Effect of Intravenous Dexamethasone on Preparing the Cervix and Labor Induction

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Abstract- The use of corticosteroids is one of the methods put forward for the strengthening and speeding up the process of labor. After identification of glucocorticoid receptors in human amnion, the role of corticosteroids in starting the process of labor has been studied in numerous studies. The purpose of this study was to determine the effect of intravenous Dexamethasone on preparing the cervix and on labor induction. A randomized, clinical, and double – blind trial was conducted on 172 women divided into a control and an experimental group. The inclusion criteria were that they had to be primparous, in or before the 40th week of pregnancy, and with Bishop scores (B.S.s) of 4 or lower. The exclusion criteria were diabetes, preeclampsia, macrosomia, twin pregnancy, rupture of the membrane (ROM), breech, and women suffering from background diseases. The B.S.s of the women was measured in charge of the study, and each woman was intravenously injected with eight milligrams of Dexamethasone or eight milligrams of distilled water. Four hours after the injections, the B.S.s of the participants was measured, and they were put under the conditions of labor induction using oxytocin. Information was collected in checklists A and B. The patients were compared with respect to B.S., the time the induction started, the average interval between the start of induction and the beginning of the active phase of childbirth, and the average length of time between the start of the active phase and the second stage of childbirth. The first and five minutes Apgar scores of the two groups of women were compared. The frequencies, the means, and the standard deviations were calculated using the SPSS – 16 software, and analysis of the results was performed with the Student's t- test and the chi-square test with $P<0.05$. There were no statistically significant differences between the two groups in terms of their age, period of pregnancy, and B.S. at the start of the study. The average B.S. of women four hours after the injections with Dexamethasone was 5.9 ± 1.57, and the corresponding figure for women in the control group was 4.6 ± 1.72. These figures were significantly different at $P<0.001$. The average interval between labor induction and the start of the active phase in the group injected with Dexamethasone was significantly less than that of the control group (2.87±0.93 versus 3.80± 0.93 at $P<0.001$). The average duration of the active phase of the second stage of childbirth was 3.47±1.10 hours in the experimental group and 3.6 ± 0.99 hours in the control group at $P<0.49$. These two figures were not significantly different. The Apgar scores of the first and fifth minutes after the birth of the children of the two groups of women were not significantly different. It was found that intravenous Dexamethasone improves the Bishop score of the cervix and thus causes softening of the cervix and reduces the length of time between labor induction and the start of the active phase of childbirth.

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Introduction

The process of childbirth starts from the axis of the hypothalamus, the pituitary gland, and the adrenal glands. Steroid substances produced in the adrenal glands of the human fetus affect the placenta and the membranes and transform the myometrium from the static to the contractile state (1). The placenta may play a role in this process because it produces a lot of CRH (Corticotropin-releasing hormone). The adrenal glands of the fetus do not

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produce a considerable amount of cortisol until the third trimester. During the last weeks of pregnancy, the cortisol and DHEA –S (Dehydroepiandrosterone sulfate) contents of the fetus rise and this leads to an increase in maternal estrogens, a particularly sterol (1). Placental CRH is not under the influence of negative feedback from cortisol. The concentration of CRH in the fetus rises during the last 12 weeks of pregnancy. This results in modification of the contractility of the uterus (1), stimulation of the membranes to produce more prostaglandins (2), stimulation to produce C_{19} steroids from placental adrenaline (3), and increase in the estrogen content (4). This will disturb the ratio of estrogen to progesterone and will cause expression of contractile proteins. In fact, the increase in CRH near the end of pregnancy confirms the presence of a placental-fetal clock (1).

One of the methods proposed for the strengthening and speeding up of the labor process (labor induction) is use of corticosteroids, although the effects of using these substances in the labor process is not well – understood (2-6), studies conducted on animals indicate the importance of the secretion of cortisol by adrenal glands in sheep fetuses and in fetuses of other animals on starting labor (3-7,19). Moreover, it has been observed that infusion of glucocorticoids into sheep fetuses causes premature birth induction (2,7,19). These studies have prepared the way for bringing up the role of corticosteroids in the speeding up of labor induction in women. In studies carried out, corticosteroids have been employed using extra-amniotic and intravenous methods and in some of these studies, both methods have proved successful (12-15). In various studies, researchers have shown that as in sheep, the production of steroid substances in the adrenal glands of human fetus affects the fetus and the membranes through CRH and causes the myometrium to transform from the static to the contractile state. In these studies, it has been revealed that the CRH derived from the placenta is an important factor in increasing maternal estrogens (especially sterol) in the final stages of pregnancy, and that cortisol stimulates the adrenal glands to provide a feed - forward endocrine cascade. It appears that the synthesis of the substances cortisol and DHEA – S indirectly affects the myometrium because these substances stimulate the membranes to produce more prostaglandins. Furthermore, the resulting increase in estrogen brings about a change in the ratio of estrogen to progesterone, which leads to the expression of proteins involved in myometrium contraction and destroys the static state of the fetus (8-10). However, in reviews, conflicting results have been obtained in this regard (3). In one of these reviews, it was shown that congenital hyperplasia of the fetus resulting from disturbances in cortisol production causes post - term births (10). In some studies, an association has been observed between stress in the mother and premature childbirth (16,17,20). In this research, we studied the role played by intravenous Dexamethasone in the process of labor, in the length of time between labor induction and the start of the active phase and in the duration of the active phase. We also compared the first - and five-minute Apgar scores of newborns of women in the experimental and control groups.

