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Title of the Protocol : Comparison Between Fetal Fibronectin Versus Ultrasonographic Assessment of the Cervical length in Patient with Unfavourable Cervix in Prediction of Successful Induction of Labor

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CONTENTS

Chapter	Page
Acknowledgment	*i*
List of contents	*ii*
List of Figures	*iii*
List of Tables	*iv*
List of abbreviations	*v*
Protocol	*vi*
Introduction	*1*
Aim of the work	*4*
Review of Literature	*5*
Patient & Methods	*33*
Results	*41*
Discussion	*56*
Summary & Conclusion &Recommendation	*63*
References	*69*
Arabic summary	

LIST OF FIGURES

	Page
Fig. (1):Ultrasound Mechine With Trans Vaginal Probe.	19
Fig. (2): Trans Abdominal Cervical Measurement.	20
Fig. (3): Trans Vaginal Ultrasound Measurement.	21
Fig. (4): Cervical length measurement (42.9mm in this case).	23
Fig.(5): Distribution of the studied group regarding maternal gestational age estimated fetal weight by ultrasound.	43
fig (6): Distribution of the studied group regarding Bishop, score, radiological findings, the fetal fibronectin level.	45
Fig.(7): Distribution of the studied group regarding successful induction of labor	46
Fig.(8): Relation between OSS and mode of delivery	47
Fig.(9): Relation between FFN and mode of delivery	48
Fig.(10): Relation between CX length and mode of delivery	49
Fig.(11): Relation between Bishop and FFN	50
Fig.(12): Relation between OSS and FFN	51
Fig.(13):Relation between FFN and CX length.	52
Fig. (14): Distribution of the patients with positive FFN and normal vaginal delivery to the date of delivery.	53
Fig. (15): ROC curve to detect the sensitivity, specificity and accuracy of Test Result Variable(s): Bishop	55
Fig (16): ROC curve to detect the sensitivity, specificity and accuracy of Bishop in predict successful labor induction occurring within 24hs.	54
Fig. (17): ROC curve to detect the sensitivity, specificity and accuracy of alpha feto protein in predict successful labor induction occurring within 24hs.	55

LIST OF TABLES

	Page
Table (1): Distribution of the studied group regarding maternal gestational age estimated fetal weight by ultrasound.	42
Table (2): Distribution of the studied group regarding Bishop, score, radiological findings, the fetal fibronectin level.	44
Table (3): Distribution of the studied group regarding successful induction of labor	46
Table (4): Relation between OSS and mode of delivery	47
Table (5): Relation between FFN and mode of delivery.	48
Table (6): Relation between CX length and mode of delivery	49
Table (7): Relation between Bishop and FFN	50
Table (8): Relation between OSS and FFN	51
Table (9): Relation between FFN and CX length.	52
Table (10): Distribution of the patients with positive FFN and normal	53
Table (11): Sensitivity, specificity and accuracy of Bishop in predict successful labor induction occurring within 24hs..	54
Table (12): Sensitivity, specificity and accuracy of alpha feto protein in predict successful labor induction occurring within 24hs.	55

LIST OF ABBREVIATIONS

FFN	Fetal fibronectin
CVF	Cervicovaginal fliud
TV/US	Transvaginal ultrasound
sPTL	Spontanous preterm labour
NPV	The negative predictive value

INTRODUCTION

Induction of labor is still a controversial obstetric procedure. The need to time delivery has been recognized and practiced for centuries. Although the indications have clearly changed during the past 200 years from a need to expel a dead fetus to pre-emptive action to reduce the threat to fetal or maternal health, effective and safe methods of achieving delivery must always have been the primary objectives. **(Macharey et al., 2014)**

Sonographic assessment of cervical length for predicting the outcome of labor induction has been evaluated in numerous studies. The role of ultrasound examination as a tool for selecting women likely to have a successful induction is uncertain ***(Verhoeven et al., 2013).*** Transvaginal sonographic measurements of cervical length in nulliparous women independently predict the likelihood of progress in nulliparous women undergoing labor induction. These observations strongly support that in nulliparous women undergoing labor induction preinduction cervical length plays a key role in labor progression during the latent phase,but not during the active phase of labor ***(Saccone et al.,2016).***

The Bishop score is a poor predictor for the outcome of induced labor at term and should not be used to decide whether to induce labor or not ***(Kolkman et al., 2013).***

Fibronectin is large glycoprotein (molecular mass about 420kDa) is normally present in essentially all tissues and body fluid. Its primary function is its role in cell adhesion and phagocytosis ***(Hymes and Klaenhammer, 2016).***

Fetal fibronectin,(fFN) a glycoprotein thought to act as an adherent at the maternal fetal interface, is uncommonly present in cervicovaginal secretions in the late second and early third trimesters. Although the risk for preterm birth increases as the level of fetal fibronectin rises, it has been evaluated only as a qualitative test, with a value of 50ng/dL or greater being called positive. A positive test is believed to indicate disruption of the maternal-fetal decidual attachment. Asymptomatic women with a positive fetal fibronectin test have an increased risk for preterm birth before 35 weeks, especially within 2 weeks of a positive result. Although the sensitivity of the fibronectin test at 22 to 24 weeks for all spontaneous births

before 35 weeks was only 25%, sensitivity for births before 28 weeks was 65% in one study ***(Berghella and Saccone, 2016).***

Fetal fibronectin (fFN) has been proposed as a new tool for cervical evaluation before labor induction. fFN in cervicovaginal secretion of term deliveries yield a high probability of success of induction of labor women with fibronectin negative cervicovaginal secretion and unfavorable cervix score induction of labour should not be attempted ***(Uygur et al., 2016).***

AIM OR THE WORK

The aim of this study was to assess the efficacy of Fetal fibronectin (fFN) level compared to transvaginal ultrasound of cervical length in prediction of successful induction of labor for unfavorable cervix (Bishop score 5 or less).

