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A MATHEMATICAL MODEL FOR THE EFFECT OF PROLACTIN ON DAIRY COWS'

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Abstract. In this paper, study is based on the concentration of prolactin in dairy cows in favour of Domperidone injection. The concentration of serum PRL and milk PRL was greater during DOMP period. It also shows that the proportion of steady – state serum PRL secreted daily by milk significantly raise in QN cows and in CTL cows tends to be higher. In Mathematical Model, Conway – Maxwell Poisson distributions (CMP distribution) was used. Medical result have been analysed with corresponding Mathematical model.

1. Introduction

The estimation of parameters and drawing conclusions supported the estimated parameters is one among the important aspects of inferential statistics. A two-way parameter generalisation of the Poisson distribution was introduced by Conway and Maxwell as the stationary number of occupants of a queuing system with state dependent service. This distribution is hence known as Conway – Maxwell Poisson (CMP) distribution [4]. The CMP distribution has received recent attention in the statistics literature on account of the flexibility it offers in statistical models [1]. An illustration is that the CMP distribution can model data with either under – or – over dispersed relative to the Poisson distribution. Sellers and Shmueli exploited this property and used CMP distribution to generalise the Poisson and logistic regression models [19]. Wu, Holan and Wikie used CMP distribution as the part of Bayesian model for spatio – temporal data [22]. Conway – Maxwell – Poisson distribution may be a discrete probability distribution. It is a member of the exponential family has the Poisson distribution and geometric distribution as special cases and Bernoulli distribution as a limiting case. Our purpose in this work is twofold [7].

2. Mathematical Model

The CMP distribution is defined to be the distribution with probability mass function. The CMP distribution is a natural two – parameter generalisation of the

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Poisson distribution [4]. The CMP distribution is:

$$P\left(X = u\left(h\right)\right) = f\left(u\left(h\right);;\ \lambda, \delta\right) = \frac{\lambda^{u(h)}}{\left(u\left(h\right)!\right)^{\delta}}\ \frac{1}{Z(\lambda, \delta)},\ u(h) \in \mathbb{Z}^{+} = 0, 1, \ldots$$

Where

$$Z\left(\lambda, \delta\right) = \sum_{n=0}^{\infty} \frac{\lambda^{n}}{\left(n!\right)^{\delta}}$$

The function $Z\left(\lambda, \delta\right)$ serves as normalization constant so the probability mass function sums to one. $Z(\lambda, \delta)$ is not a closed form. The domain of admissible parameters is $\lambda, \delta\ > 0$ and $0 < \lambda < 1,\ \delta = 0$ [16]. The additional parameter δ which does not appear in the Poisson distribution allows for adjustment of the rate of decay. This rate of decay is a non-linear decreasing ratio of successive probabilities,

$$\frac{P(X = u\left(h\right) - 1)}{P(X = u\left(h\right))} = \frac{u(h)^{\delta}}{\lambda}$$

When $\delta = 1$, the CMP distribution becomes standard Poisson distribution and as $\delta\ \to \infty$, the distribution approaches a Bernoulli distribution with parameter $\lambda/(1+\lambda)$.

When $\delta = 0$, the CMP distribution reduces to a geometric distribution with probability of success $1 - \lambda$ provided $\delta < 1$ [22].

For CMP distribution, moments can be found through the recursive formula

$$E\left[X^{i+1}\right] = \begin{cases} \lambda E[X+1]^{1-\delta}, & \text{if } i = 0 \\ \lambda \frac{d}{d\lambda} E\left[X^{i}\right] + E\left[X\right] E\left[X^{i}\right], & \text{if } i > 0 \end{cases}$$

For general δ, there does not exist a closed form formula for the cumulative distribution function of $X \sim CMP\left(\lambda, \delta\right)$. If $\delta \geq 1$ is an integer, can obtain the formula in terms of generalized hypergeometric function

$$F\left(k\right) = P\left(X \leq k\right) = 1 - \frac{F_{\delta-1}(;k+2,\ \ldots\ldots,\ k+2; \lambda)}{\left\{(k+1)!\right\}^{\delta-1} F_{\delta-1}\left(;1,\ \ldots\ldots, 1; \lambda\right))}$$

The probability generating function is $Es^{X} = \frac{Z(s\lambda, \delta)}{Z(\lambda, \delta)}$ and the mean and variance are given by

$$E\ X = \lambda \frac{d}{d\lambda}\{\ln\left(Z\left(\lambda, \delta\right)\right)\ \}$$

$$var\ (X) = \lambda \frac{d}{d\lambda} E\ X$$

The cumulant generating function is

$$g\left(t\right) = \ln\left(E\left[e^{tX}\right]\right)\ = \ln\left(Z\left(\lambda e^{t}, \delta\right)\right)\ - \ln\lambda(Z\left(\lambda, \delta\right))$$

The normalizing constant does not have closed form, the following asymptotic expansion is of interest.

