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Research Article

IMPACT OF STERIOD AND ANTIBIOTIC ON THE POTENTIAL TOCOLYTICS

PUSHPENDRA KUMAR SINGH*, HARPREET SINGH, SANJITA DAS

Department of Pharmaceutical Technology N.I.E.T College Greater Noida ,UP, India,Email: pushpendrapharma21@gmail.com

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ABSTRACT

To prevent premature labor always attempts are taken by the medication with Tocolytic. Along with Tocolytic, steroid and antibiotic are used for the proper therapy to prevent premature labor. The present study will evaluate the impact of the selected steroid (bethamethasone) and antibiotic (ampicillin) on the uterine relaxant effect of the selected Tocolytic (indomethacine).This study will be helpful for the proper medication during the preventation of premature labor along with a better medication and better result. Evaluation of impact of the selected drugs (betamethasone,ampicillin) on the efficacy of the selected Tocolytic (indomethacine) by in vitro method using oxytocin as a uterine contractile agent on rat uterus. The rat's uterine preparation is used for the present study and the sensitivity of uterus is depends upon the oestrus cycles.Oxytocin cause the contraction of the uterine muscle by acting on the muscuarinic receptor. Tocolytic block muscarinic receptor of uterine muscle. Therefore, in this study the Tocolytic reduce oxytocin induced contraction in rat uterine. The concentration response cruve of oxytocin was shifted to the right in the presence of Tocolytic. Afterwards the effect of the selected steroid and antibiotic in presence of the Tocolytic are evaluated on the kymograph of oxytocin.it was observed that steroid and antibiotic decrease the potency of Tocolytic.

Keywords: Premature Labour,Tocolytic,Steroid,Antbiotic,Oxytocin,Betamethasone, Ampicillin,Indomethacin

INTRODUCTION

Neonatal morbidity & mortality, is a major contributor to loss of life,caused by preterm birth. Special education are given for children born before 37-32 week. World data on the incidence of preterm birth are unreliable, but incidence ranges between About 5% of children die due to pre term birth in developed countries and about 25% of children die due to preterm birth in developing countries. Wide scale national data is lacking in this respect to show the incidence in our country. Perinatal mortality rate is 159/1000 pregnancies according to Pakistan Demographic & Health Survey (PDHS) 2006-2007.Tocolytic therapy is used to reduce neonatal mortality & morbidity by delaying birth, allowing for corticosteroid administration & maternal transfer to a tertiary care centre . An effective tocolytic agent work rapidly to ensure that labor does not progress beyond the point of no return especially in settings where in utero transfer is necessary.The choice tocolytic agent which could improve neonatal outcome with no maternal or neonatal side effects, has not yet surfaced [1].

Respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), sepsis and overall neonatal mortality has been significantly reduced by the use of antenatal corticosteroid.National Institutes of Health (NIH) (1994) recommended the administration of a single course of antenatal corticosteroid for women at risk of preterm birth presenting between 24-34 weeks of gestation.

The course of antenatal steroid is maximally beneficial if the newborn is delivered after 24 hours and within 7 days of the last dose of steroid. On this basis, weekly courses of antenatal steroid have been proposed. The major concern of those opposing multiple courses has been the adverse outcomes on growth and neuro-development. Many others opine that neonatal morbidity and mortality decreases after repeated courses of antenatal steroid with no significant adverse effects.Multiple courses should be used only in the context of well-conducted randomized controlled trials (RCT) recommended by (NIH).

There is a paucity of data on this issue from developing countries. In the context of inaccessibility and unaffordability of advanced neonatal interventions, a low cost universally accessible intervention such as multiple courses of antenatal corticosteroid has immense potential. [2].

