Preventing preterm birth in high-risk pregnant women: cerclage or Pessary? A retrospective cohort study

Prevención del parto prematuro en mujeres embarazadas de alto riesgo: cerclaje o pesario? Un estudio de cohorte retrospectivo

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Received/Recibido: 12/28/2020 Accepted/Aceptado: 01/15/2021 Published/Publicado: 03/10/2021 DOI: http://doi.org/10.5281/zenodo.4710676

Abstract

Although preterm birth is considerably more prevalent in pregnant women with a history of previous preterm birth, there is no universal consensus on how to prevent preterm birth in high-risk pregnant women individually. Pessary and cerclage are currently among the two main approaches for preventing preterm birth; however, each method's effectiveness in different high-risk pregnant women is relatively unknown. Therefore, the present study compared the use of cerclage and pessary as methods to prevent preterm birth in high-risk pregnant women. In the current retrospective cohort study, data regarding 88 high-risk pregnant women who were admitted to Kamali Hospital, Karaj, Iran, and had short cervical lengths were collected. Each pregnant woman was either implanted with a pessary or had a cerclage performed. Regression modeling was performed to adjust for the possible confounders, and the odds of preterm birth before the 37th week in each treatment group was calculated. The regression modeling showed that pregnant women who received a pessary implant had lower odds of preterm birth (OR=0.3, 95%CI= 0.1-0.9, p<0.05). Age, gestational age, and cervical length at the time of receiving treatment were considered as the confounding variables. The present study shows that pessary is a more effective method for preventing preterm birth in high-risk pregnant women with cervical lengths ≤25 mm in comparison to the cerclage.

Keywords: Preterm labor, Pessary, Cerclage.

Resumen

Aunque el parto prematuro es considerablemente más prevalente en mujeres embarazadas con antecedentes de parto prematuro previo, no existe un consenso universal sobre cómo prevenir el parto prematuro en mujeres embarazadas de alto riesgo individualmente. El pesario y el cerclaje se encuentran actualmente entre los dos enfoques principales para prevenir el parto prematuro; sin embargo, la efectividad de cada método en diferentes mujeres embarazadas de alto riesgo es relativamente desconocida. Por ello, en el presente estudio se comparó el uso de pesario y el cerclaje como métodos para prevenir el parto prematuro en mujeres embarazadas de alto riesgo. En el actual estudio de cohorte retrospectivo, se recopilaron datos sobre 88 mujeres embarazadas de alto riesgo que fueron ingresadas en el Hospital de Kamali, Karaj, Irán y que tenían longitudes cervicales cortas. A cada mujer embarazada se le implantó un pesario o se le realizó un cerclaje. Se realizó un modelo de regresión para ajustar los posibles factores de confusión y se calcularon las probabilidades de parto prematuro antes de la semana 37 en cada grupo de tratamiento. El modelo de regresión mostró que, en comparación con el grupo de tratamiento con cerclaje, las mujeres embarazadas que recibieron un implante de pesario tuvieron menores probabilidades de parto prematuro (OR = 0,3, IC del 95% = 0,1-0,9, p <0,05). La edad, la edad gestacional y la longitud cervical en el momento de recibir el tratamiento se consideraron variables de confusión. El presente estudio muestra que el pesario es un método más efectivo para prevenir el parto prematuro en mujeres emba-

razadas de alto riesgo con longitudes cervicales ≤ 25 mm en comparación con el cerclaje. Trabajo de parto prematuro, pesario, cerclaje.

Palabras clave: Trabajo de parto prematuro, Pesario, Cerclaje

Introduction

Preterm birth is among the leading causes of perinatal mortality[1]. The prevalence of preterm birth ranges from 5 to 18% worldwide, according to the World Health Organization (WHO)[2]. As a developing country, Iran also has a high prevalence of preterm delivery, which is around 9% of all pregnancies[3]. Although extensive developments in neonatal care have significantly decreased the mortality associated with preterm births, early identification and effective treatment of pregnant women at risk of preterm delivery is the true answer for effectively reducing neonatal mortality[4].