Fix $\delta > 0$, then as $\lambda \to \infty$,

$$Z\left(\delta, \infty\right) = \frac{\exp\{\delta \lambda^{1/\delta}\}}{\lambda^{\delta - 1/2 delta (2\pi)^{\delta - 1/2}\sqrt{\delta}}} \sum_{j=0}^{\infty} c_{j} \left(\delta \lambda^{1/\delta}\right)^{-j}$$

where c_k are uniquely determined by the expansion

$$(\Gamma(t+1))^{-\delta} = \frac{\delta^{\delta(t+\frac{1}{2})}}{(2\pi)^{\delta-1/2}} \sum_{k=0}^{\infty} \frac{c_k}{\Gamma(\delta t + \frac{1+\delta}{2+k})} \qquad [15]$$

2.1. Parameter Estimation. There are few methods of estimating the parameters of the CMP distribution from the data. Two methods are going to be discussed: weighted method of least squares and maximum likelihood [14]. The weighted least squares approach is simple and efficient but lack precision. But maximum likelihood is more precise but is more complex and computationally intensive.

a. Weighted Least Squares. The weighted least squares provide a simple, efficient method to derive rough estimates of the parameters of the CMP distribution and determine if the distribution would be an appropriate model. An alternative method should be used to compute more accurate estimates of the parameters if the model is deemed appropriate [18].

$$\log \frac{P_{u(h)-1}}{P_{u(h)}} = -log\lambda + \delta \log u(h)$$

where $p_{u(h)}$ denotes $\Pr(X = u(h))$. When estimating the parameters, the probabilities can be replaced by the relative frequencies of $u(h)$ and $u(h) - 1$. To determine if the CMP distribution is an appropriate model, these values should be plotted against $\log u(h)$ for all ratios without zero counts. If the data appear to be linear, then the model is likely to be good fit [14].

The inverse weighted matrix will have the variances of each ratio on the diagonal with the one – step covariance on the first off – diagonal, given below

$$var\left[\log \frac{\hat{P}_{u(h)-1}}{\hat{P}_{u(h)}}\right] \approx \frac{1}{np_{u(h)}} + \frac{1}{np_{u(h)-1}}$$

$$cov\left(\log \frac{\hat{P}_{u(h)-1}}{\hat{P}_{u(h)}}\ ,\ log\log \frac{\hat{P}_{u(h)}}{\hat{P}_{u(h)+1}}\right) \approx \frac{1}{np_{u(h)}}$$

b. Maximum Likelihood. The CMP likelihood function is

$$\mathcal{L}(\lambda, \delta | u(h_1), \ldots, u(h)_k) = \lambda^{S_1} \exp(-\delta S_2) Z^k(\lambda, \delta)$$

where $S_1 = \sum_{r=1}^{k} u(h)_r$ and $S_2 = \sum_{r=1}^{k} \log u(h)_r!$.

Maximizing the likelihood yields the following two equations
$E[X] = \overline{X}$ and $E \log X! = \overline{\log X!}$ Which do not have an analytic solution.

Instead, the maximum likelihood estimates are approximated numerically by the Newton – Raphson method. In each iteration, the expectations, variances and covariance of X and $\log X!$ are approximated by using the estimates for ? and d from the previous iteration in the expression.

$E[f(u(h))] = \sum_{n=0}^{\infty} f(n) \frac{\lambda^n}{(n!)^d Z(\lambda,\delta)}$ This is continued until convergence of $\hat{\lambda}$ and $\hat{\delta}$ [5].

2.2. Power-biasing. For any non-negative random variable W with finite δ -th moment, we say that $W^{(\delta)}$ has the δ -power-biased distribution of W if

$$\left(\mathbb{E}W^{(\delta)}\right)\mathbb{E}\, f\left(W^{(\delta)}\right) = \mathbb{E}\left[W^{(\delta)} f(W)\right]$$

For all $f : \mathbb{R}^+ \to \mathbb{R}$ such that the expectations exist. In this paper, it is interested in the case that W is non-negative and integer-valued. In this case, the mass function of $W^{(\delta)}$is given by

$$\mathbb{P}\left(W^{(\delta)} = n\right) = \frac{n^\delta \mathbb{P}\left(W = n\right)}{\mathbb{E}W^{(\delta)}},\ n \in \mathbb{Z}^+[19]$$

Properties of an outsized family of such transformations, of which power-biasing may be a part, are discussed by Goldstein and Reinert [6]. The case $\delta = 1$ is the usual size-biasing, which has often previously been employed in conjunction with the Poisson distribution [14]. The power-biasing employed here is the natural generalisation of size-biasing that may be applied in the CMP case.

