Molecular techniques for the Neonatal Screening of Spinal Muscular Atrophy

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Spinal muscular atrophy (SMA) is neurodegenerative disease mainly caused by the homozygous deletion of the functional telomeric survival motor neuron 1 gene (SMN1) exon 7. This absence causes a lack of the ubiquitous SMN protein which selectively destroys alfa motor neurons. Due to the disease severity, it is the leading genetic cause of infant death. The copy number of the centromeric SMN2 gene has an inverse correlation with the phenotype. SMA is currently classified in 5 types – Type 0 (lethal in womb or in the first weeks of life), Type I (approximately 50% of cases), Type 2 (children can sit alone), Type 3 (children can walk independently) and Type 4 (mildest form that appears in adults). Diagnosis is only made when symptoms arise and, by then, motor neurons are already irreversibly lost. Three therapies are now available, but they are most effective in the asymptomatic phase. To achieve this objective, the strategy is to include SMA in the panel of diseases screened in the Neonatal Screening (NS) Programs. In this sense, we describe the implementation of an in-house assay, that detects the absence of exon 7 of the SMN1 gene through the real-time polymerase chain reaction technique, adapted to NS. Normal controls and pathological samples collected from Guthrie cards were used. Our results show 100% concordance with the known genotypes (100% sensitivity and specificity). This method is a reliable, simple and affordable way to screen for this lethal disease.

Keywords: Neonatal Screening; Muscular Atrophy, Spinal; Real-Time Polymerase Chain Reaction