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Original Article

Serum decorin measurement in prediction of the risk for preterm birth

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ABSTRACT

Objective: To define serum decorin (sDEC) levels in healthy pregnants and in patients with preterm labor (PTL), and to introduce possible role of sDEC in predicting the risk for preterm birth (PTB).
Materials and methods: Thirty-one women with diagnosis of PTL between 24th to 32nd weeks of pregnancy were compared with 44 healthy pregnants in this prospective case–control study. Maternal blood sDEC and uterine cervical length (CL) measurements were conducted at referral.
Results: Median sDEC level was significantly decreased in PTL group ($p = 0.013$). Median CL was significantly shorter in PTL group ($p < 0.001$). There was not any correlation between sDEC level and maternal age, BMI, and gestational age at blood sampling time within PTL ($p = 0.955$, $p = 0.609$, $p = 0.079$, respectively) and control groups ($p = 0.652$, $p = 0.131$, and $p = 0.921$, respectively). There was not any association between sDEC level and PTB within 7 days, before 34th weeks, but before 37th weeks there was ($p = 0.206$, 0.091, and $p = 0.026$, respectively). There was not any correlation between sDEC level and the CL in PTL group ($p = 0.056$).
Conclusions: sDEC has a limited effect in prediction of PTB within a week or before 34th weeks. Combination of sDEC with CL measurements predicted PTB before 37th weeks.conclusion

Introduction

Preterm birth (PTB) is a pathological process related to infection in a significant proportion of the cases [1]. It is also related with early maturation of physiological processes, which normally occur at term. Incidence of the PTB is as high as 12%–13% of all pregnancies [2]. In recent years, with the achieved advances in newborn facilities, prognosis of the low-birth weighted-premature infants has been recovered, but still the rate of prematurely delivered newborns has not been alleviated with the improved diagnostics. It is the leading cause of perinatal morbidity and mortality of the newborn [3]. As well, PTB is the major decision-making event in evolution of a healthy non-disabled fetus.

Tocolytic treatment is indicated in a patient with a diagnosis of preterm labor (PTL). Randomized controlled trials have indicated that tocolytic treatment could postpone PTB in patients with PTL for up to 7 days, however, a satisfactory reduction in the perinatal morbidity could not be demonstrated [3,4]. Therefore, determining the specific risk factors and introducing superb diagnostic modalities prior to the onset of PTB would be a more efficient strategy in decreasing the frequency of PTB and related morbidity.

Decorin is a short chained-proteoglycan, and one of the small leucine-rich proteoglycans (SLRPs), which is found in extracellular matrix [5]. It belongs to class I SLRPs. SLRPs are, like larger proteoglycans, comprised of a protein core and glycosaminoglycan side chains. The distinguishing feature of SLRPs is the presence of a central domain containing leucine-rich repeats in the protein core. This domain is responsible for most of the functional activity of these molecules. Decorin is located on the collagen fibrils. It was readily demonstrated that decorin regulates fibrillogenesis, cell organization and stabilization in connection with type I collagen *in vivo* [5,6]. The influence of transforming growth factor beta 1 reduces the synthesis and chain length of decorin [7,8]. Decorin is

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found in every tissue where proteoglycans exist. These include bone, cartilage, gum, vascular endothelium, endometrium, connective tissue of the cervix, placenta, and decidua [9–11]. Targeted deletion or alteration of any of the SLRPs lead to disruption in collagen fibrils in tissues.

To date, studies have concentrated on role of decorin in patients with preterm rupture of membranes [12–14]. The role of decorin in pathophysiology of PTL has not been investigated so far. As changes in collagen levels and the proteoglycan levels occur through the cervical ripening theoretically [15,16] we hypothesized that alterations in serum decorin (sDEC) levels could be found in women with the diagnosis of PTL prior to 32nd gestational weeks when compared to healthy pregnant women of the same gestational age.

