

B2 ADRENERGIC AND OXYTOCIN RECEPTOR POLYMORPHISMS AFFECT THE PROGRESS OF LABOR IN NULLIPAROUS WOMEN

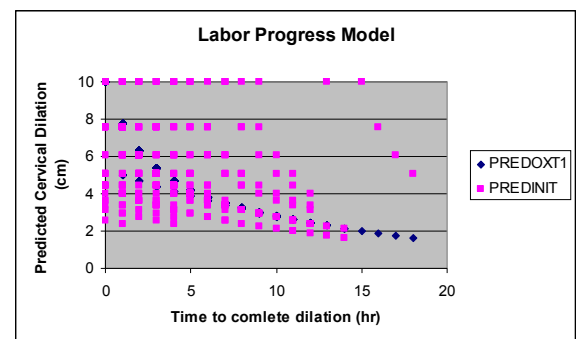
Abdullah S. Terkawi, M.D., William M. Jackson, M.D., Shehnaz Hansoti, M.D., Rabeena Tabassum, M.D., Mazen Al-Suhaibani, M.D., Khalid Al-Shuaibi, M.D., Anandhi Nadarajah, M.D., Pamela Flood, M.D.
Department of Anesthesiology Columbia University, New York, New York

Background: While demographic characteristics have been shown to affect labor progress, it is not known to what degree genotypic factors contribute. Beta-2 adrenergic (B2AR) and oxytocin receptors (OXTR) are known to modulate uterine contractility. We examined the effect of genotype at 2 common polymorphic sites in the B2AR (rs1042713, rs1042714) and 3 at the OXTR (rs2258485, rs2224298, rs53576) on the progress of the latent phase, active phase, and transition point of labor.

Methods: 76 parturients were prospectively enrolled in KFMC, Riyadh – Saudi Arabia. Cervical dilation and labor management data were recorded with respect to time. Genomic DNA was prepared with a Purgene kit and genotyping at the above sites was provided by Sequenom. Labor progress was modeled with a bi-exponential function, and analysis of the effect of covariates was tested with NONMEM using PLTTools.

Results: Meperidine administration ($P < 0.00005$), caesarean delivery ($P < 0.02$), and OXTR rs2254298 genotype AA ($P < 0.04$) were associated with a slower active labor, OXTR rs2228485 genotype CC ($P < 0.007$) was associated with a faster active labor, and B2AR-16 genotype AA ($P < 0.04$), as well as B2AR-27 genotype CC ($P < 0.04$), were associated with an earlier transition to active labor.

Conclusions: Polymorphisms in both the B2AR and OXTR influence the progress of labor. Individual differences in uterine contractility and labor progress may be explained in part by inherited differences in modulatory proteins. With greater patient enrollment we plan to construct a full mixed effects model that will take into account demographic differences as well as the impact of multiple genes.



Initial Model	Value	P value	MPE (cm)	MAPE (cm)
Active rate constant ^{-hr}	0.581		0	0.91
Latent rate constant ^{-hr}	0.0634			
Transition (cm)	5.1			
Meperidine		4E-05	0.006	0.78
Active rate constant ^{-hr} (meperidine)	(meperidine)	0.574		
Active rate constant ^{-hr} (no meperidine)	0.821			
Latent rate constant ^{-hr}	0.0545			
Transition (cm)	5.1			
OXT-1 Genotype CC		6E-03	0.173	0.74
Active rate constant ^{-hr} (CC)	17.6			
Active rate constant ^{-hr} (not CC)	0.525			
Latent rate constant ^{-hr}	0.0654			
Transition (cm)	5.4			
Caesarean Section		0.016	0.063	0.93
Active rate constant ^{-hr} (CS-2nd stage)	0.273			
Active rate constant ^{-hr} (no CS)	0.617			
Latent rate constant ^{-hr}	0.0629			
Transition (cm)	5.1			
B2AR-16 Genotype AA		0.032	0.079	0.72
Active rate constant ^{-hr}	0.52			
Latent rate constant ^{-hr}	0.0555			
Transition (cm) (AA)	3.9			
Transition (cm) (not AA)	5.2			
OXT-2 Genotype AA		0.033	0	0.84
Active rate constant ^{-hr} (AA)	0.051			
Active rate constant ^{-hr} (not AA)	0.547			
Latent rate constant ^{-hr}	0.0687			
Transition (cm)	5.2			
B2AR-27 Genotype CC		0.039	0	0.70
Active rate constant ^{-hr}	0.522			
Latent rate constant ^{-hr}	0.0594			
Transition (cm) (CC)	4.7			
Transition (cm) (not CC)	5.6			

Table 1: Labor Progress Model. Initial model and the covariates that significantly affect the model in univariate analysis.

MPE - Median Predicted Error

MAPE - Median Absolute Predicted Error