

Deficiency of Uridine Monophosphate Synthase : A Recessive Disorder in Holstein Friesian Cattle

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Abstract

The present review is to summarise findings on one of the most important recessive hereditary disorder deficiency of uridine monophosphate synthase (DUMPS) in cattle. It is a disease of Holstein cattle characterized by lowered blood activity of enzyme uridine monophosphate synthase (UMPS). DUMPS leads to embryonic death in early stage of pregnancy. So some serious reproductive problems take place in dairy herds. Several investigations were carried out in different countries. No carrier animals were found among Holstein populations in Poland, Iran, India and Turkey, but the mutant allele was detected in the studies carried out in U.S.A. and Argentina. DUMPS of Holstein cattle is a component of the hypothesized multi-component complex. It is transmitted as an autosomal recessive trait. A carrier-normal mating results in one-half carriers, regardless of sex. Embryo homozygous for DUMPS die early in gestation and do not survive to the birth. The embryos often are resorbed during the first two-month of gestation, leading to more services per calving and longer than normal calving intervals (Shanke and Robinson, 1989). The only way to avoid economic losses is an early detection of DUMPS carriers. The use of PCR based molecular technologies promises quick detection of carriers enables their culling therefore, controlling and preventing the spread of DUMPS in the population.

Keywords: Autosomal recessive disorder, DUMPS, Holstein Friesian, Pyrimidine nucleotide, Orotic acid

Introduction

There are more than 5000 autosomal recessive genetic diseases in humans. Similarly, a small number of such diseases are also identified in animals and many of them are equivalent to human diseases. In cattle, the autosomal recessive genetic diseases are breed-specific. Some of them are Holstein specific, which include mainly factor XI deficiency Syndrome (Brush et al. 1987), Complex vertebral malformation (Steffen 2001), bovine leukocyte adhesion deficiency syndrome (Kerhli et al. 1990), bovine citrullinaemia (Harper et al. 1986) and deficiency of uridine monophosphate synthase (Robinson et al. 1993). Inherited disorders affect all kinds of farm animals. Functional and physiological defects arising from inherited disorders have negative impact on health and productivity of farm animals. Autosomal recessive disorders lead to economic loss in the dairy cattle industry, which is kept on with Holstein cattle, due to difficulty in detection of carrier individuals. Increased use of artificial insemination and worldwide use of service bull cause to widespread of this kind of disorders via carriers seem to be normal (Patel et al., 2006).

The Uridine Monophosphate Synthase (UMPS) is an enzyme, which has a key role on the pyrimidine nucleotide synthesis, which is essential for normal growth and development for several ruminant and nonruminant species (Healy and Shanks, 1987). Inactivation of this enzyme is caused by an autosomal-recessive heredity mutation, which occurs in the gene of UMPS. The mutation (C \pm T) leads to the loss of the restriction site of Aval site in codon 405 of the gene (Schwenger et al., 1993). This disorder is named as Deficiency of Uridine Monophosphate Synthase (DUMPS) in the Holstein cattle and characterized by lowered blood activity of enzyme UMPS (Healy and Shanks, 1987). DUMPS leads to embryonic death in early stage of pregnancy (Ghanem et al., 2006). So some serious reproductive problems take place in dairy herds. Several investigations were carried out in different countries. No carrier animals were found among Holstein populations in Poland (Kaminski et al., 2005), Iran (Rahimi et al., 2006), India (Patel et al., 2006) and Turkey (Meydan et al., 2006; Akyüz and Ertugrul, 2008), but the mutant allele was detected in the studies carried out in U.S.A (Shanks et al., 1987) and Argentina.

History

The deficiency of uridine monophosphate synthase results in early embryonic death of homozygous offspring. In late 1987, the condition was declared an undesirable enzyme defect by the Holstein Association of America (HAA) and a screening programme was initiated by using a biochemical assay involving estimation of erythrocyte UMP synthase. Heterozygous or carriers have half of the normal activity of this enzyme (Shanks and Robinson, 1990). Most of the DUMPS carriers identified in North America (n = 438) and Europe (n = 314), were the offspring of Happy Herd Beautician, a 5th best U.S. Holstein bull in 1987 (Holstein Association, 1987). Two HF carriers were found among 314 AI bulls in Hungary (Fesus et al. 1999). Mutation in the UMPS gene was also identified in 1.79% bulls 0.96% cows in Argentina (poli et al. 1996). Taiwan also recently reported two carrier out of 1468 HF animals screened for DUMPS (Lin et al. 2001).

Patel et al. (2006) screened DUMPS in Indian Holstein cattle. The polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analysis was performed on a group of 642 animals, mainly HF and HF crossbred cattle, to identify carriers of these diseases. None of the animals were carriers of DUMPS. It is possible that with the mounting selection pressure, the international gene pool may diminish, and consequently the risk of dissemination of inherited defects will increase. It is therefore recommended to screen breeding bulls for their breed-specific genetic diseases before they are inducted in artificial insemination programmes, to minimize the risk.

Molecular basis of DUMPS

DUMPS is a genetic disorder which interferes with pyrimidine biosynthesis. The enzyme uridine monophosphate synthase catalyses the conversion of orotic acid to UMP, the precursor of all other pyrimidine nucleotides and a normal constituent in the milk of cows and other ruminants (Shanks and Robinson 1989, Shanks et al. 1989). It was observed that several cows in the University of Illinois dairy herd produced in their milk five to ten times higher concentrations of orotic acid than normal. These elevations of milk orotic acid were evident at all stages of lactation and persisted from one lactation to other.

DNA test for identifying different genotypes of DUMPS

The genomic structure of UMP synthase gene was determined and a PCR- based diagnostic test for carrier detection has been established. DUMPS is caused by point mutation (C-T) at codon 405 within exon 5 (Viana et al. 1998). The UMP synthase gene was mapped to the bovine chromosome 1 (q31-36) (Harlizus et al. 1996).

A possible method of genotyping is given by Schwenger et al. (1993) and Grzybowski et al. (1998). A 108-bp product surrounding the mutation was amplified from genomic DNA with primers 5'GCA AAT GGC TGA AGA ACA TTC TG3' and 5'GCT TCT AAC TGA ACT CCT CGA GT3'. The PCR product was digested with Aval; normal homozygote shows bands of 53, 36, and 19bp, heterozygote of 89, 53, 36, and 19bp, the recessive genotype is 89 and 19bp.

The designation DP is added to the name of known heterozygotes and appears on official pedigrees, while TD designates animals that have tested normal for the condition (Shanks and Robinson 1990).

Checklist for managing DUMPS in a herd

- 1) A system should be set up for accurate recording of sire and maternal grandsire ID for all cows in the herd.
- 2) List or spreadsheet file should be made showing the DUMPS status of the sire and maternal grandsire of each cow in the herd.
- 3) Selection index should be used such as Lifetime Net Merit, to identify the group of AI sires likely to be used in the herd during the next three months.
- 4) DUMPS carrier bulls should be avoided for using on any cow whose sire or maternal grandsire is a carrier.
- 5) Modern genetic tools help us to identify undesirable genes and to eliminate them in a rapid and efficient manner and should be utilized.

Conclusion

With the wide use of artificial insemination (AI) and international trading of semen and breeding bulls, these genetic diseases have already been spread to a large population, as animal carriers of the diseases look normal. In India, where Holstein Friesian (HF) bulls and their semen are extensively used for crossbreeding programmes with indigenous cattle, it has become necessary to screen all HF and HF crossbreds, especially AI bulls, to minimize the risk of spreading these diseases among future bulls or bull mothers.

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