

ECONOMIC OPTIMIZATION OF THE NUMBER OF RECIPIENTS IN BOVINE EMBRYO TRANSFER PROGRAMS

Renato Travassos Beltrame¹; Luis Gustavo Barioni^{2*}; Breno Dala Maestri³; Celia Raquel Quirino¹

¹UENF/CCTA/LMGA - Depto. de Produção Animal, Av. Alberto Lamego, 2000 -28013-600 - Campos dos Goytacazes, RJ - Brasil.

²Embrapa CERRADOS, C.P. 08223 - 73301-970 - Planaltina, DF - Brasil.

³UVV - Centro Universitário Vila Velha - 29102-770 - Vila Velha, ES - Brasil.

*Corresponding author <barioni@cpac.embrapa.br>

ABSTRACT: Purchase and maintenance of recipient females account for a large proportion of the costs and determine the number of calves that can be produced in an embryo transfer program. However, the large variability of embryo production by the donors and the need to purchase and synchronize the recipients before knowing the number of embryos collected make it difficult for the decision maker to identify the ideal number of recipient females to allocate. An ex-ante evaluation to determine the optimal number of recipient females was carried out through a sensitivity analysis for the ratio between the number of recipients and donors in a simulation model. The variability for the number of embryos collected was accounted for by applying the Monte Carlo simulation technique, assuming normal distribution and known values for mean and variance. The simulation considered monthly intervals between collections, during a 24 months program. The effect of embryo freezing on the number of pregnancies was considered by introducing a stock of frozen embryos into the mathematical model. Optimal recipient/donor ratio and the cost per pregnancy were compared for three recipient synchronization protocols (prostaglandin, progesterone - P₄ and Ovsynch), based on the expected performance for synchronization, conception and transfer/treated rates for each protocol. Stochastic simulation associated with sensitivity analysis was effective in identifying the optimal donor to recipient ratio. Freezing embryos is effective to reduce the operational costs per pregnancy. The estimated optimal recipient/donor ratio was 20 for prostaglandin and 16.7 for the other protocols. The P₄ protocol, although the most expensive, resulted in the lowest pregnancy cost estimation followed by prostaglandin and Ovsynch.

Key words: Monte Carlo, mathematical model, simulation, cost estimation, estrus synchronization

OTIMIZAÇÃO ECONÔMICA DO NÚMERO DE RECEPTORAS EM PROGRAMAS DE TRANSFERÊNCIA DE EMBRIÕES EM BOVINOS

RESUMO: A aquisição e manutenção de receptoras representam grande proporção dos custos e determinam o número de produtos gerados em um programa de transferência de embriões. Entretanto, a grande variabilidade na produção de embriões e a necessidade de adquirir e sincronizar receptoras antes de conhecer o número de embriões na coleta geram dificuldades na identificação do número ideal de receptoras pelo tomador de decisão. Nesse contexto, uma avaliação ex-ante para determinação do número ótimo de receptoras foi realizada por meio de análise de sensibilidade para a razão entre o número de receptoras e de doadoras em um modelo de simulação. Considerou-se a variabilidade no número de embriões coletados aplicando-se a técnica de simulação de Monte Carlo, assumindo-se distribuição normal com média e variância do número de embriões viáveis conhecidos. Consideraram-se coletas e transferências de embriões em intervalos mensais durante um período de 24 meses. O efeito do congelamento de embriões no número de prenhez foi representado modelando-se a dinâmica de um estoque de embriões congelados. Foram comparados a razão ótima entre receptoras e doadoras e o custo por prenhez de três protocolos de sincronização de receptoras (prostaglandina, Progesterona - P₄ e Ovsynch) com base em suas respectivas taxas de sincronização, aptidão e prenhez. A simulação estocástica associada com análise de sensibilidade foi efetiva em identificar a razão receptora / doadora ideal. O congelamento de embriões foi efetivo para reduzir o custo por prenhez. A razão ótima de receptoras por doadora foi afetada pelo protocolo de sincronização, sendo de 20 para a prostaglandina

e de 16,7 para os demais protocolos. Apesar do maior custo, o protocolo P₄ resultou na menor estimativa de custo por prenhez seguido pelo protocolo utilizando prostaglandina e pelo protocolo Ovsynch. Palavras-chave: Monte Carlo, modelo matemático, simulação, estimativa de custo, sincronização de estro

INTRODUCTION

A steady increase in the adoption of Embryo Transfer (ET) has been observed in Brazil (Sociedade Brasileira de Tecnologia de Embrões, 2004) as a means of increasing the contribution of high genetic merit females to the genetic progress of bovine populations (Fortune et al., 1991; Christiansen, 1991).

