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Mathematical Model for the Secretion of Oxytocin after Vaginal Delivery or Caesarean in Breastfeeding Women

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ABSTRACT
Oxytocin, which is produced in the supraoptic (SON) and paraventricular (PVN) nuclei of the hypothalamus, is released in to circulation from magnocellular neurons which extend down to the posterior pituitary. In addition, oxytocin is produced and released from parvocellular neurons in the PVN, which project to many areas within the brain such as other parts of the hypothalamus, the amygdala , the striatum, the raphenuclei, the LC, the vagal motor and sensory nuclei, the dorsal horn of the spinal cord as well as the preganglionic sympathetic neurons of the intermediolateral column of the spinal cord . The structure of the nonapeptide oxytocin differs by only two amino acids from that of vasopressin, which is produced in separate neurons of the PVN and SON. Only one oxytocin receptor, i.e. the uterine type of receptor, has been identified. This type of receptor also has been demonstrated in the central nervous system. Oxytocin release into the nervous system during the early postpartum period may strengthen the expression of maternal behaviors and prolong breastfeeding. Comparisons between woman following vaginal delivery (VD) versus caesarean section (CS) suggest that exposure to oxytocin during labor and in the postpartal period can influence the subsequent function of oxytocin-producing neurons during the lactation period. In the Mathematical model, both the cases are compared by finding the Renewal density and Failure Density functions. Renewal density is higher if we compare the caesarean case with vaginal delivery during the labor and in the early post partum period. In a similar manner, we obtain the bounds of the failure density functions in both the cases.
MATHEMATICAL SUBJECT CLASSIFICATION: 60GXX, 60E05.
KEYWORDS: The Renewal Function, Density, Oxytocin, Stress

I. Mathematical model

The event $\{N_R(t) \geq n\}$ is equivalent to the event $\{\tau_n < t\}$. Thus,

$$\Pr\{N_R(t) \geq n\} = \Pr\{\tau_n < t\}$$
$$= \Pr\{C_1 + \ldots\ldots + C_n < t\}$$
$$= K_n(t), \qquad \ldots\ldots\ldots\ldots\ldots\ldots (1.1)$$

Where $K_n(t)$ is the distribution of the sum of n independent random variables, C_i $(i = 1, \ldots, n)$ each with CDF K(t). A recursive formula for $K_n(t)$ is given by

$$K_n(t) = \int_0^t K_{n-1}(x)\,k(t-x)\,dx. \qquad \ldots\ldots\ldots\ldots\ldots\ldots (1.2)$$

When a renewal is instantaneous after a failure. Then $\tau_n \sim G(n, \beta)$ and

$$K_n(t) = 1/\Gamma(n)\beta^n \int_0^t u^{n-1} e^{-u/\beta}\,du$$
$$= 1 - \text{pos}(n-1;\, t/\beta).$$

Thus in this case it is clear that the distribution of $N_R(t)$ is poisson with parameter t/β.

The renewal function V(t) is given by

$$V(t) = \sum_{n=1}^{\infty} \Pr\{N_R(t) \geq n\}$$
$$= \sum_{n=1}^{\infty} K_n(t) \qquad \ldots\ldots\ldots\ldots\ldots\ldots (1.3)$$

It is straightforward to verify that in the case, $V(t) = t/\beta$. The renewal function V (t) also satisfies the following integral equation:

$$V(t) = K(t) + \int_0^t V(t-x)\,k(x)\,dx \qquad \ldots\ldots\ldots\ldots\ldots\ldots (1.4)$$

Although it is not always not possible to obtain a closed form solution for V(t), we can obtain useful upper and lower bounds. Since $\max_{i\le n} W_i \le \tau_n = W_1 + \ldots\ldots\ldots\ldots + W_n$,

We have $\Pr\{\max_{i\le n} W_i \le t\} \ge \Pr\{\tau_n \le t\}$ or $K_n(t) \le K^n(t)$.

Thus, $V(t) = \sum_{n=1}^{\infty} K_n(t) \le \sum_{n=1}^{\infty} K^n(t)$

$= \frac{K(t)}{1-K(t)}$ …….. (1.5)

On the other hand, $V(t) \ge K_1(t) = K(t)$.Moreover, by definition of $N_R(t)$, $t \le \tau_{N(t)+1}$.

Hence, $t \le E\{\tau_{N(t)+1}\} = \mu(V(t)+1)$, Where $\mu = E\{W\}$ is the mean time between renewals (assumed to be finite).