In the United States and other developed countries, pregnancy outcomes are considerably better than those seen in many developing countries. Range of stillbirth rates (3–7 per 1000 births versus ≥30) in many developing countries.Range of neonatal mortality rates are (≈4–6 per 1000 newborns versus ≥40 per 1000 newborns in developing countries) and range of maternal mortality rates are (5–10 per 100 000 pregnancies versus rates as high as 500–1000 per 100000 pregnancies in some developing countries). Adverse pregnancy outcomes are generally more common in the United States despite these better outcomes, than in other developed countries and causes both excessive medical costs in the perinatal period and increased long-term neurologic disability .Low birth weight (LBW) is an important cause of perinatal mortality and both short- and long-term infant and childhood morbidity in both developed and developing countries.Pre-term birth and fetal growth restriction are the two main reasons of low birth weight.LBW infant is one born weighing <2500 g according to the World Health Organization(WHO).Infants born at <37 wk from the first day of the last menstrual period are termed as preterm infants, regardless of birth weight, whereas those born weighing less than the 10th percentile of birth weight–for–gestational age, regardless of whether that weight is <2500 g,are termed as growth-restricted infants .

Death rate of Low Birth Weight infants is 40 times those of infants of normal weight, and Low Birth Weight infants are many times more likely to end up with long-term handicapping conditions [3].

Preterm labour is the major cause of perinatal morbidity and mortality.Oxytocin (OT) and prostaglandins act on the uterus, and induce contractions, that result in preterm labour. OT binds to the specific receptors, and increases the intracellular Ca^{2+} level through release of Ca^{2+} from both sarcoplasmic reticulum via inositol-1, 4, 5-triphosphate (IP_3) pathway, and extracellular fluid through voltage operated calcium channels. Calcium channel blockers, OT antagonists, b_2-agonists, magnesium sulphate, and prostaglandin synthetase inhibitors treat Pre-term labour.But sometimes, these drugs are inadequate, and show adverse effects like, hyperglycemia ,pulmonary edema, , cardiac depression, tachycardia and inhibition of neuromuscular transmission, increased cardiac output. It is therefore necessary, for search of effective and safe alternative drugs for the treatment of preterm labour [4].

MATERIAL AND METHODS

Drugs and chemicals used in the study

Standard Drugs

- Tocolytic – Indomethacine
- Steroid – Betamethasone.
- Antibiotic – Ampicillin

Drug and Dose for animal

- Oxytocin - Uterine contractile agent on rat uterus.
- Stilboestrol - 0.1 mg/kg s.c

Experimental Animals

Ethical considerations for housing and handling the animals

Wistar albino female rats weighing between 125-250 gm were used for the study. They were obtained from Central animal house of NIET, Greater Noida. They were housed in propylene cages at 25 ± 2 ºC with 12 hrs light and 12 hrs dark cycle. All the animal were fed with standard feed and water *ad libitum*. All the animals were maintained under standard laboratory condition. Study protocol was approved from the Institutional Animals Ethics Committee (IACE) and Reg. No is NIET/IACE/2011/26. The CPCSEA Reg. no is 1121/ac/CPCSEA/07.

Pharmacological Evaluation

In vitro studies

Isolated organ bath studies [5]

Examine the vaginal smear under microscope to know about the proper stage of oestrus cycle. If the rats was not in oestrus, inject 0.1 mg/kg of stilboestrol and wait for 24 hr.Vaginal smear was prepared by taking a drop of the vaginal wash and putting on the slide glass, check the frank oestrus (cornified epithealial cells and liukocytes) stage.The animal was sacrificed by blow on the head and carotid bleeding.The pelvic region was cut open and exposed both horn of uterus and then these were to be separated gently from the surrounding fatty material and transfer them to a dish contaning De Jalon's solution. When the rat was in oestrus generally the uterus was fleshy and pink in colour.Two separate pieces (2-3 cm long) of uterine preparations can be made for experiments use.The uterine preparation was mounted in the organ bath contaning De Jalon solution at 30-32 ºC. Tension of 0.5 g and was applied and allow the tissue to equilibrate for 30 min.The concentration dependent responses was recorded due to oxytocin using frontal writing lever. Contact time of 60 sec, and 5 min time cycle kept for proper recording of responses. Tocolytic was added to the reservoir.The tissue with tocolytic was irrigated with oxytocin in presence of given tocolytic, steroid and antibiotic and exposed both horn of the modified ringer for 20 min.The C.R.C(Concentration Response Curve) of oxytocin was repeated in presence of given tocolytic ,steroid and antibiotic.

First of all the base line was taken . After that Oxytocin (utertine contratile agent) peeks were obtain until the maximum concentration peek was observed. Maximum concentration peek was observed at (0.4 ml) concentration of oxytocin.The peek observed at (0.4 ml) concentration was considered as standard peek. So (0.4ml) concentration of oxytocin was a standard dose for contraction.