In ET programs recipient females are necessary to gestate the embryos produced by the donor cows (Reichenbach, et al., 2002). Purchase and maintenance of recipient females account for a large proportion of the costs (Fernandes, 1999; Beltrame, 2002) and determines the number of calves that can be produced in an ET program.

The large variability of embryo production by the donors (Galli et al., 2003) and the need to purchase and synchronize the recipients, before knowing the number of embryos collected, however, makes it difficult for the decision maker to identify the ideal number of recipient females to allocate for ET.

Although a considerable number of mathematical models have been developed for decision support on human interventions in bovine reproduction (Slennings & Wheelera, 1989), none have definitively addressed the problem of determining the optimum number of recipients in ET programs. In this context, this article presents a model used to estimate, through computer simulation, the performance of an ET program in approximating the economic optimum number of recipients for different recipient synchronization protocols.

MATERIAL AND METHODS

A mathematical model was developed to calculate the number of pregnancies at the *i*th embryo collection event. The model can be described as follows (equations 1 to 5):

$$G_i = \alpha_c \cdot \alpha_r \cdot \alpha_a \cdot (\text{Min}(E_i, I_i) \cdot \alpha_{gf} - \text{Min}(\Delta C_i, 0) \cdot \alpha_{gd}) \quad (1)$$

$$I_i = R_i \cdot \alpha_c \cdot \alpha_r \cdot \alpha_a \quad (2)$$

$$(3)$$

$$\Delta C_i = \text{Max}(E_i - I_i, -C_i) \quad (4)$$

$$C_i = \sum_{j=1}^{i-1} \Delta C_j \quad (5)$$

where: G_i is the total number of pregnancies; R_i is the total number of recipients; N_i is the available number of donors, μ and ρ are respectively the expected mean and standard deviation of the number of embryos per donor, E_i is the number of embryos, I_i is the number of recipients ready for embryo transfer, ΔC_i is the change in the stock of frozen embryos; C_i is the number of frozen embryos in stock; α_c is the proportion of cycling recipients; α_r is the proportion of recipient that responds to the synchronization protocol; α_a is the proportion of transferred / treated recipient at an ET event; α_{gf} and α_{gd} are, respectively, the pregnancy rates for fresh and thawed inactivated embryos; and $\eta(N_i \cdot \mu, N_i \cdot \rho^2)$ is a normal distribution with mean $N_i \cdot \mu$ and variance $N_i \cdot \rho^2$. A value of ΔC_i greater than 0 represents a surplus of embryos (number of collected embryos is greater than the number of recipients). The model assumes that all the embryos in surplus are frozen. $\Delta C_i < 0$ represents a deficit of embryos ($E_i - I_i$) in the *i*th collection and determines the number of embryos to be thawed.

Costs were calculated assuming that: (a) the recipients purchase price is 20% higher than of cows for slaughter with same liveweight; (b) a two month delay is necessary before the first utilization of recipients due to the need for exams, adaptation and establishment of adequate body condition; (c) a three month period is required between embryo transfer and the re-introduction of non-pregnant recipients into the program; (d) after two unsuccessful embryo transfers, non-pregnant recipients are sold at slaughter price; (e) at the end of the simulated period, all non-pregnant recipients are sold. A liveweight gain of 45 kg is estimated in the period from purchase to sale, independent of how long the recipient stayed in the program. Slaughter price was assumed for selling the recipients after the program (US\$ 236.25). Maintenance costs for the recipients were estimated from opportunity costs of renting the pastures for beef cattle. The costs appropriated to donors did not consider animal purchase.