Hence, $V(t) \ge \frac{t}{\mu} - 1$. Thus we have the inequalities

$$\max\left(K(t), \frac{t}{\mu} - 1\right) \le V(t) \le \frac{K(t)}{1-K(t)}.$$

For small values of t, $V(t) \approx K(t)$.

The renewal density $v(t)\ can$ be expressed as

$$v(t) = \int_0^t w(x)g(t-x)dx, \qquad 0 < t < \infty \qquad \ldots\ldots\ldots\ldots\ldots (1.6)$$

where the failure density is related to $v(x)\ according$ to

$$w(t) = f(t) + \int_0^t v(x) f(t-x)dx, \quad 0 < t < \infty. \qquad \ldots\ldots\ldots\ldots\ldots..(1.7)$$

Let $v^*(s)$, $w^*(s)$, $f^*(s)$ and $g^*(s)$ denote the Laplace transforms of v(t), w(t), f(t) and g(t), respectively, i.e., $v^*(s) = \int_0^{\infty} e^{-ts} v(t)\, dt$, etc. Equations (1.6) and (1.7) yields Laplace transforms

$$v^*(s) = \frac{f^*(s)g^*(s)}{1 - f^*(s)g^*(s)} \qquad \ldots\ldots\ldots\ldots\ldots(1.8)$$

and $w^*(s) = v^*(s)/g^*(s), \qquad 0 < s < \infty$ ……. (1.9)

In principle, the renewal density v(t) can be obtained by inverting (1.8).

Suppose that the time till failure has an exponential distribution E(β),and the time till repair has an exponential distribution E(γ). Let $\lambda=1/\beta$ and $\mu=1/\gamma$. Accordingly,

$$f(t) = \begin{cases} 0, & t \le 0 \\ \lambda e^{-\lambda t}, & t > 0 \end{cases} \quad \text{and}$$

$$g(t) = \begin{cases} 0, & t \le 0 \\ \mu e^{-\mu t}, & t > 0 \end{cases}$$

The corresponding Laplace transforms are $f^*(s) = \lambda/(\lambda+s)$ and $g^*(s) = \mu/(\mu+s)$, respectively. According to (1.8) , the Laplace transform of the renewal density is

$$v^*(s) = \frac{\lambda\mu}{s^2 + (\lambda+\mu)s} = \frac{\lambda\mu}{\lambda+\mu}\left(\frac{1}{s} - \frac{1}{s+\lambda+\mu}\right) \qquad \ldots\ldots\ldots\ldots(1.10)$$

Every Laplace transforms are $f^*(s)$ on $(0,\infty)$ has a unique inverse f(t) on $(0,\infty)$.

The inverse transform of (1.10) as can be easily checked, is

$$V(t) = \frac{\lambda\mu}{\lambda+\mu} - \frac{\lambda\mu}{(\lambda+\mu)} e^{-t(\lambda+\mu)}, \quad 0 < t < \infty \qquad \ldots\ldots\ldots\ldots\ldots.. (1.11)$$

In a similar fashion we obtain the failure density

$$w(t) = \frac{\lambda\mu}{\lambda+\mu} + \frac{\lambda^2}{(\lambda+\mu)} e^{-t(\lambda+\mu)}, \quad 0 < t < \infty \qquad \ldots\ldots\ldots\ldots\ldots (1.12)$$

Integrating (1.11) and (1.12) we obtain, for $0 < t < \infty$,

$$V(t) = \frac{\lambda\mu}{\lambda+\mu}t - \frac{\lambda\mu}{(\lambda+\mu)^2}(1-e^{-t(\lambda+\mu)}) \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1.13)$$

and $$W(t) = \frac{\lambda\mu}{\lambda+\mu}t + \frac{\lambda^2}{(\lambda+\mu)^2}(1-e^{-t(\lambda+\mu)}) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1.14)$$

Finally, the unavailability function is

$$Q(t) = W(t) - V(t)$$

$$= \frac{\lambda}{\lambda+\mu} - \frac{\lambda}{\lambda+\mu}e^{-t(\lambda+\mu)} \quad , \ 0 < t < \infty \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1.15)$$

and the availability function is

$$A(t) = 1 - Q(t)$$

$$= \frac{\mu}{\lambda+\mu} + \frac{\lambda}{\lambda+\mu}e^{-t(\lambda+\mu)} \quad , \quad 0 < t < \infty. \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1.16)$$

Notice that $\lim_{t\to\infty} A(t) = A_\infty = \frac{\mu}{\lambda+\mu} = \frac{\beta}{\beta+\gamma}$