Tissue was washed 3-4 times.Then combined peeks of oxytocin (0.4 ml concentration) and (antiuterine contractile agent) tocolytic (0.1 ml,0.2 ml,0.4 ml,0.8 ml concentration) were observed.It was concluded that at oxytocin (0.4 ml) and tocolytic (0.8 ml) concentration , the peek meets the base line.

Tissue was again washed 3 – 4 times. Then combined peeks of oxytocin (0.4 ml concentration), steroid (0.1 ml concentration) and tocolytic (0.1 ml,0.2 ml,0.4 ml,0.8 ml,0.16 ml concentration) were observed.It was concluded that at oxytocin (0.4 ml) and steroid(0.1 ml concentration tocolytic (0.16 ml concentration) , the peek meets the base line.

Tissue was again washed 3 – 4 times. Then combined peeks of oxytocin (0.4 ml concentration), antibiotic (0.1 ml concentration) and tocolytic (0.1 ml,0.2 ml,0.4 ml,0.8 ml,0.16 ml,0.32 ml concentration) were observed.It was concluded that at oxytocin (0.4 ml) and antibiotic (0.1 ml concentration) tocolytic (0.32 ml concentration) , the peek meets the base line.

DISCUSSION

Preterm birth is one of the greatest challenge obstetrical practice the currently used medication are not able to stop or sufficiently delay the process of the preterm birth.Mostly we use steroid and antibiotic before labour .Tocolytic are used when there is any lung disorder or bacterial infection. Tocolytic is an Anti-contraction drugs.Delievery can be delayed for some time period by using Tocolytic. During this time period, steroidal drugs and Antibiotic can be given to mother to prevent any lungs disorder or bacterial infection.

From the study it had been concluded that when steroid and antibiotic are used along with tocolytic at the time of labour, sterods and antibiotic decreases the anticontraction activity of tocolytic so an increased dose of tocolytic was given.It was essential to increase the dose of tocolytic in order to enhance the labour time period.During the enhanced period of labour any bacterial infection or lung disorder can be cured by steroid and antibiotic.So, all these results led to conclude that the tocolytic potency may be decrease significantly by combination with steroid and antibiotic . To the best of our Knowledge , our study was the first to test the impact of steroid and antibiotic on potential tocolytic.

RESULT

At (0.4 ml) concentration was considered as standard peek. So (0.4ml) concentration of oxytocin was a standard dose for contraction. At oxytocin (0.4 ml) with tocolytic (0.8 ml) concentration , the peek meets the base line. At oxytocin (0.4 ml) with steroid(0.1 ml concentration tocolytic (0.16 ml concentration) , the peek meets the base line as shown in fig 1. At oxytocin (0.4 ml) with antibiotic (0.1 ml concentration) and tocolytic (0.32 ml concentration) , the peek meets the base line.It was observed that an increased concentration of tocolytic was needed with steroid(0.1 ml) and antibiotic (0.1 ml) as shown in fig 2.

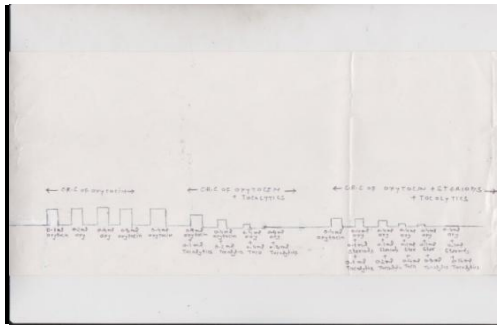

Fig 1

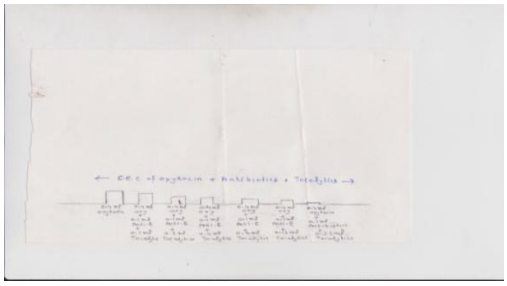

Fig. 2

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