increases, women may have the sensation of pelvic pressure and an urge to begin pushing. At the beginning of the normal second stage, the head is fully engaged in the pelvis; the widest diameter of the head has passed below the level of the pelvic inlet. The fetal head then continues descent into the pelvis, below the pubic arch and out through the vaginal introitus (opening). This is assisted by the additional maternal efforts of "bearing down" or pushing. The appearance of the fetal head at the vaginal orifice is termed the "crowning". At this point, the woman will feel an intense burning or stinging sensation.⁴⁷

When the amniotic sac has not ruptured during labour or pushing, the infant can be born with the membranes intact. This is referred to as "delivery en caul".⁴⁷ Complete expulsion of the baby signals the successful completion of the second stage of labour.⁴⁷

The second stage of birth will vary by factors including parity (the number of children a woman has had), fetal size, anesthesia, and the presence of infection. Longer labours are associated with declining rates of spontaneous vaginal delivery and increasing rates of infection, perineal laceration, and obstetric hemorrhage, as well as the need for intensive care of the neonate.⁵⁵

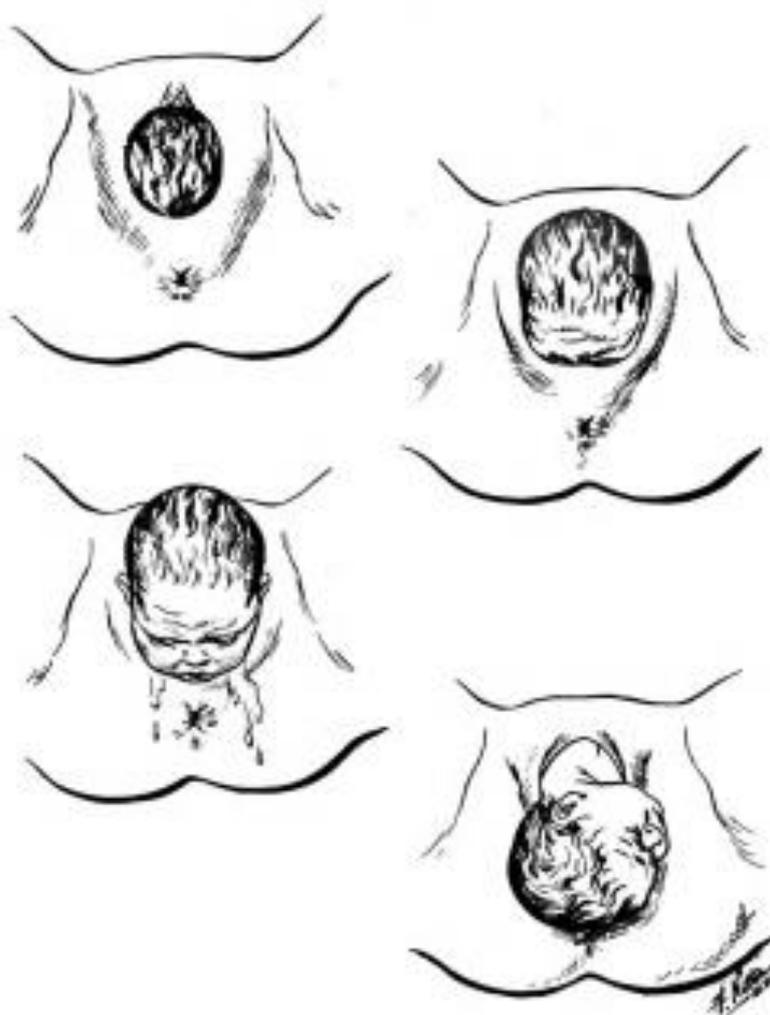


Fig iii: Stages in the birth of the baby's head⁴⁷

Third stage: placenta delivery

The period from just after the fetus is expelled until just after the placenta is expelled is called the third stage of labour or the involution stage. Placental expulsion begins as a physiological separation from the wall of the uterus. The average time from delivery of the baby until complete expulsion of the placenta is estimated to be 10–12 minutes dependent on whether active or expectant management is employed.[46] In as many as 3% of all vaginal deliveries, the duration of the third stage is longer than 30 minutes and raises concern for retained placenta.⁵⁶