Materials and Methods

In a randomized, clinical, and double – blind trial (IRCT code 2013052613468N1), among pregnant women visiting the maternity ward of the Kossar Hospital of the Qazvin University of Medical Sciences in 2012 for the termination of their pregnancy, 172 women were selected. These women who were primparous, had Bishop scores of 4, and were in their 40th week of pregnancy, were randomly put into an experimental group (the members of which were injected with Dexamethasone four hours before labor induction) and a control group (the members of which were injected with distilled water four hours before the start of labor induction.

Primiparity, GA (Gestational age) 40 weeks, and Bishop scores of 4 were the criteria for enrollment of participants. The Bishop score index was defined as follows (Table1):

Table1. The original Bishop score table

Component	Subscore			
	0	**1**	**2**	**3**
Dilatation (cm)	0	1-2	3-4	5-6
Station	-3	-2	-1 or 0	+1 or +2
Effacement (%)	0-30	40-50	60-70	80
Consistency	Firm	Medium	Soft	--
Position	Posterior	Mid	Anterior	--

Participants with diabetes, preeclampsia, underlying diseases, breech, macrosomia (LGA), twins, women who were already in labor, women with spontaneous rupture of the amniotic sac (ROM), and patients who

refused to take part in the study were omitted.

The active phase of childbirth includes uterine contractions and dilations of 3-5 centimeters or more, and, if uterine contractions are strong enough to increase cervix dilation from 3-5 centimeters, it continues until the start of the second phase of childbirth. The duration of the active phase can also be considered as the interval between the start of the active phase and the completion of cervix dilation.

We used checklists in the present study to collect and record data. When these 172 patients were admitted to the maternity ward, the person in charge of the study examined them and determined their B.S.s. Every other one of these women was then intravenously injected with either 8 milligrams of Dexamethasone or 8 milliliters of distilled water.

The Dexamethasone and distilled water were provided for the person in charge of the study in syringes marked with A or B. This person was unaware of the contents of these syringes for the duration of the study .

The patients were re-examined four hours after the injections to determine their B.S.s and oxytocin was used for labor induction. The related information was stored in checklists A and B.

Finally, the patients were examined with respect to improvements in the condition of their crevixces during the average periods extending from the start of induction to the beginning of the active stage and from the start of the active stage to the beginning of the second stage of childbirth. The first- and the fifth - minute Apgar scores of their newborns were also determined. The related information was recorded in checklists A and B. Using the statistical software SPSS - 16, this information was entered into a computer, the frequencies, means and standard deviations were calculated. The obtained results were analyzed by employing the student's t–test and Chi-square test at $P<0.05$.

The procedures used in conducting the study were thoroughly explained to the patients, and if any problem arose for any of the patients, they would be omitted from the study. The patients were given written informed consent forms, and they participated in the study voluntarily.

It was explained to the patients that prescription of Dexamethasone did not increase the risk they were exposed to, and that since the useful effects of this drug had not been proved yet, not prescribing it would not be ethically wrong. This study was started and completed with the approval of the ethics committee of the Qazvin University of Medical Sciences, and patients participating in it did not incur any extra costs.

Results

A total number of 172 patients composed of 86 women in the experimental group and the same number in the control group took part in the study. The average age of the experimental group was 21.7 ± 0.67, and that of the control group 22.4 ± 0.67 (which did not show a significant difference at $P<0.28$). Bishop Score at entrance in case (2.95 ± 0.9) and control groups (2.82 ± 0.9) was not different significantly but this score difference in the first time of induction in case (5.9 ± 1.57) and control (4.6 ± 1.72) was significant. In addition the interval between the start of induction and the beginning of the active phase in case and control groups was different significantly ($P<0.001$) but the interval between the start of the active stage and the beginning of the second stage of childbirth between case and control groups was not different significantly ($P<0.3$). There was no significant difference in the first and fifth minute Apgar score between case and control groups ($P<0.98$, $P<0.79$) (Table 1).