Simulations were carried out for two cases: (1) deterministic, where the number of embryos recovered in each collection was equal to the expected mean ($\mu = 6$ and $\sigma = 0$), based on Beltrame (2002), and; (2) stochastic with freezing embryos, where the number of embryos produced was generated using Monte Carlo simulation (Freitas Filho, 2001; Perin Filho,

1995), through a normal distribution ($\mu = 6$, $\sigma = 6$) with absence of covariance among collections. In both cases, 24 embryo collections were simulated. A herd of 100 recipient females was kept constant through the acquisition of new animals during the period simulated.

In case (2) simulations were run 50 times. Mean and standard deviation of the number of pregnancies, and associated costs were estimated. The least cost of pregnancy was adopted as the optimality criteria.

It was assumed that donor synchronization was carried out using a protocol using progesterone releasing internal device (PRID) and superovulation using FSH (Folltropin[®]). For the recipient, three recipient synchronization protocols were considered (Spell et al., 2001; Bó et al., 2002; Bó et al., 2004):

1 - **Prostaglandin:** PGF_{2 α} , two doses eleven days apart;

2 - **Progesterone -P₄:** Day 0 → PRID + BE 2mg → Day 8 remove PRID + 0.15 mg PGF_{2 α} → Day 9 → BE 1mg → Day17 → Embryo transfer;

3 - **Ovsynch:** Day 0 GnRH → Day 7 PGF_{2 α} → Day 9 GnRH → Day17 → Embryo transfer.

Costs were based on market prices of October, 2005 (see Tables 2 and 3 for costs specifications). Table 1 presents the technical coefficients considered in the simulations:

The operating cost per donor was estimated at US\$ 319.59 (Table 3). Both donor-related costs and

donor performance were assumed constant across protocols (Table 3). Consequently, all variation in pregnancy costs is associated with differences in the expected performance and costs for each of the protocols for recipient synchronization. Initial costs for the recipients ranged from US\$ 275.76 to US\$ 287.99 during the first ET (Table 2).

RESULTS AND DISCUSSION

Comparing the pregnancy costs for each protocol at different recipient/donor ratios and identifying the near-optimal number of donors to minimize the pregnancy cost for each protocol (Figure 1), it is observed that with the expected values of technical performance, the P₄ protocol produced the lowest costs per pregnancy for all the range of recipient/donor ratios studied (US\$ 240.61, Figure 1). Pregnancy costs of prostaglandin and Ovsynch pro-

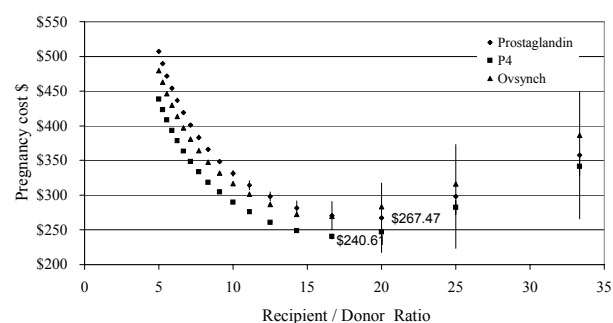


Figure 1 - Mean and standard deviation (error bars) of estimated pregnancy costs as a function of the number of donors per 100 recipients.

Table 1 - Technical coefficients assigned to the model for the three synchronization protocols in this study.

	PGF _{2α}	P ₄	Ovsynch
Number of recipients	100	100	100
% cycling recipients ^a	70	70	70
% treated recipients	80 ^b	95	94
% transferred / treated recipients	55 ^b	50	55
% Pregnancy recipient rate	55 ^b	60	50
% Pregnancy rate w/ freezing embryos	45 ^b	50	40

^{a,b}based on: Baruselli et al., 2000; Del Rey, 2001; Spell et al, 2001; Bó et al, 2002; Bó et al 2004, Tecnopec, 2004

Table 2 - Estimated cost of recipient at the 1st ET.