Placental expulsion can be managed actively or it can be managed expectantly, allowing the placenta to be expelled without medical assistance. Active management is described as the administration of a uterotonic drug within one minute of fetal delivery, controlled traction of the umbilical cord and fundal massage after delivery of the placenta, followed by performance of uterine massage every 15 minutes for two hours. In a joint statement, World Health Organization, the International Federation of Gynaecology and Obstetrics and the International Confederation of Midwives recommend active management of the third stage of labour in all vaginal deliveries to help to prevent postpartum hemorrhage.^{57, 58}

Delaying the clamping of the umbilical cord until at least one minute after birth improves outcomes as long as there is the ability to treat jaundice if it occurs. In some birthing centers, this may be delayed by 5 minutes or more, or omitted entirely. Delayed clamping of the cord decreases the risk of anemia but may increase risk of jaundice. Clamping is followed by cutting of the cord, which is painless due to the absence of nerves.⁴⁷

Fourth stage

The "fourth stage of labour" is the period beginning immediately after the birth of a child and extending for about six weeks. The terms postpartum and postnatal are often used to describe this period. The woman's body, including hormone levels and uterus size, return to a non-pregnant state and the newborn adjusts to life outside the mother's body. The World Health Organization describes the postnatal period as the most critical and yet the most neglected phase in the lives of mothers and babies; most deaths occur during the postnatal period.^{59, 60}

Following the birth, if the mother had an episiotomy or a tearing of the perineum, it is stitched. The mother has regular assessments for uterine contraction and fundal height, vaginal bleeding, heart rate and blood pressure, and temperature, for the first 24 hours after birth. The first passing of urine should be documented within 6 hours. Afterpains (pains

similar to menstrual cramps), contractions of the uterus to prevent excessive blood flow, continue for several days. Vaginal discharge, termed "lochia", can be expected to continue for several weeks; initially bright red, it gradually becomes pink, changing to brown, and finally to yellow or white. Some women experience an uncontrolled episode of shivering or postpartum chills, after the birth.⁶⁰

Most authorities suggest the infant be placed in skin-to-skin contact with the mother for 1 –2 hours immediately after birth, putting routine cares off till later.⁴⁷

Until recently babies born in hospitals were removed from their mothers shortly after birth and brought to the mother only at feeding times. Mothers were told that their newborn would be safer in the nursery and that the separation would offer the mother more time to rest. As attitudes began to change, some hospitals offered a "rooming in" option wherein after a period of routine hospital procedures and observation, the infant could be allowed to share the mother's room. However, more recent information has begun to question the standard practice of removing the newborn immediately postpartum for routine postnatal procedures before being returned to the mother. Beginning around 2000, some authorities began to suggest that early skin-to-skin contact (placing the naked baby on the mother's chest) may benefit both mother and infant. Using animal studies that have shown that the intimate contact inherent in skin-to-skin contact promotes neurobehaviors that result in the fulfillment of basic biological needs as a model, recent studies have been done to assess what, if any, advantages may be associated with early skin-to-skin contact for human mothers and their babies.

A 2011 medical review looked at existing studies and found that early skin-to-skin contact, sometimes called kangaroo care, resulted in improved breastfeeding outcomes, cardio-respiratory stability, and a decrease in infant crying. A 2016 Cochrane review found that skin-to-skin contact at birth promotes the likelihood and effectiveness of breastfeeding. Evidence on physiological outcomes, such as crying or temperature was unclear.⁴⁷

As of 2014, early postpartum skin-to-skin contact is endorsed by all major organizations that are responsible for the well-being of infants, including the American Academy of Pediatrics. The World Health Organization states that "the process of childbirth is not finished until the baby has safely transferred from placental to mammary nutrition." They advise that the newborn be placed skin-to-skin with the mother, postponing any routine procedures for at least one to two hours.