Materials and methods

Study protocol and the participants

The study was conducted as prospective case–control study between May 2012 and August 2014 in a tertiary care university hospital. Pregnant women with 24–32 weeks of pregnancy who referred with a complaint of inguinal, abdominal or dorsal pain were defined as the target population. PTL was defined as presence of regular uterine contraction cycles frequent than once in 10 min together with a longitudinal cervical length (CL) measurement shorter than 25 mm. Among those candidates, women with preterm rupture of membranes, cervical insufficiency, multiple pregnancy, hypertensive disorders of pregnancy, pre-gestational or gestational diabetes mellitus, systemic disorders including connective tissue diseases and vasculitis, polyhydramnios, placenta previa, recent vaginal bleeding, placental abruption, and unfavorable fetal conditions including fetal growth restriction, congenital fetal anomalies, and fetal demise were excluded from the study. Patients between 24th and 32nd gestational ages who met the definition of PTL, with contractions and or shorter than 25 mm CL measurements designated the *PTL group*. Gestational age-matched healthy singleton pregnant women without uterine contractions and CL > 25 mm were assigned in the *control group*. Institutional Review Board approval was obtained (2012-9/14). All participants were fully informed and gave written informed consent.

Gestational age was calculated with respect to the last menstrual period or crown-rump length at first trimester ultrasonography, as appropriate. Frequency and amplitude of uterine contractions were recorded with external fetal monitor for at least 30 min. CL was evaluated by transvaginal ultrasonography. Following the obstetric evaluation, peripheric venous sampling from the participants was performed before any treatment has been started. All patients with PTL were administered 10 mg of oral nifedipine tablets 6 times daily or intravenous beta agonist (ritodrine hydrochloride) as the first-line tocolytic treatment. Betamethasone administration has been started to patients in PTL group.

Blood samples for serum decorin levels from healthy pregnants constituting the control group, were also taken between 24 and 32 weeks during their routine controls. All the patients included in the study were followed until birth.

Sample collection and analysis

3 mL of peripheric venous blood samples were drained into EDTA-containing test tubes. Materials were centrifuged at 1000 cycles for 15 min within 30 min after collection. Supernatants were isolated and stored in cryo tubes at −27 °C until being studied. sDEC levels were measured by enzyme linked-immunosorbent assay (ELISA) method. Human Decorin Elisa Kit (Adipo Bioscience, Santa Clara, CA, USA) was used for the sDEC measurements. Standard work-up for Elisa procedure was conducted according to the manufacturer's instructions.

Statistical analysis

Statistical analyses were performed using SPSS for Windows 20.0 statistical package program (SPSS Inc., Chicago, Ill). For the comparison of the continuous variables between the two groups, depending on the distribution of the sample group, Student's *t*-test or Mann–Whitney *U* test were carried out, as appropriate. Chi-square test was used in the comparison of categorical variables. Correlation analysis was performed with the Pearson's correlation coefficient or Spearman's rank correlation coefficient, as appropriate. ROC analysis was conducted to define cut-off values for predicting the risk of PTB within a week, before 34th, and 37th gestational weeks. $P < 0.05$ was considered as statistically significant.

Results

One hundred and sixteen patients were assigned in the study in order to constitute the PTL group. Fifty-two participants who meet the exclusion criteria subtracted from the study group. Among 64 remainders, 31 participants who obey the PTL criteria constituted the PTL group. Gestational aged matched 44 women were assigned in control group.

Table 1 demonstrates the characteristics of the study population. Mean maternal age and body mass index (BMI) and also median values of gravidity, parity, abortion, and gestational age at blood sampling between groups were not significantly different.

Median CL was significantly shorter in PTL group compared to control group (20 mm vs. 37 mm, $p < 0.001$) (Table 2). Median sDEC was significantly lower in PTL group compared to the controls (3026.2 pg/mL vs. 4021.2 pg/mL, $p = 0.013$). Median gestational age at delivery was significantly earlier in PTL group than the controls ($36^{2/7}$ vs. $38^{3/7}$, $p < 0.001$).

