**Optimization of Recipient Management to Improve Embryo Transfer Success in Cattle**

**ABSTRACT**

Embryo transfer (ET) is a key advancement in reproductive biotechnology, with its success hinging on various factors related to the embryo, recipient, and their intricate interactions. Environmental conditions, for example, heat stress impedes embryonic development and escalates early embryonic loss. It affects the embryo at its pre-attachment stage, but the magnitude of the impact decreases as the embryo develops. In cattle, ET represents a significant financial commitment, mainly due to the costs associated with managing and maintaining recipient animals. Enhancing pregnancy rates in recipients can lead to more efficient embryo utilization, resulting in cost savings by minimizing transfer expenses and the care needed for non-pregnant animals. This review emphasizes the importance of comprehensive management practices, including optimal nutrition, synchronization of the recipient's cycle with the donor's, precise procedural techniques during embryo transfer, and effective post-transfer management, all of which are essential for improving ET outcomes in recipient cattle. Moreover, strategic handling, proper nutrition, and health monitoring, directly contribute to enhanced outcomes.

**Keywords:** Embryo transfer, Management, Recipient, Synchronization

**INTRODUCTION**

Embryo transfer is a significant advancement in reproductive biotechnology, offering opportunities for genetic improvement and expanding marketing potential in purebred cattle. Once transferable embryos are harvested from a donor cow, the decision must be made regarding which recipients should receive the embryos to maximize the number of successful pregnancies [1]. The suitability of recipients depends on several factors, including management practices, nutrition, and estrous cycle control, to ensure the presence of a functional corpus luteum at the time of transfer [2]. The success of an embryo transfer program relies more on the recipient than the donor, as the recipient must achieve and sustain a healthy pregnancy, calve independently, and rear a high-quality calf [3]. Therefore, emphasis must be placed on selecting the right recipient and implementing strategies that allow both customers and practitioners to effectively utilize embryos from superovulation, in vitro production, or nuclear transfer to maximize the number of pregnancies [4]. Selecting recipients with a higher likelihood of successful conception and pregnancy maintenance is one of the most crucial factors affecting the efficiency of using IVF embryos in timed embryo transfer programs [5,6].

**EMBRYO TRANSFER TECHNIQUE**

The first successful embryo implantation in a cyclic female was accomplished in rabbits in 1891, but it became widely practiced in cattle only during the 1970s [7]. Embryo transfer (ET) is a biotechnological procedure in which an embryo is harvested from a female donor and subsequently implanted into a recipient female, where the embryo continues its development [8]. ET represents a significant advancement in reproductive biotechnology, enabling the exploitation of genetic potential in bovine production, enhancing the quality and efficiency standards, and increasing reproductive rates in elite females [9]. Key benefits of ET include the acceleration of desirable genetic dissemination, the ability to produce a greater number of offspring from genetically superior donors, enhancement of reproductive efficiency in repeat breeders, and the mitigation of fertility issues caused by heat stress during breeding and the early stages of pregnancy [10]. Embryos intended for transfer are either produced in vivo through multiple ovulation embryo transfer (MOET) or in vitro through in vitro fertilization (IVF), and may be transferred fresh or following cryopreservation [11]. In vitro embryos are generated by extracting oocytes from follicles, typically via ultrasound-guided transvaginal aspiration, although oocytes can also be retrieved from ovaries outside the body. These oocytes are then matured in a controlled culture environment before being fertilized with prepared sperm. The resulting zygotes are cultured until they reach the morula or blastocyst stage for transfer [12]. In vitro embryo production (IVP) techniques are attractive because of the possibilities for the low-cost mass production of bovine embryos for transfer, embryo diagnosis, somatic cell and embryo cloning and for the production of transgenic cows, as well as for basic research on the mechanisms of fertilization and embryogenesis. The two most common methods used to improve the efficiency of in vitro maturation (IVM) and in vitro embryo culture (IVC) are the addition of serum and co-culture. The beneficial effects of serum supplementation in culture media are considered to be due to the supply of nutrients, vitamins, growth factors, hormones, and anti-oxidative compounds for oocyte maturation and embryo development [45].