The World health organization suggests that any initial observations of the infant can be done while the infant remains close to the mother, saying that even a brief separation before the baby has had its first feed can disturb the bonding process. They further advise frequent skin-to-skin contact as much as possible during the first days after delivery, especially if it was interrupted for some reason after the delivery. The National Institute for Health and Care Excellence also advises postponing procedures such as weighing, measuring, and bathing for at least 1 hour to insure an initial period of skin-to-skin contact between mother and infant.⁴⁷



Fig iv: A 30 minute old infant receiving routine care⁴⁷

Drotaverine

Drotaverine is an effective medicine to treat spasm or twitches of the smooth muscles in the stomach and heart. It is used to relieve pain caused due to irritable bowel syndrome, headache, menstrual periods, and is also used to relieve cervical spasm during labor.

It is structurally related to papaverine, is a selective inhibitor of phosphodiesterase 4, and has no anticholinergic effects.⁶¹

It is available in Asian and Eastern European countries under several brand names.⁶¹

An article from 2013 described the effects from overdose (in a 19-year-old woman) as including vomiting, seizures and fatal cardiac toxicity.

In 2016, the young Russian chess player Ivan Bukavshin died of a massive overdose (or poisoning) of the drug, which was originally thought to be a stroke.⁶¹

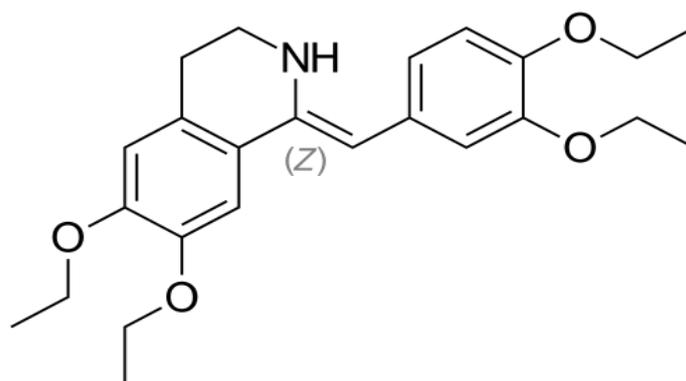


Fig v: Drotaverine⁶¹

Efficacy of drotaverine versus valethamate on cervical dilatation during labour

Of all the journeys ever we make, the most dangerous is the very first one we make through the last 10cms of the birth canal. In the strategy of labour, the duration of the labour which has great influence on both maternal and perinatal morbidity. Years ago when watchful expectancy was the attitude of midwives, prolonged labour increased the risk of dehydration, ketoacidosis, infection traumatic delivery and fetal morbidity viz, hypoxia, infection. Modern times, “Active Management” trends towards curtailing the total duration of labour compatible with the safety of the mother and foetus.⁶²

Drotaverine, an isoquinoline derivative, inhibits specifically phosphodiesterase IV which in turn increases the intracellular concentration of cAMP and cGMP and causes smooth muscle relaxation. Inj. Drotaverine Hydrochloride 40mg is given intramuscularly. Valethamate is a mixture of diphenylpiperidino-propane ethylamide HCL. It has atropine like parasympatholytic action, Papaverine – like action on plain muscle and antihistaminic action. The drug reduces the hyperexcitability of parasympathetic system and lowers the spasm of smooth muscle system. Each ampoule of valethamate bromide 80 mg is given intravenously.⁶²

Prolonged labour has been a dreaded problem for obstetricians. The most common cause of prolonged first stage of labour is cervical spasm leading to cervical dystocia. Many times it is observed that inspite of good uterine contractions; cervix fails to dilate or dilates very slowly.

This is functional cervical dystocia. Methods that aim at minimizing the incidence of functional cervical dystocia and cutting short the first stage of labour are welcome by both obstetricians and women.^{3,4} Many spasmolytic drugs have been used and tried in the past, Drotaverine is a newer Spasmolytic drug acts by inhibiting phosphodiesterase enzyme IV, which is claimed to reduce the duration of labour by accelerating cervical dilatation without causing side effects.⁶²

Epidosin (valethamate bromide) is also an antispasmodic which helps in cervical dilatation due to its neurotropic or atropine like action and musculotropic or papaverine like action. Hence this study was carried out to compare the efficacy of Inj. Drotaverine with Inj Valethamate on duration of active phase of labour, the rate of cervical dilatation and its effect on mother and foetus.⁶²

THIS STUDY

OBJECTIVE:

To compare the outcome for acceleration of labour in terms of mean duration of 1st stage in laboring patients receiving drotaverine versus control group

Operational Definitions

Drotaverine:

Drotaverine is a drug which given intravenously in active phase of first stage of labour i.e; >3cm dilatation in the dose of 40mg and repeated after 2 hours if rate of cervical dilatation was less than 1cm/hr in primigravida and 1.5cm/hr in multigravida.