Six (19.4%) of the patients in PTL group and 9 of (20.5%) control participants were between 24th and 28th gestational weeks, whereas 25 (81.6%) of the patients in PTL group and 35 (79.5%) of the controls were between 28th and 32nd gestational weeks during the inclusion.

When pregnancies smaller than 28th weeks of gestation at diagnosis were analyzed, mean values of maternal age and BMI between groups were not significantly different. There was a significant difference in median gestational age at blood sampling between PTL and control groups ($p = 0.026$; $26^{1/7}$ vs. $26^{4/7}$). sDEC levels did not differ significantly between groups (Table 3).

When pregnancies greater than 28th weeks of gestation at diagnosis were considered, mean values of maternal age and BMI and median value of gestational age at blood sampling between groups did not differ significantly. Median sDEC level was significantly lower in PTL group compared to controls ($p = 0.043$) (Table 4).

We did not establish any correlation between sDEC level and maternal age, BMI, and gestational age at blood sampling within PTL ($p = 0.955$, $p = 0.609$, $p = 0.079$, respectively) and control groups ($p = 0.652$, $p = 0.131$, and $p = 0.921$, respectively).

In PTL group, there was an association between sDEC level and PTB before 37th gestational weeks ($p = 0.026$), but there was not between sDEC level and PTB within 7 days and before 34th gestational weeks ($p = 0.206$ and 0.091, respectively) (Table 5). We did not find any correlation between sDEC and the CL in PTL group ($p = 0.056$).

However, CL was associated with PTB within 7 days, before 34th and 37th weeks of gestation in PTL group ($p < 0.001$, $p < 0.001$, and

Table 1
Demographic characteristics of the study participants.

	PTL group ($n = 31$)	Control group ($n = 44$)	p
Age (years)	27.3 ± 5.06	28.9 ± 5.06	0.176
BMI (kg/m^2)	27.6 ± 6.28	29.6 ± 4.58	0.113
Gravidity	1 [1–7]	2 [1–6]	0.166
Parity	1 (0–3)	1 (0–3)	0.105
Abortions	1 (0–4)	1 (0–2)	0.951
GW at blood sampling time (GWs ^{days})	$29^{6/7}$ ($24^{6/7}$–$31^{6/7}$)	$29^{2/7}$ ($24^{2/7}$–$31^{6/7}$)	0.771

GW: Gestational weeks, PTL: Preterm labor.

Table 2
Clinical data of the study participants.

	PTL group ($n = 31$)	Control group ($n = 44$)	p
Cervical length (mm)	20 [7–24]	37 (31–44)	**<0.001**
Serum decorin (pg/mL)	3026.2 (1724.9–6959.4)	4021.2 (1848–7709.7)	**0.013**
GW at delivery (GWs ^{days})	$36^{2/7}$ ($25^{5/7}$–$40^{5/7}$)	$38^{3/7}$ (37–$41^{1/7}$)	**<0.001**
Birth weight (gr)	2950 (930–4300)	3000 (1700–4150)	0.693

GW: Gestational weeks, PTL: Preterm labor.
Bold indicates significant difference of $p < 0.05$.

p = 0.003, respectively). CL predicted PTB within the first week with 100% sensitivity, 80% specificity, 54.5% positive predictive value (PPV) (p < 0.001; LR = 5.0, 95% CI, 2.3–11), before 34th gestational weeks with 100% sensitivity, 65.2% specificity, and 50% PPV (p < 0.001; LR = 2.87, 95% CI, 1.6–5), and before 37th gestational weeks with 72% sensitivity, 77% specificity, and 81.2% PPV (p = 0.003; LR = 3.13, 95% CI, 1.1–8.8).

Combination of sDEC and CL predicted PTB within the first week with 100% sensitivity, 80% specificity, and 54.5% PPV (p < 0.001; LR = 5.0, 95% CI, 2.3–11), before 34th gestational weeks with 100% sensitivity, 65.2% specificity, and 57.1% PPV (p < 0.001; LR = 3.83, 95% CI, 1.9–7.6), and before 37th gestational weeks with 77.8% sensitivity, 77% specificity, and 84% PPV (p = 0.003; LR = 3.37, 95% CI, 1.2–9.4).