Table 1. The table of the means and standard deviations of the age of the mothers, the average duration of pregnancy, the Bishop score, the interval between the start of induction and the beginning of the active phase, the interval between the start of the active stage and the beginning of the second stage of childbirth, and the first – and fifth – minute Apgar scores of the newborns (a total of 141 newborns)

	Case (Mean ± SD)	Control (Mean ± SD)	*P*
Age of the mother (years)	21.7 ± 0.67	22.4 ± 0.67	0.28
Age of pregnancy (weeks)	40.1 ± 0.3	40.2 ± 0.4	0.14
Bishop Score (entrance)	2.95 ± 0.9	2.82 ± 0.9	0.3
Bishop Score (first of induction)	5.9 ± 1.57	4.6 ± 1.72	0.001
The interval between the start of induction and the beginning of the active phase (hours)	2.87 ± 1.57	3.8 ± 1.72	0.001
The interval between the start of the active stage and the beginning of the second stage of childbirth (hours)	3.47 ± 1.1	3.6 ± 0.99	0.3
The first minute Apgar score	8.9 ± 0.39	8.9 ± 0.39	0.98
The fifth minute Apgar score	9.9±0.03	9.9±0.02	0.79

The frequency of C/S (Caesarian Section) in case and control group was 9.9% and 8.1%, respectively. The frequency of NVD (Normal Vaginal Delivery) and C/S was not significant between case and control groups (P<0.69) (Table 2).

Table 2. Distribution of the types of childbirth in the experimental and control groups

	NVD	C/S
Case (n=86)	41.3	9.9
Control (n=86)	40.7	8.1
Total (n=172)	82	18
***P*-value**	0.69	

NVD (Normal Vaginal Delivery)
C/S (Caesarian Section)

Discussion

In this study, the average Bishop score at the start of induction in the experimental group was significantly higher than that of the control group. It was also found that the mean interval from the start of induction to the beginning of the active phase in the experimental group was shorter than that of the control group.

In a study conducted by Ziaee *et al*., the average length of time between labor induction and the active phase in the experimental group (n=32) was considerably shorter than that of the control group. This agrees with the shortening of the active phase we found in the current study (but the number of patients in their research was smaller than that of ours). Of course, they had employed muscular injection of 10 milligrams of Dexamethasone in two doses 12 hours apart and had used intravenous oxytocin the next day to induce labor (13).

Kashanian *et al*. concluded indicated that the average length of time between labor induction and the start of the active phase and the duration of the second stage of childbirth in the group receiving Dexamethasone (n=60) were significantly shorter than the corresponding durations for the control group. However, the number of the patients in their study was smaller than that of ours, and they prescribed a muscular injection of 8 milligrams of Dexamethasone followed six hours later by labor induction using oxytocin. They did not compare cervix preparation between the experimental and control groups either. Results of their study somewhat agrees with those of ours (that the average length of time between labor induction and the start of the active phase in the experimental group was shorter than that of the control group).

Barkai *et al*., conducted a randomized study to evaluate the effects of corticosteroids on childbirth. They injected the members of the experimental group (n=50) with 20 milligrams of Dexamethasone in a saline solution and used a Foley catheter to extra-amniotic deliver just the saline solution to the members of the control group (n=48). The results obtained showed that the average interval between labor induction and the active phase in the experimental group was significantly shorter than that of the control group (7.8 ± 3.1 versus 11.9 ± 3.9 hours), and that the duration between labor induction and childbirth was much shorter, too (11.9 ± 3 versus 14.5 ± 4.8 hours) (12). These results also conform to those of present research. Many of the studies carried out on animals (usually on sheep) found results similar to those obtained by Barkai *et al*., (2,7,19).

However, reviews have yielded conflicting results regarding this issue. Kavanagh *et al*., reviewed a clinical trial conducted on 66 pregnant women in which the effects of prescribing muscular Dexamethasone together with oxytocin was compared with the effects of using oxytocin alone. They raised the point that corticosteroids were not effective in inducing labor and that this method had not become popular and required further research. Results obtained in this research prove that, contrary to their study, Dexamethasone is effective in labor induction and causes softening of the cervix.

In all, taking studies that have been conducted (including our research) into consideration, it appears that prescription of Dexamethasone can play a role in improving the preparation of the cervix and in speeding up labor induction, and that it may be possible to use Dexamethasone to help speed up the childbirth process and improve cervix preparation. Considering the results achieved in this research, it is recommended that this

study be repeated using a larger sample and that the side effects of using Dexamethasone for labor induction on newborns and the effects of Dexamethasone on inducing labor in multiparous women be investigated, too.

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