Generally, the availability function A(t) is given by the formula

$$A(t) = 1 - F(t) + \int_0^t v(x)[1 - F(t-x)]dx \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1.17)$$

Or $$A(t) = R(t) + \int_0^t v(x)R(t-x)dx, \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1.18)$$

Where F(t) is the CDF of the TTF and R(t) is the reliability function of a nonrepairable system. Thus, if $R^*(s)$ is the Laplace transform of the reliability function, and $A^*(s)$ is that of the availability function, We obtain from (1.8) and (1.18) that

$$A^*(s) = R^*(s)\,(1+v^*(s))$$

$$= \frac{R^*(s)}{1 - f^*(s)g^*(s)} \qquad 0 < s < x. \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1.19)$$

The Laplace transform (1.19) should be inverted either analytically or numerically to obtain the availability function of the system.

II. Application

2.1. Oxytocin

Oxytocin released by the suckling stimulus during lactation causes ejection of milk by contracting the myoepithelial cells in the mammary glands. As will be discussed below, other suckling - induced behavioral, physiological and endocrinological changes occurring during lactation also may be caused by oxytocin.

Oxytocin, which is produced in the supraoptic (SON) and paraventricular (PVN) nuclei of the hypothalamus, is released in to circulation from magnocellular neurons which extend down to the posterior pituitary. In addition, oxytocin is produced and released from parvocellular neurons in the PVN, which project to many areas within the brain such as other parts of the hypothalamus, the amygdala , the striatum, the raphenuclei, the LC, the vagal motor and sensory nuclei, the dorsal horn of the spinal cord as well as the preganglionic sympathetic neurons of the intermediolateral column of the spinal cord [2]. The structure of the nonapeptide oxytocin differs by only two amino acids from that of vasopressin, which is produced in separate neurons of the PVN and SON. Only one oxytocin receptor, i.e.the uterine type of receptor, has been identified. This type of receptor also has been demonstrated in the central nervous system [1].

2.2 Role of oxytocin in psychological adaptations in breastfeeding women:

Mothers having had their newborns skin to skin immediately after birth, spend more time with their babies, they interact more with their infants during breast feeding [3], and breastfeed for a longer period [5,4]. It is possible that postpartum skin to skin contact facilitates interactions between mother and baby because the newborn, when put on the mother's chest, expresses an inborn 'prefeeding' behavior. This behavior involves massage of the breast by hand movements and suckling by the baby [7]. These stimuli both result in the circulation and into the brain in response to suckling [6]. Oxytocin release into the nervous system during the early postpartum period may strengthen the expression of maternal behaviors and prolong breastfeeding.

Comparisons between woman following vaginal delivery (VD) versus caesarean section (CS) suggest that exposure to oxytocin during labour and in the postpartal period can influence the subsequent function of oxytocin-producing neurons during the lactation period [11]. After VD oxytocin is initially non pulsatile, but spikes of oxytocin are detectable by day 2 postpartum (Fig 2.2.1). However, mothers that are delivered by CS have significantly fewer oxytocin spikes measured in plasma during a breastfeed. These results suggest that the CS mothers have a more immature type of oxytocin pattern. Two factors are of particular importance for the lack of breastfeeding induced oxytocin peaks in the mothers after a CS; one is the absence of the second stage of labour, and the second is a delayed contact between mother and baby after birth. Both labour and the immediate postpartal skin- to -skin contact are associated with an intense release of oxytocin. A relative lack of oxytocin in the CS mothers might be responsible for the different oxytocin patterns seen 2 days later [11].

If oxytocin release is intensely stimulated, morphological and functional changes occur in the PVN. The glia cells normally interposed between the oxytocin cells retract following closer contact and communication between the oxytocin cells. During these circumstances the cells start to fire simultaneously leading to a synchronized bursting activity, which is paralleled by a pulsatile release of oxytocin into the circulation [9]. It is therefore tempting to suggest that such structural and woman having given birth by CS as in woman after a VD, due to the lack of exposure to oxytocin during labour and in the early post partum period.