Discussion

Approximately half of the cases with PTL encounter PTB, which is responsible from the two thirds of the neonatal mortality [17]. The frequency of PTL and thus PTB are substantially increasing and continue to be the most important factor for neonatal morbidity and mortality. Shortening or funneling of the cervix in the second trimester could be easily demonstrated by ultrasonography [2]. Therefore, evaluation of the cervix with transvaginal ultrasonography is a noninvasive and a reproducible method. Nevertheless,

Table 3
Demographic and clinical data of study participants with pregnancies '*lower than 28th week of gestation*'.

	PTL group <28 weeks ($n = 6$)	Control group <28 weeks ($n = 9$)	p
Age (years)	28 ± 5.19	29.3 ± 4.67	0.603
BMI (kg/m^2)	27.1 ± 4.52	28.9 ± 4.31	0.328
GW at blood sampling time (GWs ^{days})	$26^{1/7}$ ($24^{6/7}$–$27^{6/7}$)	$26^{4/7}$ ($24^{2/7}$–$27^{6/7}$)	**0.026**
Cervical length (mm)	19.5 [8–23]	37 (32–39)	**<0.001**
Serum decorin (pg/mL)	3039.3 (1724.9–4216.1)	4016.8 (2744.8–7012.1)	0.113
GW at delivery (GWs ^{days})	33 ($25^{5/7}$–$38^{5/7}$)	$38^{1/7}$ (37–$41^{1/7}$)	**0.008**

GW: Gestational weeks, PTL: Preterm labor.
Bold indicates significant difference of $p < 0.05$.

Table 4
Demographic and clinical data of study participants with pregnancies '*greater than 28th week of gestation*'.

	PTL group >28 weeks ($n = 25$)	Control group >28 weeks ($n = 35$)	p
Age (years)	27.2 ± 4.87	28.7 ± 5.1	0.267
BMI (kg/m^2)	28.4 ± 6.11	29.9 ± 5.42	0.185
GW at blood sampling time (GWs ^{days})	$30^{2/7}$ (28–$31^{6/7}$)	$29^{4/7}$ (28–$31^{6/7}$)	0.816
Serum decorin (pg/mL)	3026.2 (1774.7–6959.4)	4025.6 (1848–7709.7)	**0.043**
GW at delivery (GWs ^{days})	$37^{1/7}$ ($29^{6/7}$–$40^{5/7}$)	$38^{4/7}$ ($37^{2/7}$–41)	**0.020**

Bold indicates significant difference of $p < 0.05$.

Table 5
Use of cervical length and serum decorin in '*predicting risk of PTB*' in patients with PTL by ROC analysis.

	Serum decorin		Cervical length		Cervical length + serum decorin	
	p	LR (95% CI)	p	LR (95% CI)	p	LR (95% CI)
<7days[a]	0.206	5.25 (0.77–35.98)	**<0.001**	5.0 (2.3–11)	**<0.001**	5.0 (2.3–11)
<34 GW[b]	0.091	6.66 (1.05–42.06)	**<0.001**	2.87 (1.6–5)	**<0.001**	3.83 (1.9–7.6)
<37 GW[c]	**0.026**	1.75 (1.0–2.9)	**0.003**	3.13 (1.1–8.8)	**0.002**	3.37 (1.2–9.4)

GW: Gestational weeks, LR: Likelihood ratio, PTB: preterm birth, PTL: Preterm labor. Occurrence of delivery.
Bold indicates significant difference of $p < 0.05$.
[a] within first 7 days following the diagnosis and sample collection, and occurrence of delivery.
[b] before 34th.
[c] before 37th gestational weeks are given.

measurement of the CL alone has been indicated to be insufficient for the estimation of PTB in low risk group [18]. Biochemical markers have been combined to the CL measurement in order to increase the detection rate of PTB. In Preterm Prediction Study, chance of delivery prior to 32nd week was given as 50% in patients who have a history of PTB and a CL shorter than 25 mm together with positive fetal fibronectin testing in cervicovaginal fluids [19]. Still, there is a need for more valuable diagnostic tools. Improved diagnostics would help to decrease economic costs, medical insufficiency and psychological disappointments.