3. Applications

In most mammals, prolactin (PRL) is important for maintaining lactation, and therefore the suppression of PRL inhibits lactation [9]. In many mammalian species including some livestock (sheep, pigs) also as in rodents and primates depletion of prolactin during lactation either prevents or depresses milk secretion, but in the major dairy species (goat, cow) this is often not so; if yield is reduced in the least it's only by a little amount. However, the involvement of PRL within the control of ruminant lactation is a little amount clear, because inconsistent effects on milk yield are observed with the short-term suppression of PRL by bromocriptine [10]. Recently, a study showed that stimulated PRL secretion with daily injections of the dopamine antagonist domperidone for 5 week. Milk production increased gradually and was greater in domperidone-treated cows. In late-lactation cows, quinagolide and cabergoline decreased milk production within the primary day of treatment and induced more rapid changes in several markers of mamma [12].

For several decades, the galactopoietic role of prolactin (PRL) in ruminants has been controversial. Knight 1993 concluded in a study that the inhibition of PRL with quinagolide (QN) decreases milk production in dairy cows [8]. Meanwhile Lacasse and Ollier in 2015 found that injecting dopamine antagonist, domperidone (DOMP) increases milk production and basal PRL concentration in dairy cows [10]. Therefore now there is a good evidence in dairy cows that PRL is galactopoietic.

Throughout the year without change in milk production, basal PRL concentration is affected by the environment. In 1973, Koprowski and Trucker winded in their study that mammary gland's sensitivity to PRL is adaptable [9]. During dry period, Lacasse et all, 2014 found that there is less circulation of PRL but increase subsequent milk production [11, 13]. Furthermore, in 2013 Tao and Dahl found a conversed conclusion in their study. They have found that heat stress increases PRL concentration and cooling cow during dry period subsequently enhance milk production [20]. McKinnon et al in 1988 observed that PRL binding capacity of the mammary gland can be increased by increasing the milk frequency. To increase mammary glands responsiveness to PRL, the only mechanism is to increase the number of PRL receptor [17]. Knight (1993) administrated in goats and found that a unilateral increase in milking frequency increased the milk response to PRL administration in goats [8]. Bernier – Dodier et al (2010) and Thompson et al (2015) in their study revealed that goats milked more frequently have higher gene expression of long and short isoform receptors in mammary gland [3, 21].

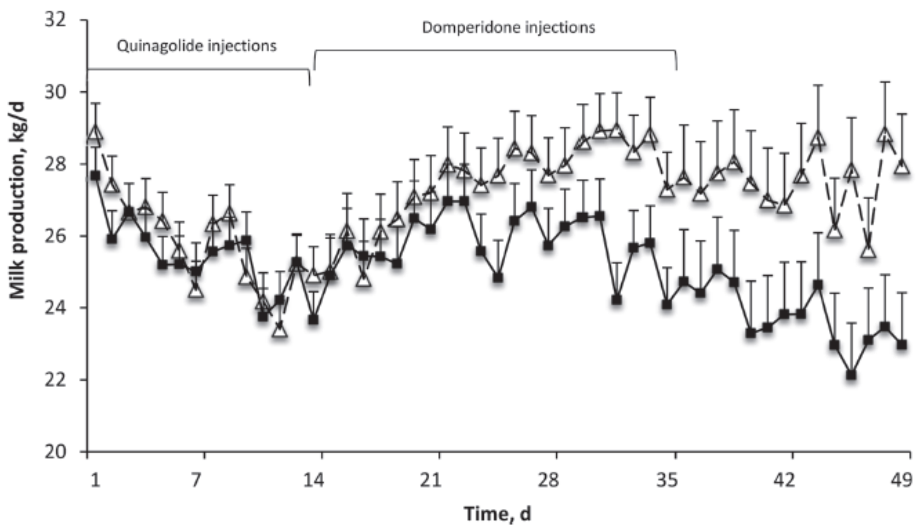

FIGURE 1. denotes the milk production of CTL (■) cow and QN(Δ) cows

In both QN and CTL cows before starting of the experiment, level of milk production was almost similar. The above Figure 1 clearly shows that during the treatment milk production was declined but was not affected. During DOMP period, the injected cows with QN secreted greater milk than the control group. When compared to control cow, milk production in QN injected cow is greater during post treatment. Throughout the experiment, milk fat content was not affected by the treatments. In QN cows the milk protein is greater when compared to CTL cows during the treatment period but was unaffected in the other period. During the treatment period there is no clear pattern of changes in milk lactose content.