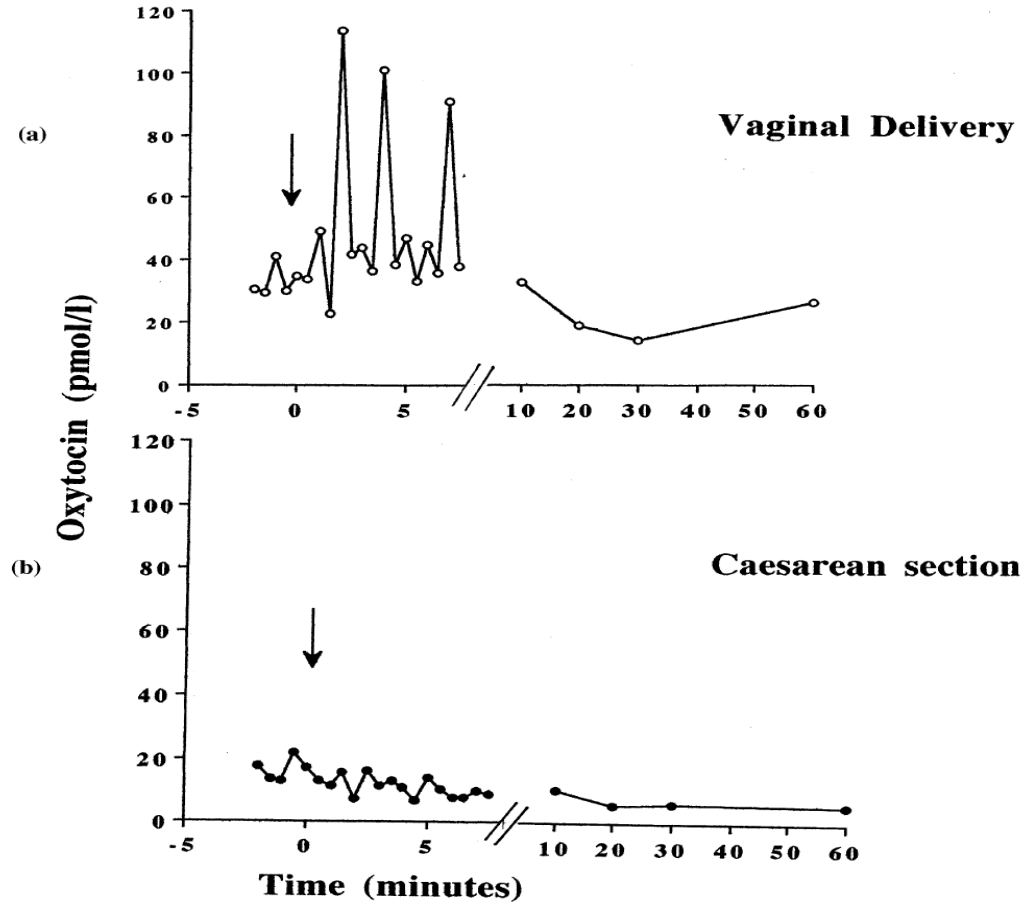


Figure -2.2.1 Oxytocin levels (pmol/1) in response to breastfeeding in individual women after (a) vaginal delivery or (b) after caesarean section [12]. At '0' the infant started sucking the breast.

Personality patterns of breastfeeding women change within a few days after birth. Breastfeeding women become more social, calmer and more tolerant to monotony. Oxytocin levels are positively correlated with scores obtained on personality tests, reflecting social interactions and calmness; this finding supports the hypothesis that oxytocin may play a role in these psychological adaptations [11,10]. In breastfeeding women, the analysis of correlations between oxytocin levels and personality traits indicated that increased levels of social interaction , and decreased levels of anxiety correlated with different aspects of oxytocin release – for example, the number of oxytocin pulses occurring in response to breastfeeding correlated with openness to social interactions, while basal oxytocin levels correlated with calmness.

The number of oxytocin pulses and the openness to social interactions also correlated with the amountof milk given by the mother. Thus , a Pulsative oxytocin release pattern was associated with both physiological and physical components of the 'giving' aspects of the Oxytocin induced effect pattern. The increased levels of calm may instead represent a psychological aspect of the 'antistress-stress' effects of oxytocin [11].

As described above, the nonadrenergic system emanating from the LC plays an important role in vigilance and arousal and, in the suppression of emotionality and social competence, possibly by inducing 'left brain dominance'[13]. These activating effects of noradrenalin are mediated by stimulation of a variety of receptors belonging to the α- and β- subclasses of adrenergic receptors [12]. Oxytocin may, as mentioned above, and in particular after repeated administration, enhanced the activity of central α_2-adrenoceptors to reduce blood pressure. Recently, oxytocin also has been shown to enchance the ability of clonidine, an α_2-receptor agonist, to inhibit firing of noradrenergic LC neurons.

The personality profile of breastfeeding women is characterized by increased social competence and calmness; this profile may be regarded as an antithesis to the behavioral pattern of the fight-flight response. Because the fight-flight response reflects a strong LC activation, it is tempting to speculate that the physiological as well as the physiological antistress effects of oxytocin may be related to an enhanced α_2-adrenoceptor activity in the CNS. A particularly clear example of this effect may be seen in breast feeding women.