Biochemical changes including modifications in the collagen and connective tissue component of the cervix occur towards the end of pregnancy [20,21]. Concentrations of collagen fibrils decrease while reorganization of the collagen fibrillar network takes place in cervical tissue prior to the labor [21,22]. Consequently, we hypothesized in this study that alterations in serum decorin (sDEC) levels could be found in women with the diagnosis of PTL as decorin has a role in remodeling of the type I collagen of the cervix. There were studies investigating decorin in myometrium, placenta, amniotic fluid, and cervical stroma [23–26]. There were studies that have concentrated on the role of decorin in patients with preterm rupture of membranes [12–14]. However, the role of decorin in pathophysiology of labor has not been clearly elucidated so far. According to our best knowledge, there is no other study, which investigates decorin levels as a serum marker in pregnant women who bear low to moderate risk for preterm birth in clinical obstetrics to date.

In this study, we demonstrated that sDEC levels were decreased in patients with PTL compared to healthy pregnancies at same gestational aged controls. This result was in accordance with the study of Meinert et al. [27] which has investigated decorin levels in amniotic fluid of 9 patients who delivered with cesarean section because of inactive contractions and immature cervix, and 11 patients with spontaneous vaginal delivery. In that study, decreased levels of decorin in amniotic fluid were determined in patients with spontaneous delivery. Accordingly, the authors have suggested that this feature represented a part of physiological maturation process, in which decorin levels decreased prior to the delivery. In addition to our previous finding, we also demonstrated sDEC levels to be decreased in patients with PTL when we investigated pregnancies before and after 28th gestational week. Therefore, we assume that similar pathways lead to a decrease in sDEC levels prior to delivery before and after 28th gestational week.

Some of the cervical proteoglycans were shown to be changed throughout pregnancy [21]. Thus, cervical decorin is also suggested to change with advances in time during the pregnancy. In one of those studies, Hjelm et al. have demonstrated a 46% increase in heparin sulphate and a 40% decrease in proteoglycans like decorin and biglycan at cervix throughout the pregnancy [28]. They hypothesized that these changes were necessary for the myometrial contractions to happen. However, Leppert et al. have demonstrated that decorin immunostaining increased progressively at the subepithelial zone of cervical stroma of the pregnant rats as their pregnancies advanced until term [26]. Ogita et al. also, have investigated immunoexpression levels of decorin mRNA in choriodecidual membranes during labor, and found increased decorin mRNA immunoexpression [24]. Accordingly, they speculated that increase in decorin mRNA was a part of arrangement procedures of the labor. Our results which indicated a decline in sDEC levels in patients with PTL supported some of the previous studies but against the study of Ogita et al. [24]. However, apart from the work of Leppert et al. [26] we could not demonstrate a relationship between sDEC levels and gestational ages of the study participants neither in patients with PTL nor in the healthy pregnant women. This could be evaluated with further studies investigating especially the correlation between the amount of systemic serum and local decorin levels. We could say from our results that sDEC levels do not increase with the increase in gestational age particularly between 24th and 32nd gestational weeks. In addition to the previous findings, we showed that sDEC levels were not influenced from maternal age and BMI neither in patients with PTL nor in healthy pregnant women.

Previous studies have addressed a positive predictive value of less than 50% for PTB prior to 32nd week in patients whose CL is shortened [19,29]. Similar to them, Melamed et al. asserted a limited value of cervical shortening in the prediction of preterm delivery among women with threatened preterm labor [30]. Apart from the specific aim of this research, shortening of CL < 25 mm alone correlated with PTB in our patients with PTL. PPV of cervical shortening for predicting PTB within a week, before 34th, and 37th weeks of gestation were found to be 54.5%, 50%, and 81.2%, respectively. These results were in accordance with the previous studies.