1- Recipient cost at 1 ^a ET	Purchase	Labour	Hormone	Antibiotic	Maintenance	Total cost
a) P ₄ (US\$)	259.29	-	16.70	2.50	9.50	287.99
b) PGF _{2α} (US\$)	259.29	0.56	3.90	2.50	9.50	275.76
c) "Ovsynch" (US\$)	259.26	-	11.00	2.50	9.50	282.29

¹BIONICHE Animal Health, Bellville, ON, Canada.

Table 3 - Estimated costs per donor (Bos Taurus - Simmental) for each event of embryo collection

1- Maintenance	US\$
Total month	11.57
Total per program	23.14
2 -Superovulation protocol	
PRID + BE + GnRH	25.00
FSH	60.17
Prostaglandin	2.95
Total	88.12
3 - Semen	
Two dose	37.50
4 - ET honorary	
Collection / donor	170.83
5 - Total cost / donor	319.59

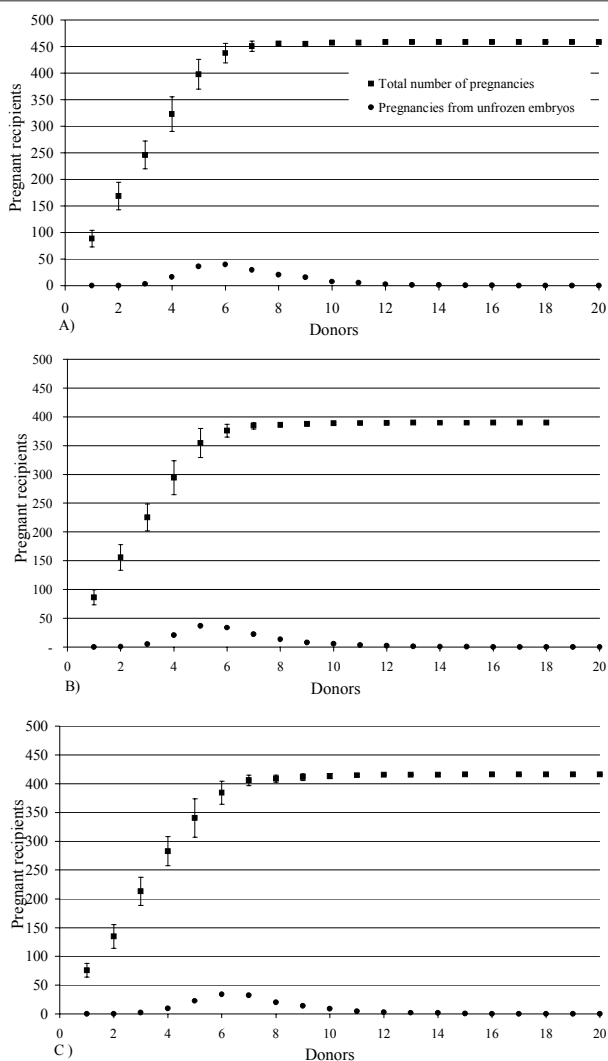


Figure 2 - Total number of pregnancies and pregnancies from thawed embryos in a 24 months period for (A) recipient synchronized using the PRID protocol; (B) recipient synchronized using the Prostaglandin protocol; (C) recipient synchronized using the Ovsynch protocol. Error bars represent standard deviation of the number of pregnancies.

protocols were similar at optimum recipients/donor ratio (US\$ 267.47 and US\$ 269.64, Figure 1). However, an inversion in rank is observed between prostaglandin and Ovsynch, with the first presenting lower costs when recipients/donors ratio is lower than the optimum and the latter being less expensive from that point on.

The optimal recipient/donor ratio was also different among protocols. While the least cost per pregnancy occurred at 16.7 recipients per donor for the P₄ and Ovsynch protocols, it occurred at 20 recipients per donor for prostaglandin.

Figure 2 illustrates the variation in total number of pregnancies, number of pregnancies from thawed embryos and costs per pregnancy, for each protocol. The optimum number of donors matches the maximum number of pregnancies from thawed embryos (Figures 1 and 2). This highlights the importance of the embryo freezing in reducing pregnancy costs in ET programs. The risk related to the number of pregnancies decreases with a higher number of donors (Figure 2). The reason is that with excessive number of donors, there is always a surplus of embryos, so that the number of pregnancies is always limited by the number of recipients. However, at a near-optimum number of donors, embryo freezing buffers the variation between collections with surplus and collections with deficit in number of embryos.