REVIEW OF LITERATURE

Induction of labor should be undertaken when the benefits of delivery to either mother or fetus outweigh the risks of pregnancy continuation. Many accepted medical and obstetric indications for labor induction like maternal medical conditions (Hypertensive disorders, Preeclampsia/ eclampsis, Gestational hypertension Diabetes mellitus, Renal disease, Chronic pulmonary disease,) obstetric conditions, (Chorioamnionitis and Oligohydramnios) ***(Parkes et al., 2016).***

The safety of the procedure and the possibility to manage labor during daytime is an often heard argument in favor of "day light obstetrics". Also the possibility to prevent intrauterine fetal morbidity and mortality of known or unknown cause and the possibility to apply intra partum fetal surveillance and monitoring from the beginning of labor are put forward as arguments in favor of induction of labor. ***(American Association of Birth Centers. 2013).***

Feelings of the dangers of induced delivery as long term perspectives for the society are the most often heated arguments against it. Techniques for inducing labor have also

changed from dietary delicacies and verbal threats giving way to physical stimulation mainly achieved by cervical stretching and amniotomy to sophisticated pharmacological manipulation using oxytocin and prostaglandins, based on our expanding knowledge of the physiological processes involved in spontaneous parturition. Thus to initiate the artificial means for initiation of labor we need to understand the parturition cascade with the biophysio-chemical changes to evolve and establish normal labor and thus realize the impact of induction of labor on achieving it. ***(Toivonen et al., 2012)***

Physiological background of the onset of Normal Labor:

The physiological processes that regulate parturition to onset of labor are difficult to define as various mechanisms are functioning at the same time. Exact factor which initiates labor remains unknown. The uterus and cervix undergoes considerable physiological, biochemical and anatomical changes during the transition between the antenatal and intrapartum period. The gravid uterus is hormonally prepared by estrogen, progesterone and prostaglandin to function in a coordinated manner. In primiparous women cervical dilatation

and effacement were related to the time of gestation at which labor started ***(Zwelling, 2008).***

Complex maturational cascade of events in the fetus may also play a role in the initiation of labor. The idea of the fetus playing a central role in the initiation of labor is supported by experimental data. In humans the activation of the fetal hypothalamic pituitary adrenal axis results in the release of C-19 steroid (dehydroepiandrostenedione) which serves as an essential precursor for placental estrogen (estriol) production at the level of the fetoplacental- maternal unit for the onset labor. ***(Lindstrom et al., 2005)***

It is likely that a "parturition cascade" is responsible for the quiescent uterus to be activated by the removal of mechanisms and recruitment of factors promoting awakening phase with progressive changes in the uterine myometrium, cervix and the fetal membranes as pregnancy climaxes for the preparation of labor.***(Elliott et al, 2001)***

a) **Myometrial changes:** The increased myometrium irritability and the responsiveness to the uterotoninc and estrogen increases the gap junctions, oxytocin and

prostaglandin receptors causing alterations in the expression of key enzyme connexin 43 with calcium channels being functionally prepared to respond as the pregnancy advances to activation. The contraction-associated protein CAP also controls the myometrium contractility. Also the myometrial oxytocin receptors increase with upregulation of the myometrial cell gap junction protein (ex connexin-43) facilitating the influx of calcium from outside the myocyte through calcium channels or the release of calcium deposited in the endoplasmic reticulum causing uterine contraction. Calcium binds to calmoudin to form a complex with the enzyme myosin light chain kinase to phosphorylate the short chains of myosin causing ATP production and muscle contraction ***(Norwitz et al.,, 2002).***

b) Cervical changes:- The cervix possesses a unique construction as described by ***(Norwitz et al.,, 2002)*****,** to enable it to perform its various roles. It consists predominantly of a stromatous body of connective tissue that can be subdivided into a superficial loose zone and a deeper dense stromal zone. The main elements of this connective tissue are collagen together

with a small amount of elastic tissue and an even smaller component of muscle fibres. ***(Norwitz et al.,, 2002).***

The collagen is composed of dense regular fibrils arranged in parallel bundles held together by cross-links, with a few interspersed mast cells and other cellular elements. The ground substance is composed of proteoglycan complexes consisting of glycosaminoglycan side chains (GAGs) on core proteins linked to a hyaluronic acid chain that bind tightly. ***(Akgul et al., 2012)***

The dominant GAGs in the cervix are dermatan sulphate and chondroitin sulphate, both of which contain hyaluronic acid conferring additional binding strength and have hydrophilic properties. Fibroblasts with numerous long cytoplasmic processes radiating from one cell body to another, possibly similar to myometrial gap junctions, infiltrate the ground substance ***(Akgul et al., 2012).***

With the advance of pregnancy, increased vascularity is seen and the fibroblasts become secretory, white cells and macrophages migrate out of vessel walls into the cervical