In this study, we demonstrated an association between sDEC and PTB before 37th gestational weeks in patients with PTL, but there was not any association between sDEC and PTB within 7 days and before 34th gestational weeks. It was interesting for us that we did not find a correlation between sDEC levels and CL measurements in this group. We think that these results eventuated because of the insufficiency of quantity of the study population, selection of the cases with low to moderate risk for PTB based on ultrasonographic criteria, and administration of tocolytic treatment following the diagnosis of PTL.

In conclusion, although we could talk about presence of significant reduction of sDEC levels in patients with PTL compared to healthy pregnancies with regard to previous results in this study, further analyses indicated that sDEC level had no effect in prediction of PTB within a week or before 34th gestational weeks.

Conflict of interest

The authors declare that they have no conflict of interest.

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References

[1] Romero R, Espinoza J, Gonçalves LF, Kusanovic JP, Friel L, Hassan S. The role of inflammation and infection in preterm birth. Semin Reprod Med 2007;25:21–39.
[2] Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet 2008;371:75–84.
[3] Gyetvai K, Hannah ME, Hodnett ED, Ohlsson A. Tocolytics for preterm labor: a systematic review. Obstet Gynecol 1999;94:869–77.
[4] Miyazaki C, Moreno RG, Ota E, Swa T, Oladapo OT, Mori R. Tocolysis for inhibiting preterm birth in extremely preterm birth, multiple gestations and in growth restricted fetuses: a systematic review and meta-analysis. Reprod Health 2016;13:4.
[5] Neame PJ, Kay CJ. Small leucine rich proteoglycans. In: Iozzo RV, editor. Proteoglycans: structure, biology and molecular interactions. New York: Marcel Dekker; 2000. p. 216–9.
[6] Weber IT, Harrison RW, Iozzo RV. Model structure of decorin and implications for collagen fibrillogenesis. J Biol Chem 1996;271:31767–70.
[7] Kähäri VM, Larjava H, Uitto J. Differential regulation of extracellular matrix proteoglycan (PG) gene expression. Transforming growth factor-beta 1 up-regulates biglycan (PGI), and versican (large fibroblast PG) but down-regulates decorin (PGII) mRNA levels in human fibroblasts in culture. J Biol Chem 1991;266:10608–15.
[8] Ferdous Z, Wei VM, Iozzo R, Höök M, Grande-Allen KJ. Decorin transforming growth factor interaction regulates matrix organization and mechanical characteristics of three-dimensional collagen matrices. J Biol Chem 2007;282:35887–98.