Outcome:

Outcome will be measured in terms of;

Duration of first stage of labour:

Duration in minutes from administration of drug at 3cm cervical dilatation till full dilatation of cervix assessed on vaginal examination. Duration was assessed in hours. Patients in labour i.e pain at least 3/10 minutes, cervical dilatation upto 3cm was included in the study.

Hypothesis:

There is a difference in the outcome of laboring patients receiving drotaverine versus control group.

MATERIAL AND METHOD:

Study design:

Randomized controlled trial

Settings:

Department of Obstetrics and Gynaecology unit 1 GMC Teaching hospital Guranwala

Duration of study:

Six months after approval of synopsis

Sampling technique:

Non-probability consecutive sampling.

Sampling size:

Sample size of 248 cases (124 cases in each group) is the ??? and expected mean cervical dilation in receiving group as $2.43 \pm 84/\text{hr}$ and in placebo group as $1.85 \pm 1.38/\text{hr}$.²

Selection criteria:

Inclusion criteria

- Both primigravidas and multigravidas.
- Term gestation i.e 37-42 weeks assessed by last menstrual period.
- Cervical dilatation of upto 3cm with rupture of membranes.
- Singleton fetus with cephalic presentation assessed by ultrasound.
- No evidence of fetal compromise assessed by cardiotocograph and colour of liquor.
- Regular uterine contractions at a rate of 3 to 4 contractions every 10 minutes.

Exclusion criteria

- Cephalopelvic disproportion assessed by clinical and abdominopelvic examination.
- Patients known allergic to drotaverine.
- Any history of cervical injury.
- Cervical surgery in the past.
- Patient on antihypertensive therapy.

Data Collection Technique

The study was approved by ethical committee, the study comprised of those patients who fulfilled the inclusion criteria. Patients were admitted from labour room, after informed consent, patients biodata including name, age, parity was noted. A detailed history was taken and routine investigations were performed.

Patients were divided in two group's i.e; Group A and Group B by lottery method. Group A was given 40mg of i/v drotaverine in active phase of first stage of labour and its effect was assessed by digital pelvic examination and results were plotted on partogram, the dose was repeated after 2 hours if the rate of cervical dilatation was less than 1cm/hr in primigravida and 1.5cm/hr in multigravida, while group B not received any drug and were the control group. The results were noted in terms of duration of first stage of labour in two groups. All this information was recorded in a predesigned performa(attached).

Data Analysis

SPSS version 11.0 was used for data analysis. Quantitative variable like patient's age, gestational age and duration of labour in both groups were presented by mean and standard deviation. T-test was applied for significance difference between groups for duration of first stage of labour taking P-value < 0.05 as significant. Data was stratified for parity, age, gestational age, BMI. Post stratification t-test would be used. p-value < 0.05 was considered significant.

RESULTS:

In our study total 248 cases were enrolled. The mean age of the group A patients was 27.47 ± 6.66 years and its mean value in group B was 30.09 ± 6.18 years. **Table#1**

In our study 65(26.21%) patients were with no parity status, the patients with parity one were 53(21.37%), the patients with parity two were 46(18.55%), the patients with parity three were 32(12.90%), the patients with parity four were 26(10.48%) and the patients with parity five were 26(10.48%). **Fig#1**

In this study the mean gestational age of the group A patients was 39.41 ± 1.82 weeks and in group B patients was 39.44 ± 1.75 weeks. **Table#2**

In this study the mean BMI of the group A patients was 24.28 ± 3.41 kg/m² and in group B patients was 24.28 ± 3.41 kg/m². **Table#3**

