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2. What is Melatonin doing during Pregnancy?

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The diurnal release of melatonin from the pineal gland is known to play an important role in circadian rhythmicity and reproduction, especially in seasonally breeding animals. The role and regulation of maternal melatonin during pregnancy is not fully understood.

Serum melatonin concentrations were measured in normal pregnant women throughout the pregnancy. The nighttime serum melatonin levels gradually increased from 24 weeks of gestation to 36 weeks, rapidly decreased after delivery, and got to the non-pregnant levels on the 2nd day of puerperium. The daytime serum melatonin levels were very low during pregnancy. The data suggest a possibility that the maternal melatonin may play a role in parturition. Therefore, the role and regulation of melatonin are further investigated using pregnant rat model. Serum melatonin (nighttime) concentrations gradually increased from day 12 of pregnancy to day 21, and rapidly decreased after delivery. The change in serum melatonin levels during pregnancy in rats was similar to that in humans. We focused on the finding that serum melatonin levels are highest at the end of pregnancy and examined the role of melatonin on parturition time. Cycling rats were subjected to pinealectomy (PINX) or sham operation. All rats were maintained under the same photoperiod conditions (14h Light: 10h Dark) and induced pregnancy. Pregnant PINX rats received subcutaneous injection of melatonin (10 ug) at 8: 00h (PINX + day-melatonin) or at 20:00h (PINX + night-melatonin) from day 15 to the end of pregnancy. As an additional group, PINX rats underwent subcutaneous implantation of a melatonin capsule and were induced pregnancy (PINX + whole day-melatonin). Parturition times were recorded on days 22 and 23 of pregnancy. Parturition times in the sham-operation group (n = 19) were between 12:00h and 17:00h (light period) on day 22, or 8:00h and 16:00h (light period) on day 23 of pregnancy. Five (26.3%) of 19 rats in the PINX group, 3(16.7%) of 18 rats in the PINX + day-melatonin group, and 3(16.7%) of 18 rats in the PINX + whole day-melatonin group initiated parturition during the dark period. However, all rats in the PINX + night-melatonin group (n = 15) initiated parturition during the light period. The results suggest that melatonin rhythm synchronizing with photoperiodic rhythm is likely to be an important determinant of parturition time.

We secondly examined the regulation of melatonin secretion during pregnancy in rats. When the number of conceptuses (fetus and placenta) was experimentally reduced to one, serum melatonin concentrations were significantly lower than normal pregnancy bearing more than 10 conceptuses. When the fetuses were removed by fetectomy, serum melatonin concentrations were not decreased. RT-PCR revealed that rate limiting enzyme for melatonin synthesis, N-acethyltransferase, is not expressed in the rat placenta. Injection of the conditioned medium made by placenta incubation significantly increased serum melatonin concentrations. Taken together, it is suggested that maternal circulating melatonin is from the maternal pineal gland and increased by placental hormones during pregnancy.