III. Mathematical Results

Fig.3.1

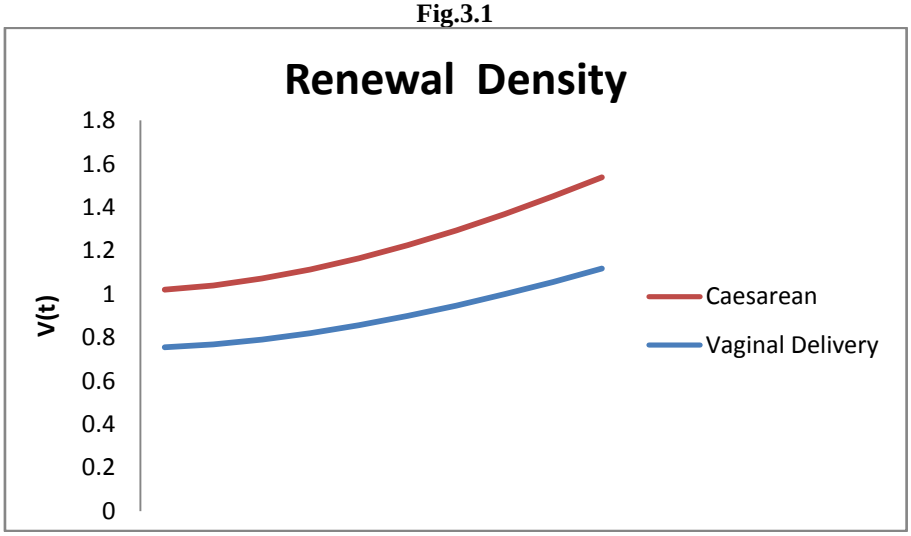
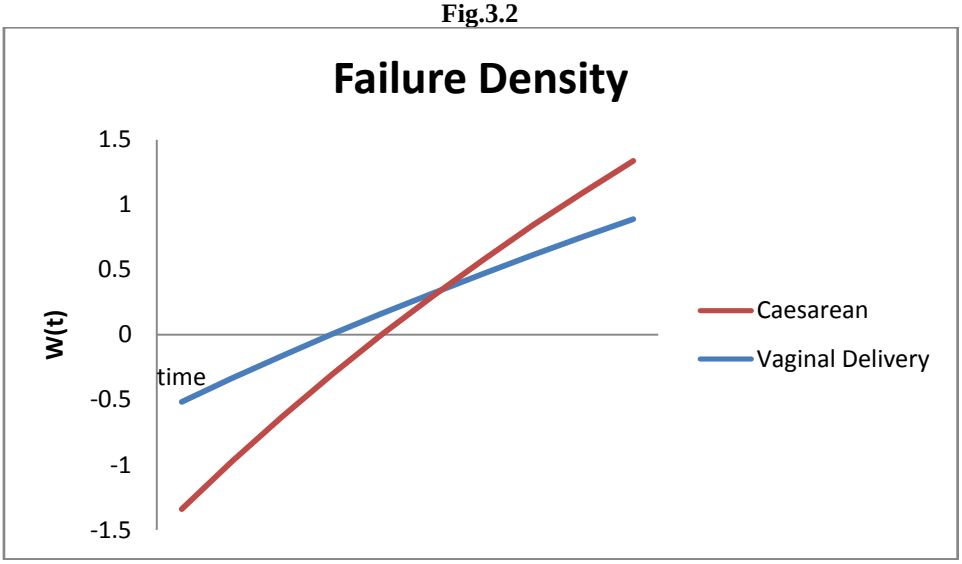


Fig.3.2



Renewal density is higher if we compare the Caesarian case with Vaginal Delivery during the labor and in the early post partum period. In a similar fashion we obtain the Failure Density function also and here we can see the bounds of the failure density functions in both the cases.

IV. Conclusion

Oxytocin release into the nervous system during the early postpartum period may strengthen the expression of maternal behaviors and prolong breastfeeding. Comparisons between woman following vaginal delivery (VD) versus caesarean section (CS) suggest that exposure to oxytocin during labor and in the postpartal period can influence the subsequent function of oxytocin-producing neurons during the lactation period. In the Mathematical model, both the cases are compared by finding the Renewal density and Failure Density functions. Renewal density is higher if we compare the caesarean case with vaginal delivery during the labor and in the early post partum period. In a similar manner, we obtain the bounds of the failure density functions in both the cases.

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