A similar behavior in the response curves of the number of pregnancies can be observed for all the protocols (Figure 2). The rate of increase in the number of pregnancies in relation to number of donors is the same for all protocols until embryo freezing/thawing begins. Up to that point, the rate of change in pregnancy numbers depends only on the number of embryos available, and consequently on the number of donors (Figure 3). Further increases on the number of the embryos lead to decreasing increments where the number of pregnancies converges to the asymptotic value (Figure 3).

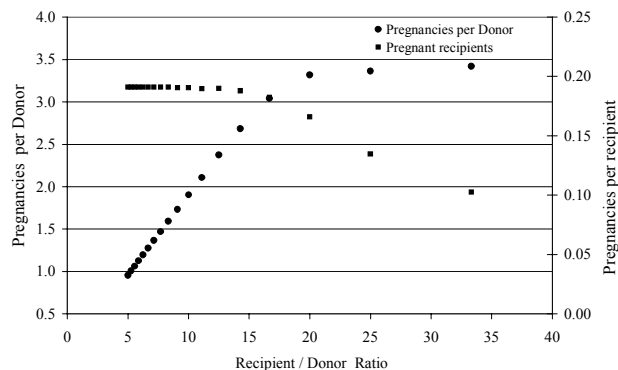


Figure 3 - Pregnancies per donor and per recipient in each collection for different recipient / donor ratios.

Within the decreasing increment phase, there is a point where the increments in the number of pregnancies produced by a new donor are not sufficient to overcome the marginal costs of having it. Therefore an optimal point can be identified.

Figure 3 illustrates the variation in the efficiencies of use of donors and recipients at different recipient/donor ratios. Up to a certain level of recipient/donor, the number of pregnancies is limited by the availability of recipients and there is always a surplus of embryos which are not transferred. Therefore the efficiency of the recipients (i.e. the number of pregnancies per recipient) is at a maximum. With the increasing availability of recipients, there is a range where ET events alternate surplus and deficits in the number of embryos. In that range neither the donor nor the recipient efficiencies are maximized. However, it tends to be the range where the maximum overall economic efficiency is found (compare Figures 1 and 3). With recipient/donor ratios above that range there is always a deficit of embryos and, therefore, maximum number of pregnancies per donor.

Comparisons among synchronization protocols has been done through a computer simulation, as in the research of Slenning & Wheeler (1989) who suggested significant economic differences among superovulation protocols. However, the decision on the number of recipients have been usually based on empirical observation, trial and error or with the use of a deterministic relationship with the expected number of embryos, which was proven to be biased (Barioni et al., 2003).

Usefulness of this method of stochastic simulation for the decision on the number of recipients has still to be validated. Incomplete information regarding the factors influencing the expected number of embryos and its probability distribution besides the variation in the recipients' reproductive performance may limit the capacity of this analysis in providing improved decision support. Therefore, further studies regarding the factors related to the reproductive performance of donors and recipients in embryo transfer programs are required.

CONCLUSION

The use of stochastic simulation associated with sensitivity analysis was effective in identifying near-optimal donor to recipient ratio and can be used as a method to compare different technological and management options with potential to be incorporated into decision support systems. The optimal donor/recipient ratio, evaluated with the model, varied with the

efficiency of the synchronization protocol used for the recipients, with the Progesterone protocol resulting in the lowest pregnancy cost estimation followed by PGF_{2α} and Ovsynch. Optimal donor/recipient ratio for the studied scenario was estimated as 20 for prostaglandin and 16.7 for the other protocols. For all cases, embryo freezing was found to be important in reducing cost and production risk in embryo transfer programs.

ACKNOWLEDGEMENTS

To CAPES for the scholarship of Renato T. Beltrame.