**SELECTION AND SYNCHRONIZATION OF RECIPIENT CATTLE**

In embryo transfer (ET) programs, recipients play a crucial yet often overlooked role in the overall success of the operation [13]. Therefore, the accurate selection of recipients stands as one of the primary objectives for achieving success in an ET program [14]. The process of selecting recipients for embryo transfer is based on specific breeding criteria, which include the reproductive health of the cows, their ability to calve without difficulty, proficiency in milking and mothering, adequate nutrition, and their involvement in a thorough herd health program [15]. A clinical examination of the ovaries to confirm the presence of a corpus luteum is a critical component in selecting recipients on the day of embryo transfer [16], as the presence of a "high-quality" CL is the most vital factor in determining whether a recipient is suitable for further use in the transfer process [17]. Synchronizing donors and recipients is a pivotal component of embryo transfer that must not be overlooked. To optimize the chances of embryo survival in the recipient after transfer, the conditions within the recipient's reproductive tract should align closely with those of the donor. This requires the synchronization of estrous cycles between both the donor and the recipients, ideally within a one-day window of each other [18]. The highest pregnancy rates were observed when recipients were synchronized to be 24 hours out of phase with the donor, while the lowest rates occurred when recipients were either +36 or -36 hours out of sync with the donor [19]. Early estrous synchronization systems primarily focused on manipulating the estrous cycle by inducing luteolysis via an injection of PGF2α, followed by estrus detection. Once single PGF2α treatments proved successful, research shifted towards multiple PGF2α injections to reduce the days required for estrus detection [20,21]. For recipients synchronized with prostaglandin F2α (PGF2α), treatment must be administered 12 to 24 hours before the donor cows, as estrus induced by PGF2α in recipients occurs 60 to 72 hours later [22]. The subsequent generation of estrous synchronization systems involved the use of exogenous progestins, such as intravaginal progesterone release inserts (CIDR) or megestrol acetate (MGA), to delay estrus following natural or induced luteolysis, thereby extending the length of the estrous cycle [23,24]. The third generation of estrous synchronization systems focused on controlling follicular waves with a single GnRH injection at any stage of the estrous cycle, which induces an LH surge, thereby synchronizing ovulation or luteinization of dominant follicles [25]. As a result, a new follicular wave is initiated in more than 60% of cows within 1 to 3 days of GnRH administration. The luteal tissue formed after GnRH injection undergoes PGF2α-induced luteolysis 6 or 7 days later [26]. The use of GnRH to regulate follicular wave emergence, ovulation, and PGF2α for luteolysis led to the development of the Ovsynch protocol for dairy cows [27]. Also, pre-synchronization of estrus and ovulation using controlled internal drug release (CIDR) and PGF2 α achieved improvement in pregnancy rate from 20 to 60% in buffalo-cows and from 0 to 60% in buffalo-heifers [44]. Moreover, understanding how species respond to variations in temperature under climate warming is essential to evaluate their vulnerability. Research suggests that for mid- and high-latitude reptiles, warm incubation temperatures have been documented to enhance embryonic development by shortening the incubation period and increasing hatching success [42].

**EFFICIENT MANAGEMENT OF RECIPIENT**

The primary challenges facing animal biotechnology in developing countries include limited access to resources, the distinctiveness of animal breeds, a lack of trained technicians and fieldworkers, the high cost of acquiring technology from developed nations, expensive technological inputs, minimal investment in animal biotechnology, neglect of indigenous knowledge, and the disregard for local agricultural management practices [28]. To ensure the successful application of embryo transfer technology, several critical factors must be established. Therefore, producers, veterinarians, and all members of the herd management team must be well-versed in both the short-term and long-term elements that contribute to a successful embryo transfer program [3].

Examples of recipient factors that negatively impact pregnancy rates following embryo transfer (P/ET) include low body condition score, inadequate weight gain, lactation or parity in dairy cattle, temperament, and the presence of periparturient or postpartum diseases [30].