Measured by transvaginal ultrasound at around the 20th week of gestation can identify pregnant women at the risk of preterm delivery by measuring cervical length[5]. After identifying at-risk pregnant women, in addition to the recommended oral or vaginal progesterone, there are currently 2 main approaches for preventing preterm birth: performing a cerclage or implanting a pessary, both of which have been practiced for years[6]. Although there are many reports on the efficacy of each method separately, reports on the comparison of effectiveness between the mentioned methods are scarce[7]. Also, certain aspects of the history of pregnant women such as the previous history of preterm birth, parity, cervical length, and gestational age can significantly affect the efficacy of each method[8]. Additionally, a combination of these methods can be practiced as well. As a result, choosing the optimum method for preventing preterm birth in each pregnant woman is still a matter of controversy.

In the present retrospective cohort study, we aim to compare the effectiveness of pessary and cerclage in preventing preterm birth before the 37th week in singleton pregnant women with a history of previous preterm birth in Iran.

Materials and methods

In this retrospective cohort study, the medical data of pregnant women at risk of preterm birth who were treated with either cerclage or pessary between January 2017 through January 2018 was collected from Kamali Hospital, Karaj, Iran. Pregnant women with a history of previous preterm birth were considered at risk and their cervical lengths were evaluated with transvaginal ultrasonography in the 12th-24th week of gestation. Pregnant women with a cervical length ≤25 millimeters before the 24th week of gestation were considered as candidates for either cerclage or pessary. Treatment choice was made by the physician on an individual basis. The cerclage was performed using Mc Donald's technique between 12-24th week of gestation. Smith's pessary was implanted by the physician during 12-28th weeks of gestation. All women who were considered for treatment also received 200mg vaginal progesterone daily. Data regarding age, gestational age, prior pregnancies, cervical length, choice of treatment (cerclage or pessary), type of delivery, date of labor, and date of last known menstrual period were extracted from the files of each patient. Pregnant women with multiple pregnancies, preeclampsia, uterine anomalies, stillbirth, a history of metabolic disorders, and patients with missing data in any of the mentioned variables were excluded from the study population. Twelve pregnant women who had their cerclage or pessary removed earlier than the 37th week of gestation were excluded from the final analysis as well. There were no reports of neonatal morbidity or mortality in the period of registered records. Finally, 88 individuals were recruited in the study population; forty-four pregnant women received the pessary implant and the other 44 pregnant women had a cerclage performed.

Statistical Analysis

The normal distribution of the data was tested through scatter plots. Fisher's Exact test was used to compare the prevalence of preterm birth before the 37th week and C-section between both treatment groups. The student's t-test was used to compare the cervical length and gestational age at the time of receiving treatment to identify possible sources of selection bias. Logistic regression was used to adjust for the possible confounding variables. Preterm birth before the 37th week was used as the outcome variable. Age (years), gestational age (weeks), and cervical length at the time of receiving treatment were considered as the possible confounders. Choice of treatment (pessary or cerclage) was considered as the only predictor.

The study was approved by the ethics committee of Alborz University of Medical Sciences.

Continuous variables are presented as mean ± standard deviation. All statistical analyses were conducted using SPSS version 15.0 or R 3.5.1. A value of $p<0.05$ was considered significant.

Results

The baseline characteristics of the study population are presented in (Table 1). In summary, 88 pregnant women, aged 28.6±6.1, with singleton pregnancies and gestational age of 17±2.2 weeks at the time of the receiving treatment were included in the study. Gestational age at the time of delivery was 34.3±4.7 weeks and 55.3 percent had preterm births before the 37th week of gestation. Prevalence of preterm birth was 32% and 75% in the pessary and the cerclage group, respectively.

Table 1. Baseline characteristics of the study population		
Row	Treatment group	
	Cerclage (n=44)	Pessary(n=44)
Age (mean ± SD)	27.2 ± 5.7	30.1 ± 6.3
Gestational age at the time of the study (mean ± SD)	16.3 ± 2.0	17.6 ± 2.2
Cervical length (mean ± SD)	22.3 ± 3.3	24 ± 2.4
Type of delivery (number, %)		
C-section	(13) 29.5%	(14) 31.8%
Vaginal delivery	(31) 70.5%	(30) 68.2%
Preterm birth before 37th week (number, %)	(33) 75% *	(14) 32%

*p<0.05 compared with Pessary procedure

Prevalence of C-section was not different in pregnant women with different choices of treatment. However, the prevalence of preterm birth before the 37th week was significantly higher in pregnant women treated with performing a cerclage (33 pregnant women) compared to those implanted with a pessary (14 pregnant women, p<0.05).