Out of 248 patients the mean duration of labour was 2.59 ± 0.98 hours with minimum and maximum duration values of 1 & 4 hours respectively. **Table#4**

Among of 248 respondents the mean duration of active stage labour in group A was respondents was 2.08 ± 0.82 hours and in group B was 3.10 ± 0.86 hours. Statistically significant difference was found between the study groups with duration of active stage of labour i.e. $p\text{-value} = 0.001$. **Table#5**

The study results showed that in patients with age ≤ 30 years, the mean value of duration of active stage labour in group A was 2.06 ± 0.81 hours and its mean value in group B was 3.22 ± 0.86 hours. Similarly in patients with age > 30 years, the mean value of duration of active stage labour in group A was 2.11 ± 0.85 hours and its mean value in group B was 3.00 ± 0.85 hours. Statistically significant difference was found between the study groups with duration of active stage labour stratified by age i.e. $p\text{-value} < 0.05$. **Table#6**

The study results showed that in primary parity patients, the mean value of duration of active stage labour in group A was 2.02 ± 0.81 hours and its mean value in group B was 3.11 ± 0.84 hours. Similarly in multiparity patients, the mean value of duration of active stage labour in group A was 2.14 ± 0.84 hours and its mean value in group B was 3.10 ± 0.89 hours. Statistically significant difference was found between the study groups with duration of active stage labour stratified by parity i.e. $p\text{-value} < 0.05$. **Table#7**

The study results showed that in patients with gestational age 37-39 weeks, the mean value of duration of active stage labour in group A was 2.08 ± 0.84 hours and its mean value in group B was 3.25 ± 0.87 hours. Similarly in patients with gestational age 40-42 weeks, the mean value of duration of active stage labour in group A was 2.08 ± 0.82 hours and its mean value in group B was 2.97 ± 0.84 hours. Statistically significant difference was found between the study groups with duration of active stage labour stratified by gestational age i.e. $p\text{-value} < 0.05$. **Table#8**

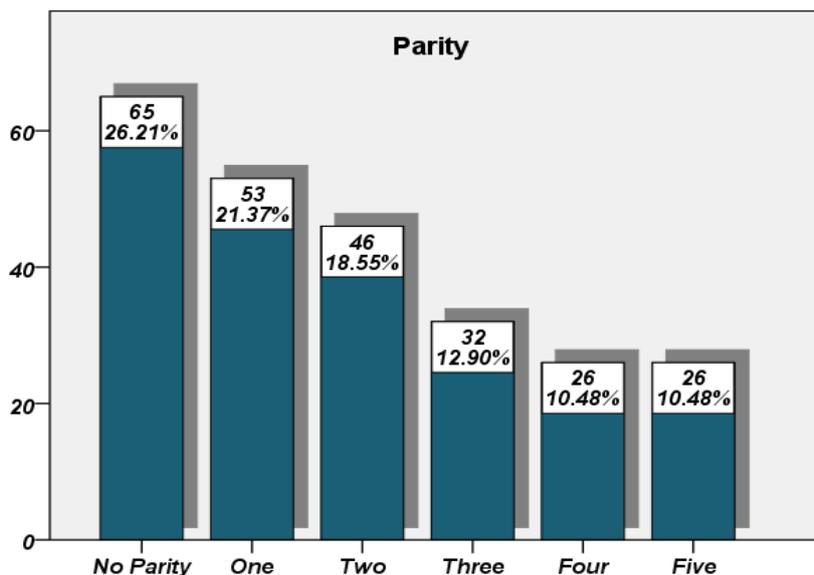
The study results showed that in patients with normal BMI, the mean value of duration of active stage labour in group A was 2.00 ± 0.82 hours and its mean value in group B was 3.04 ± 0.89 hours. Similarly in patients abnormal BMI, the mean value of duration of active stage labour in group A was 2.19 ± 0.83 hours and its mean value in group B was 3.19 ± 0.83 hours. Statistically significant difference was found between the study groups with duration of active stage labour stratified by BMI i.e. $p\text{-value} < 0.05$. **Table#9**