During the period of pre-treatment, treatment and DOMP treatment, the yield of fat, protein and lactose were similar. The yield of fat was greater in QN cows when compared to CTL cows, yield of protein and lactose was also greater in QN cows during the post treatment period. Also energy corrected milk was greater in QN cows during post treatment periods.

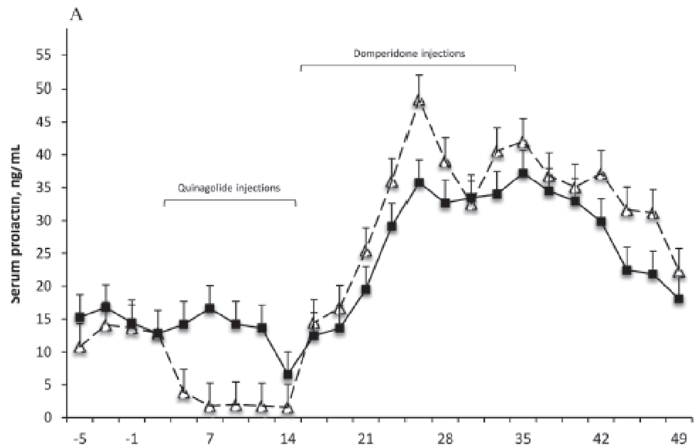

FIGURE 2A: denotes the milk production of CTL (■) cow and QN(Δ) cows

In both group of cows, before the start of experiment basal serum PRL concentration was similar. In the above Figure Figure 2a clearly shows that the concentration of PRL was comparatively very low in QN cows than the CTL cows during the treatment periods. The concentration of serum PRL was greater during DOMP period. There was no difference between QN and CTL group of cows during post treatment period.

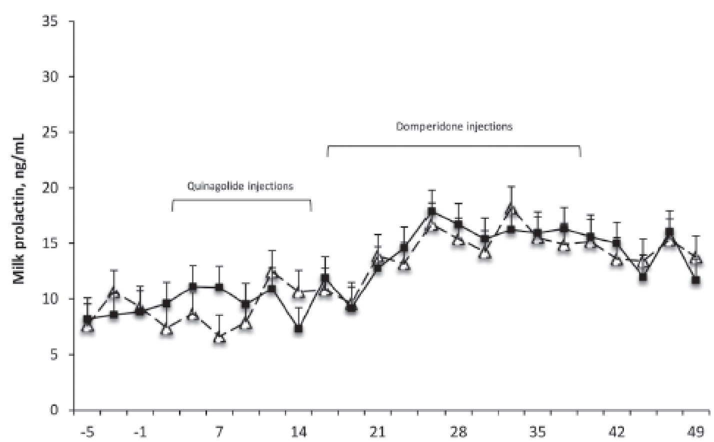

FIGURE 2B: denotes the milk prolactin of CTL (■) cow and QN(Δ) cows

In the above Figure Figure 2b clearly shows that the concentration of milk PRL throughout the experiment was unaffected. But during DOMP and post treatment period there is variation in the concentration of milk PRL.

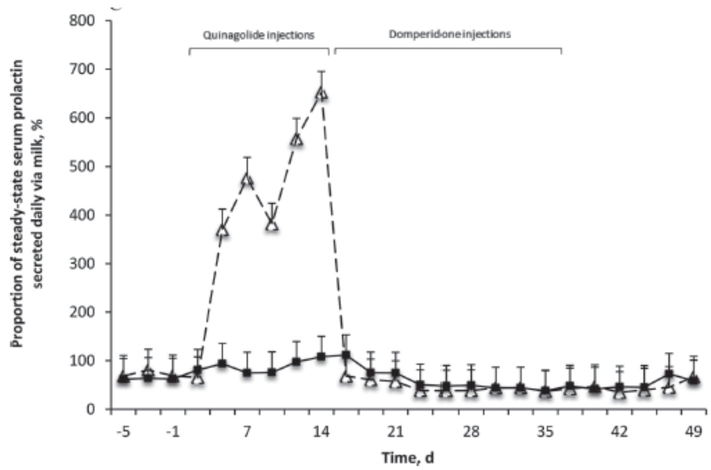

FIGURE 2C: denotes the proportion of steady – state serum PRL secreted daily by milk in both QN(Δ) and (■) CTL cows

In the above Figure Figure 2c clearly shows the proportion of steady – state serum PRL secreted daily by milk does not differ in both QN and CTL cows during post and pre – treatment. But during treatment period there is significant raise in QN cows and in CTL cows tends to be higher. The proportion of steady – state serum PRL secreted daily by milk started to decrease in both QN and CTL cows during DOMP period.