Independent sample Student's t-test revealed that pregnant women who had pessary implanted, received treatment later (16.3±2 vs 17.6±2.2 weeks for cerclage and pessary respectively, p<0.05) and had lower levels of cervical dilation at the time of receiving treatment (22.3±3.3 vs 24±2.4 millimeters for cerclage and pessary respectively, p<0.05). The logistic regression model showed that in comparison to the cerclage treatment group, pregnant women with pessary implants had reduced odds of preterm birth before the 37th week (OR=0.3, 95% CI= 0.1-0.9, p<0.05) after adjusting for confounding variables. Overall, the logistic model included the choice of treatment as the primary predictor, and age, gestational age, and cervical length at the time of treatment were considered as the confounding variables. Preterm birth before the 37th week was considered as the primary outcome. The model was statistically significant (Chi-squared= 18.6, p<0.001), explained 30% of the variation in the outcome variable (Nagelkerke R-squared method), and correctly predicted the outcome in 73% of the cases.

Discussion

The results of the present study show that implanting a pessary significantly reduces the odds of preterm birth in comparison to performing a cerclage in singleton pregnant women with a history of preterm birth and a cervical length ≤ of 25 mm. However, choice of treatment did not affect the prevalence of C-sections performed in either group.

Our results are similar to another retrospective cohort conducted on singleton pregnant women by Tsikouras et al., with high risk for preterm birth that found pessary a more effective method than cerclage in preventing preterm birth before 33 weeks of gestation. These findings are also in agreement with the PECEP trial (2012) on singleton pregnant women with a short cervical length identified through the routine second-trimester transvaginal screening. In this trial, Goya et al. compared pessary implants to conservative management, and the prevalence of spontaneous preterm birth before the 37th week was 22 vs 59 percent in each treatment group, respectively. However, in a trial similar to PECEP conducted by Hui et al., not only pessary was not effective in preventing preterm birth, the prevalence of preterm birth before the 34th week was even higher in the pessary group[10]. Of note, the overall prevalence of preterm birth in their respective study population was significantly lower than that of the PECEP trial. Interestingly, both these trials have a lower prevalence of preterm birth than that of the present study. The higher prevalence of preterm birth in our study can at least partly be attributed to the inclusion criteria of our study population, which only selected high-risk pregnant women. While both trials conducted by Goya et al. and Hui et al. only were recruited pregnant women with a short cervix found on routine sonograms, while our study population comprised of pregnant women with a history of preterm birth as well as a short cervix. The retrospective cohort conducted by Tsikouras et al. also recruited a high-risk population and had a higher prevalence of preterm birth than expected, but their inclusion criteria were not as specific as the present study. Although pessary is not as well studied as other methods of preventing preterm birth, the existing literature suggests that apparently, pessary implants are more beneficial in pregnant women with a higher risk of preterm birth. Additionally, other risk factors besides the history of previous preterm birth such as ethnicity, body mass index (BMI), and history of smoking may contribute to increased prevalence of preterm birth as well, and not all risk factors and their relative contribution to the prevalence of preterm birth are known. Although a history of previous preterm birth is among the best known risk factors, only 10% of pregnant women with confirmed preterm birth had a previous history. Identifying a short cervical length in otherwise healthy pregnant women will only recognize 40% of the ensuing preterm births as well [11]. Further studies are required to elucidate the impact of each possible risk factor. As a result, study populations are not entirely comparable; considering the unknown exact mechanism of action of the pessary, outcomes may not be entirely comparable as well. This may partly explain the heterogeneity. However, despite all the controversies, the pessary is still considered a viable mechanism for the prevention of preterm birth in most of the published studies and systematic reviews [12-15].

Conclusion

Our study had several limitations. First, the study is designed as a retrospective cohort and as a result, the study is inherently prone to selection and information biases; also causality cannot be inferred. Second, some of the previously identified risk factors are not measured in the present study and could have affected our analyses. However, the level of contribution of these factors and their subsequent impact on the present study is not known. Third, our treatment groups have significant differences in baseline characteristics but through regression modeling, the impact of these differences is mitigated significantly. Finally, a small sample size of the present

study could have reduced the power to detect specific differences between our defined subgroups.

In conclusion, the pessary is a safe, cheap, and easily accessible method for preventing preterm birth and can be more effective than cerclage in high-risk pregnant women with short cervical lengths.

Acknowledgment: The authors appreciated the contribution of the Clinical Research Development Center of Kamali Hospital in Alborz University of medical sciences to the present study.