Table#1 Comparison of age with study groups

		Study Groups	
		Group A	Group B
Age (years)	n	124	124
	Mean	27.47	30.09
	SD	6.66	6.18

Group A= Drotaverine

Group B=Control



Fig#1 Frequency distribution of parity

Table#2 Comparison of gestational age with study group

		Study Groups	
		Group A	Group B
Gestational age (weeks)	n	124	124
	Mean	39.41	39.44
	SD	1.82	1.75

Group A= Drotaverine

Group B=Control

Table#3 Comparison of BMI with study group

		Study Groups	
		Group A	Group B
BMI (kg/m ²)	n	124	124
	Mean	24.28	24.28
	SD	3.41	3.41

Group A= Drotaverine

Group B=Control

Table#4 Descriptive statistics of duration of active stage of labour with study group

Duration of active stage of Labour (Hours)	n	248
	Mean	2.59
	SD	0.98
	Minimum	1
	Maximum	4

Group A= Drotaverine

Group B=Control

Table#5 Comparison of duration of active stage of labour with study group

		Study Groups	
		Group A	Group B
Duration of active stage of labour (hours)	n	124	124
	Mean	2.08	3.10
	SD	0.82	0.86

Group A= Drotaverine

Group B=Control

Ind. t test=-9.57

p-value=0.001*

Table#6 Comparison of duration of active stage of labour with study group stratified by age

	Age (years)	Study Groups	Mean	SD	p-value
Duration of active stage of labour (hours)	≤30	Group A	2.06	0.81	0.001*
		Group B	3.22	0.86	
	> 30	Group A	2.11	0.85	0.001*
		Group B	3.00	0.85	

Group A= Drotaverine

Group B=Control

Table#7 Comparison of duration of active stage of labour with study group stratified by parity

	Parity	Study Groups	Mean	SD	p-value
Duration of active stage of labour (hours)	Primary	Group A	2.02	0.81	0.001*
		Group B	3.11	0.84	
	Multiple	Group A	2.14	0.84	0.001*
		Group B	3.10	0.89	

Group A= Drotaverine

Group B=Control

Table#8 Comparison of duration of active stage of labour with study group stratified by gestational age (weeks)

	Gestational age	Study Groups	Mean	SD	p-value
Duration of active stage of labour (hours)	37-39	Group A	2.08	0.84	0.001*
		Group B	3.25	0.87	
	40-42	Group A	2.08	0.82	0.001*
		Group B	2.97	0.84	

Group A= Drotaverine

Group B=Control

Table#9 Comparison of duration of active stage of labour with study group stratified by BMI

	BMI	Study Groups	Mean	SD	p-value
Duration of active stage of labour (hours)	Normal	Group A	2.00	0.82	0.001*

		Group B	3.04	0.89	
	Abnormal	Group A	2.19	0.83	0.001*
		Group B	3.19	0.83	

Group A= Drotaverine

Group B=Control

DISCUSSION:

This present randomized control trial was carried out in a teaching hospital situated in district Gujranwala to compare the outcome for acceleration of labour in terms of mean duration of 1st stage in laboring patients receiving drotaverine versus control group.

Of all the journeys ever we make, the most dangerous is the very first one we make through the last 10cms of the birth canal. In the strategy of labour, the duration of the labour which has great influence on both maternal and perinatal morbidity. Drotaverine, an isoquinoline derivative, inhibits specifically phosphodiesterase IV which in turn increases the intracellular concentration of cAMP and cGMP and causes smooth muscle relaxation.⁶²

In our study among 248 respondents the mean value of duration of active stage labour in Drotaverine group was respondents were 2.08±0.82 hours and its mean value in control group was 3.10±0.86 hours. Statistically significant difference was found between the study groups with duration of active stage of labour. i. e p-value=0.001. Some of the studies are discussed below showing the results in favour of our study as.

A study by Meena Thapa et al⁶³ presented that the injection-delivery interval was studied in both Groups. The duration of injection-delivery interval was found to be almost equal in primigravidae of both Groups (p=0.72). But in multigravidae interval was significantly shorter in drotaverine Group (p=0.03).