4. Mathematical Result

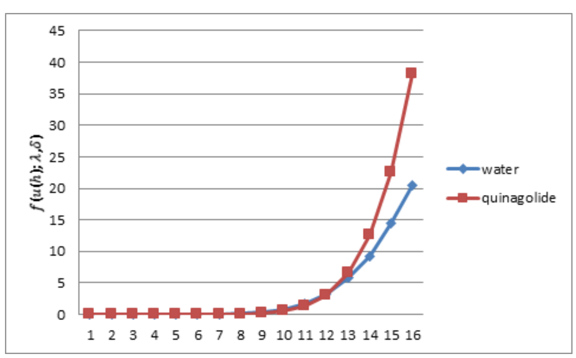

FIGURE 3A: milk production of water injected cow (control group) and quinagolide injected cow

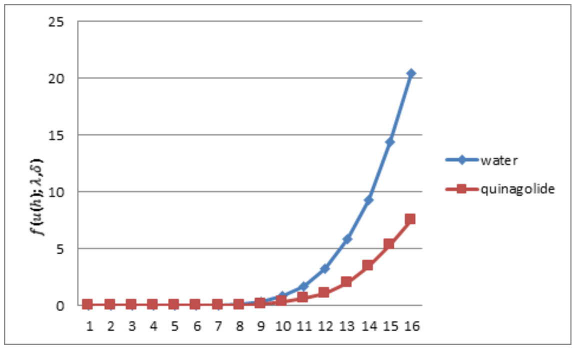

FIGURE 3B: Serum Prolactin of water injected cow (control group) and quinagolide injected cow

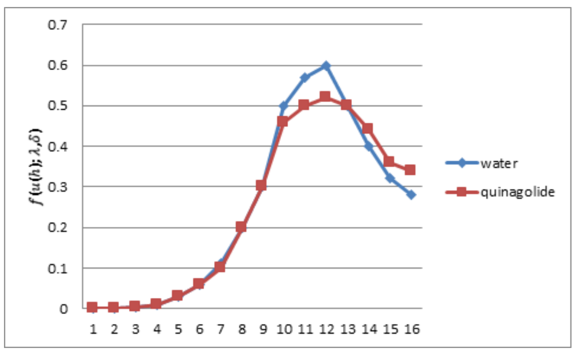

FIGURE 3C: Milk Prolactin of water injected cow (control group) and quinagolide injected cow

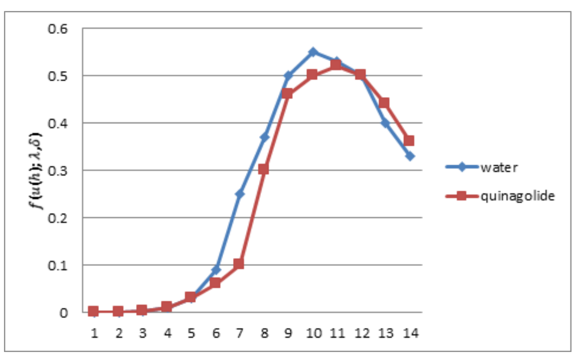

FIGURE 3D: proportion of steady – state serum PRL secreted daily by milk of water injected cow (control group) and quinagolide injected cow

5. Conclusion

The mammary gland is a complex tissue and its various functions (growth, secretion and involution) are each controlled by complex mechanisms involving combinations of hormones and locally-acting paracrine and autocrine factors. Prolactin may be a key member of those complexes, in some species the foremost important single constituent. The conclusion of the study supported that the mammary gland's responsiveness to PRL is modulated by the chronic level of the hormone. In the Mathematical model Monotonicity for the function was obtained. Milk production and serum prolactin of the cow was concave upward and monotonically increasing. Similarly the milk prolactin and proportion of steady – state serum PRL secreted daily by milk of the cow was concave downward and monotonically decreasing. In future, this paper will be much useful in the field of medical and engineering.

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Conflict of Interests

There are no conflicts of interest declared by the writers.

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