1. Insufficient intake of energy, protein, vitamins, and essential micro- and macrominerals has been linked to suboptimal reproductive performance. Body condition scoring (BCS) serves as a reliable method to assess the nutritional status of recipients, and through strategic feeding, an ideal BCS can be achieved. The effect of BCS before calving also impacts calf birth and weaning weights. When cows were fed to attain a BCS of either 4 or 6 prior to calving, both body weights and calf birth and weaning weights (with similar genetics) were higher in those cows [3].
2. Plasma progesterone concentration is closely associated with the mass, volume, and structure of the corpus luteum. Progesterone, produced by the corpus luteum (from granulosa cells), as well as by the placenta and adrenal glands in various mammals, plays an essential role in uterine development, implantation, blastocyst growth, fetal maintenance, and reduction of uterine tone during pregnancy. An immediate rise in serum progesterone levels after insemination is crucial for sustaining pregnancy and supporting the proper development of the conceptus [30].
3. For successful conception in bovine embryo transfer (ET), the presence of a functional corpus luteum (CL) and sufficient progesterone (P4) production is vital. These elements are critical for initiating and maintaining pregnancy, as CL size correlates with plasma P4 levels. Larger luteal tissue areas positively influence conception rates (CR) in bovine embryo recipients [31]. Increasing the number of corpora lutea in recipients may enhance pregnancy rates in embryo transfer programs. The continuous function of the corpus luteum ensures sustained P4 secretion, which in turn prepares the uterine environment, making it more receptive to the embryo and fostering its development [30].
4. The highest pregnancy rates are typically observed during the winter season, followed by spring, autumn, and summer. It is important to note that elevated temperatures in the summer can delay embryonic development, as embryos in warmer conditions have a reduced capacity to secrete interferon, which is essential for maternal recognition and the maintenance of pregnancy [32].
5. The experience of the operator remains a critical factor, as the operator not only determines the optimal site for embryo deposition within the selected uterine horn but also ensures that the procedure is performed with precision to minimize trauma during the transfer [33]. The procedural technique during embryo transfer is essential for creating favorable conditions for successful implantation. This includes ensuring that embryos are placed in the uterus without direct contact with the uterine fundus, which could cause contractions or trauma, potentially hindering successful implantation [34].
6. Recipient movement during embryo transfer, particularly when the embryo transfer gun is within the uterus, increases the risk of endometrial damage. Pregnancy rates have been found to be inversely correlated with the time spent in the uterus during the transfer [35]. Moreover, the manipulation of the uterus per rectum can induce the uterine release of prostaglandin F2α, which may negatively affect the success of embryo implantation [36].

**POST TRANSFER MANAGEMENT**

1. Effective recipient herd management post-embryo transfer is essential for the success of embryo transfer (ET). Managing the herd requires a fundamental understanding of the recipients' nutritional needs, post-transfer synchronization, disease management, and marketing strategies [37]. Optimal fertility is observed in herds where handling facilities are designed to minimize stress, ensuring that cattle receive ideal nutritional supplementation for at least 45 days post-transfer, as nutrition plays a pivotal role in all reproductive aspects, particularly for recipient females [38]. Understanding the timing of conception and calving enables better calving supervision, while pre-calving vaccinations can be strategically timed to ensure optimal efficacy [39]. Pregnancy rates have been shown to be lower in recipients transported between 8 and 33 days post-insemination, compared to those transported within the first 4 days. This suggests that it is preferable to transport recipients before ET. Ultrasonography is a reliable method for detecting the presence of a conceptus as early as 28 days, but it is recommended to recheck all cows after 45 days to confirm pregnancy. Hormonal protocols aid in pregnancy sustenance. For instance, Ovsynch protocol, GPG, is one of the most important estrous synchronization protocols due to the possibility of applying timed insemination with this protocol. This protocol is commonly used in many farm animals, as it aids in herd management and eliminates the need for the detection of estrus. However, there are still some shortcomings that restrict the outcomes of this protocol, such as scattering ovulation time, short luteal phase and inadequate luteal function, and low conception rates [40]. Moreover, progesterone is also known as the hormone of pregnancy because of its crucial roles in establishing and sustaining pregnancy and implantation. Progesterone facilitates blastocyst implantation to the maternal endometrium by promoting uterine secretion for conceptus growth and development, initiating window of receptivity, inducing quiescence and non-contractility of endometrium to avoid abortion and protection of embryo against maternal immune system [41]. Furthermore, effective management of a recipient herd involves preparing recipients to receive embryos and identifying open cows for resynchronization or insemination, which increases the likelihood of achieving pregnancy and producing genetically superior offspring [3]. Lastly, synchronization protocols play a vital role in the embryo survival process. For instance, embryo quality, as evaluated using IETS conventions, had the greatest effect on embryo viability in vivo. Embryos morphologically assessed as being of ‘excellent’ quality (grade 1), according to IETS conventions, had a greater rate of viability in vivo than those assessed as being of ‘good’ quality [43].

**CONCLUSION**

Effective recipient management is fundamental to improving conception rates following embryo transfer. The study highlights that adhering to standard management practices, such as strategic handling, proper nutrition, and health monitoring, directly contributes to enhanced outcomes. Nutritional interventions, in particular, play a vital role, with improved diets leading to better reproductive performance. Additionally, optimizing the uterine environment, especially through precise synchronization, significantly boosts conception rates. Moving forward, future research should focus on developing comprehensive embryo transfer protocols that incorporate these strategies, tailored to specific breeding objectives. Investigating ideal environmental conditions for recipients will be essential to further enhance the success of embryo transfer technology under field conditions, ensuring optimal outcomes and greater reproductive efficiency.

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