Sharma JB et al⁶⁴ demonstrated that injection-to-delivery interval was significantly reduced in the drotaverine group (193.96 min) in contrast to the valethamate group (220.68 min) and control group (412.84 min). The rate of cervical dilation was highest in the drotaverine group (2.04 cm/h) compared with the valethamate bromide group (1.86 cm/h) and control group (1.01 cm/h). There were no major maternal or fetal adverse effects in any group, but minor side effects were more common in the valethamate group.

One study by Madhu C et al⁵ demonstrated that there was a statistically significant difference in the mean injection-delivery times (time from first injection to delivery of the baby), which was 183.2 min (SD 78.8) in the Drotaverine group compared to 206.5 min (SD 69.7) in the Valethamate group, and 245 min (SD 70.9) in the control group. The mean cervical dilatation rate (cm/h) was 3 (SD 1.4), 2.4 (SD 0.9) and 1.9 (SD 0.6) in groups 1, 2 and 3, respectively, and these differences were statistically significant.

A randomized study conducted in 2014 concluded the results that the mean duration of first stage of labour in primigravida control group was 5 hours 48 minutes+1hour 23 minutes and in multigravida control group was 4hours and 43 minutes+1hour 7minutes while in tramadol group was 4 hours+1hour 28 minutes and 3hour 19minutes +1 hour 5 minutes respectively.⁶

Another randomized study conducted in an Academic tertiary care hospital concluded the results that laboring women who received rociverine had faster cervical dilatation than those assigned to placebo (2.43+1.84 vs 1.85+1.39 cm/hour, p=0.03).²

One more study by Singh KC et al⁶⁵ documented in their study results that In drotaverine group, there was a mean 15% reduction in the duration of the first stage of labor and a mean 19% reduction in the second stage. The maximum shortening of the first stage (28%) was observed when drotaverine was administered when cervical dilatation was 4 cm (P=0.044). Drotaverine hydrochloride is safe and effective in accelerating labor, but not effective in lessening labor pain.

Another study revealed that the Duration of active phase of first stage was 116.34 ± 59.44 and 158.78 ± 58.98 minutes in group I and II respectively. Rate of cervical dilatation was 3.99 ± 2.21 and 2.74 ± 1.72 cm/hour in group I and II respectively. They observed drotaverine to be a better drug for cervical dilatation than epidosin.⁶⁶

A randomized prospective study was carried out on 300 women in normal labour. The results were the mean duration of first stage of labour was 132.67 ± 60.24 minutes in the epidosin group, 175.92 ± 90.56 minutes in the drotaverine group and 287.68 ± 104.1 minutes in the control group. They concluded that both epidosin and drotaverine were highly effective; epidosin was better in multipara in shortening the duration of labour.⁶⁷

On the other hand study done by Gupta B et al⁶⁸ resulted that mean duration of the active phase of labor was 4.48+/-2.26 h, 3.9+/-2.42 h, and 3.6+/-2.07 h in groups 1 (drotaverine), 2 (hyoscine-N-butylbromide), and 3 (no medication), respectively. The mean rate of cervical dilation was 2.6 cm/h, 2.4 cm/h, and 2.5 cm/h, respectively. The differences were not statistically significant.

CONCLUSION:

It has been proved in our study that the drotaverine can significantly reduce mean duration of 1st stage in laboring patients. Now in future we are able to implement drotaverine in local setting. It will be more helpful in primigravidas as the duration of labour in primigravidas is longer. It will now help to decrease the risk of prolonged labour, maternal morbidity, caesarean sections rate, increase of placenta previa and morbidly adherent placenta and will increase the rate of normal vaginal births.

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PROFORMA

Drotaverine for acceleration of labour in terms of cervical dilatation

Date: _____

Registration No: _____

Name: _____ Age: _____

Parity: _____ Married from: _____

LMP: _____ EDD: _____ DOP: _____

Gestational Age: _____

BMI: _____

Group A _____ Group B _____

DOSAGE OF DRUG USED IN mg _____

Outcome _____

Duration of active stage of labour in hour's _____