[9] Iozzo RV, Murdoch AD. Proteoglycans of the extracellular environment: clues from the gene and protein side offer novel perspectives in molecular diversity and function. FASEB J 1996;10:598–614.
[10] Iozzo RV, Schaefer L. Proteoglycans in health and disease: novel regulatory signaling mechanisms evoked by the small leucine-rich proteoglycans. FEBS J 2010;277:3864–75.
[11] Keene DR, San Antonio JD, Mayne R, McQuillan DJ, Sarris G, Santoro SA, et al. Decorin binds near the C terminus of type I collagen. J Biol Chem 2000;275: 21801–4.
[12] Meinert M, Malmström A, Petersen AC, Eriksen GV, Uldbjerg N. Chorioamniontis in preterm delivery is associated with degradation of decorin and biglycan and depletion of hyaluronan in fetal membranes. Placenta 2014;35:546–51.
[13] De Miranda de Araujo LB, Horgan CE, Aron A, Iozzo RV, Lechner BE. Compensatory fetal membrane mechanisms between biglycan and decorin in inflammation. Mol Reprod Dev 2015;82:387–96.
[14] Horgan CE, Roumimper H, Tucker R, Lechner BE. Altered decorin and Smad expression in human fetal membranes in PPROM. Biol Reprod 2014;91:105.
[15] Westergren-Thorsson G, Norman M, Björnsson S, Endersen U, Stjern-holm Y, Ekman G, et al. Differential expressions of mRNA for proteoglycans, collagens and transforming growth factor beta in the human cervix during pregnancy and involution. Biochim Biophys Acta 1998;1406:203–13.
[16] Chien EKS, Feltovich H. Maternal biological, biomechanical, and biochemical changes in pregnancy. In: Reece EA, Hobbins JC, editors. Clinical obstetrics: the fetus and mother. 3rd ed. Massachusetts: Blackwell Publishing; 2007. p. 639–42.
[17] Beck S, Wojdyla D, Say L, Ana Pilar B, Mario M, Jennifer R, et al. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. Bull World Health Organ 2010;88:31–8.
[18] Lockwood CJ. The diagnosis of preterm labor and the prediction of preterm delivery. Clin Obstet Gynecol 1995;38:675–87.
[19] Goldenberg RL, Iams JD, Mercer BM, Meis PJ, Moawad AH, Copper RL, et al. The preterm prediction study: the value of new vs standard risk factors in predicting early and all spontaneous preterm births. Am J Publ Health 1998;88:233–8.
[20] Dubicke A, Ekman-Ordeberg G, Mazurek P, Miller L, Yellon SM. Density of stromal cells and macrophages associated with collagen remodeling in the human cervix in preterm and term birth. Reprod Sci 2015;23:595–603.
[21] Word RA, Li XH, Hnat M, Carrick K. Dynamics of cervical remodeling during pregnancy and parturition: mechanisms and current concepts. Semin Reprod Med 2007;25:69–79.
[22] Zanini A, Ghidini A, Norchi S, Beretta E, Cortinovis I, Bottino S. Preinduction cervical ripening with prostaglandin E2 Gel: intracervical versus intravaginal route. Obstet Gynecol 1990;76:681–3.
[23] Favaro RR, Raspantini PR, Salgado RM, Fortes ZB, Zorn TM. Long-term type 1 diabetes alters the deposition of collagens and proteoglycans in the early pregnant myometrium of mice. Histol Histopathol 2015;30:435–44.
[24] Ogita K, Kimura T, Nakamura H, Koyama S, Tsujie T, Tomiie M, et al. Differential expression and localization of decorin in human choriodecidual membrane during preterm and term pregnancy. Am J Reprod Immunol 2004;51:204–10.
[25] Nadesalingam J, Bernal AL, Dodds AW, Willis AC, Mahoney DJ, Day AJ, et al. Identification and characterization of a novel interaction between pulmonary surfactant protein D and decorin. J Biol Chem 2003;278:25678–87.
[26] Leppert PC, Kokenyesi R, Klemenich CA, Fisher J. Further evidence of a decorin-collagen interaction in the disruption of cervical collagen fibers during rat gestation. Am J Obstet Gynecol 2000;182:805–11.
[27] Meinert M, Malmström A, Tufvesson E, Westergren-Thorsson G, Petersen AC, Laurent C, et al. Labour induces increased concentrations of biglycan and hyaluronan in human fetal membranes. Placenta 2007;28:482–6.
[28] Hjelm AM, Barchan K, Malmström A, Ekman-Ordeberg GE. Changes of the uterine proteoglycan distribution at term pregnancy and during labour. Eur J Obstet Gynecol Reprod Biol 2001;100:146–51.
[29] Zhou MX, Zhou J, Bao Y, Chen YQ, Cai C. Evaluation of the ability of cervical length and fetal fibronectin measurement to predict preterm delivery in asymptomatic women with risk factors. J Matern Fetal Neonatal Med 2015;28:153–7.
[30] Melamed N, Hiersch L, Meizner I, Bardin R, Wiznitzer A, Yogev Y. Is measurement of cervical length an accurate predictive tool in women with a history of preterm delivery who present with threatened preterm labor? Ultrasound Obstet Gynecol 2014;44:661–8.