Declaration of interests: The authors declare no conflict of interests.

References

1. Goldenberg RL, Culhane JF, Iams JD, et al. Epidemiology and causes of preterm birth. Lancet. 2008 Jan 5;371(9606):75-84. doi: 10.1016/S0140-6736(08)60074-4. PubMed PMID: 18177778.
2. WHO. Preterm birth: WHO; 2018 [updated February, 2018; cited 2019 February 15th]. Available from: https://www.who.int/news-room/fact-sheets/detail/preterm-birth
3. Vakilian K, Ranjbaran M, Khorsandi M, et al. Prevalence of preterm labor in Iran: A systematic review and meta-analysis. Int J Reprod Biomed (Yazd). 2015 Dec;13(12):743-8. PubMed PMID: 27141533; PubMed Central PMCID: PMCPMC4827509.
4. Goya M, Pratcorona L, Merced C, et al. Cervical pessary in pregnant women with a short cervix (PECEP): an open-label randomized controlled trial. Lancet. 2012 May 12;379(9828):1800-6. doi: 10.1016/S0140-6736(12)60030-0. PubMed PMID: 22475493.
5. Committee on Practice Bulletins-Obstetrics TACoO, Gynecologists. Practice bulletin no. 130: prediction and prevention of preterm birth. Obstet Gynecol. 2012 Oct;120(4):964-73. doi: 10.1097/AOG.0b013e3182723b1b. PubMed PMID: 22996126.
6. Jarde A, Lutsiv O, Park CK, et al. Preterm birth prevention in twin pregnancies with progesterone, pessary, or cerclage: a systematic review and meta-analysis. BJOG. 2017 Jul;124(8):1163-1173. doi: 10.1111/1471-0528.14513. PubMed PMID: 28176485.
7. Biggio JR, Jr. Progesterone, pessary or cerclage for preterm birth prevention in twins: no answers yet. BJOG. 2017 Jul;124(8):1175. doi: 10.1111/1471-0528.14551. PubMed PMID: 28220618.
8. Falcao V, Melo C, Matias A, et al. Cervical pessary for the prevention of preterm birth: is it of any use? J Perinat Med. 2017 Jan 1;45(1):21-27. doi: 10.1515/jpm-2016-0076. PubMed PMID: 27171387.
9. Tsikouras P, Anastasopoulos G, Maroulis V, et al. Comparative Evaluation of Arabin Pessary and Cervical Cerclage for the Prevention of Preterm Labor in Asymptomatic Women with High Risk Factors. Int J Environ Res Public Health. 2018 Apr 18;15(4). doi: 10.3390/ijerph15040791. PubMed PMID: 29670041; PubMed Central PMCID: PMCPMC5923833.
10. Hui SY, Chor CM, Lau TK, et al. Cerclage pessary for preventing preterm birth in women with a singleton pregnancy and a short cervix at 20 to 24 weeks: a randomized controlled trial. Am J Perinatol. 2013 Apr;30(4):283-8. doi: 10.1055/s-0032-1322550. PubMed PMID: 22875662.
11. Mercer BM, Goldenberg RL, Moawad AH, et al. The preterm prediction study: effect of gestational age and cause of preterm birth on subsequent obstetric outcome. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Am J Obstet Gynecol. 1999 Nov;181(5 Pt 1):1216-21. PubMed PMID: 10561648.
12. Matei A, Saccone G, Vogel JP, et al. Primary and secondary prevention of preterm birth: a review of systematic reviews and ongoing randomized controlled trials. Eur J Obstet Gynecol Reprod Biol. 2019 Jan 25. doi: 10.1016/j.ejogrb.2018.12.022. PubMed PMID: 30772047.
13. Hao J, Xu B, Wang Y, Li Y, Zhao J. Low-level Progesterone on the Day of hCG Injection Has No Detrimental Effect on the Pregnancy Outcome after IVF with GnRH-a Protocol: A Retrospective Study. Archives of Obstetrics and Gynaecology. 2020 May 29;1(1).
14. O'Garae MC, O'Mearaf M, Tana X. Uterine fibroids increase the risk of hypertensive disorders of pregnancy: a prospective cohort study. Journal of Hypertension. 2020; 38:000.
15. Burd JF, Noetzel V, Walsh MJ. Lysulin Improvement in Glycemic Control Compared to Type 2 Drugs. Diabetes. 2018;1(1):103.

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