REFERENCES

- BARUSELLI, P.S.; MADUREIRA, E.H.; MARQUES, M.O. **Programas de IA em tempo fixo em *Bos Indicus***. In: CURSO DE ABORDAGEM TERICO-PRÁTICA DE NOVAS TÉCNICAS DE SINCRONIZAÇÃO SEM OBSERVAÇÃO DE CIOS EM BOVINOS, 2., São Paulo, 2000. Apostila.
- BARIONI, L.G.; BELTRAME, R.T.; VELOSO, R.F.; SAURESSIG, M.G. **Métodos para determinação do número de receptoras em programas de transferência de embriões**. Planaltina, DF: Embrapa Cerrados, 2003. 6p. (Comunicado Técnico, 99).
- BELTRAME, R.T. **Otimização da razão receptoras x doadoras para transferência de embriões em bovinos**. Vila Velha: Centro Universitário Vila Velha, 2002. 67p. (Monografia - Graduação).
- BÓ, G.; MORENO, L.; CUTAIA, L.; BARUSELLI, P.S.; REIS, E.L. Manipulação do ciclo estral em doadoras e receptoras de embrião bovino. *Acta Scientiae Veterinariae*, v.32, p.1-22, 2004.
- BÓ, G.; BARUSELLI, P.S.; MORENO, L.; CUTAIA, L.; CACCIA, M.; TRIBULO, R.; TRIBULO, H.; MAPLETOFT, R.J. The control of follicular wave development for self-appointed embryo transfer programs in cattle. *Theriogenology*, v.57, p.53-72, 2002.
- CHRISTIANSEN, L.G. Use of embryo transfer in future cattle breeding schemes. *Theriogenology*, v.35, p.141-149, 1991.
- DEL REY, A.J.M.; RENNO, F.; BARTOLOMEU, C.C.; SILVA, A.L.R.; MOREIRA, C.H.S.; BARUSELLI, P.S. Sincronização da ovulação com cidr-b para inovulação em tempo fixo de embriões bovinos congelados em etilenoglicol. *Revista Brasileira de Reprodução Animal*, v.25, p.307-310, 2001.
- FERNANDES, C.A.C. Inovulações não cirúrgicas e taxa de gestação em receptoras de embrião. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia*, v.51, p.263-266, 1999.
- FORTUNE, J.E.; SIROIS, J.; TURZILLO, A.M.; LAVOIR, M. Follicle selection in domestic ruminants. *Journal of Reproduction Fertility*, v.43, p.187-198, 1991.
- FREITAS FILHO, P.J. **Introdução a modelagem e simulação de sistemas (com aplicações em Arena)**. Santa Catarina: Visual Books, 2001.
- GALLI, C.; DUCHI, R.; CROTTI, G.; TURINI, P.; PONDERATO, N.; COLLEONI, S.; LAGUTINA, I.; LAZZARI, G. Bovine embryo technologies. *Theriogenology*, v.59, p.599-616, 2003.
- PERIN FILHO, C.P. **Introdução simulação de sistemas**. Campinas: Editora da Unicamp, 1995. 163p.
- REICHENBACH, H.D.; OLIVEIRA, M.A.L.; LIMA, P.F.; SANTOS, A.S.; ANDRADE, J.C.O. Transferência e criopreservação de embriões de bovinos. In GONÇALVES, P.B.D.; FIGUEIREDO, J.R.; FREITAS, U.J.F. **Biotécnicas aplicadas reprodução animal**. São Paulo: Varela, 2002. p.127-178.

SOCIEDADE BRASILEIRA DE TECNOLOGIA DE EMBRIÕES.

Situação atual da produção mundial de embriões em diferentes espécies. Dec, 2004. Available at: <<http://www.sbte.org.br>>. Accessed at: 20 mar. 2004

SLENNINGL, B.D.; WHEELERA, M.B. Risk evaluation for bovine embryo transfer services using computer simulation and economic decision theory. **Theriogenology**, v.31, p.653-673, 1989.

SPELL, A.R.; BEAL, W.E.; CORHA, L.R.; LAMB, C.G. Evaluating recipient and embryos factors that affect pregnancy rates of embryo transfer in beef cattle. **Theriogenology**, v.56, p.287-297, 2001.

Received June 29, 2006

Accepted March 02, 2007