INDIAN STEMCELL STUDY GROUP ASSOCIATION (ISCSG)
(An All India Registered Association)
Reg. No- LUC/07484/2018-19

To find out an appropriate protocol for the DMD patients

Aims
Step 1 Slow the degenerative process
Step 2 Complete stoppage of deterioration and maintenance of remission
Step 3 Improvement in the quality of life with regain in muscle power minimum by minimum of 25%
Step 4 Prevention of cardiorespiratory failure/ involvement

Introduction

DMD is an X-linked recessive disorder , where there is a mutation in the dystrophin gene present on chromosome Xp21.1, which causes deletion/ duplication in the various exons of dystrophin gene. The end result of which is an abnormal or truncated dystrophin protein production that expresses as partial or complete deficiency of dystrophin in muscle fibers. Dystrophin is a cytoskeletal protein, predominantly expressed in skeletal, cardiac and smooth muscles, and in the brain to a lesser extent. Dystrophin functions to maintain the structural integrity of the muscle. Therefore, as a result of abnormal dystrophin synthesis in DMD patients, the muscle fibers progressively degenerate and result into gradual muscle weakness . Furthermore, in muscular dystrophies, fibrosis is generally associated with decreased strength and elasticity of muscle and can inhibit the diffusion of nutrients to myofibers . Additionally, in DMD patients, muscle mass becomes replaced by fat tissue and fibrous tissues . Clinically DMD children present with delayed muscular milestones with difficulty in running, climbing, and frequent falls on brisk walking. Weakness in the limb girdle muscles with hypertrophy of calf muscles, gower's manoeuvre while raising from the floor and waddling gait. Mild to severe degree of mental impairment and cardiomyopathy are also observed in DMD patients .

Standard tests to detect DMD are absence of dystrophin in immunohistochemistry (IHC), raised serum creatinine kinase (CK) levels and deletion of exons in dystrophin gene.

DMD remains an incurable disease, although several medicines including corticosteroids are used to delay the process of muscle degeneration. Glucocorticoids are widely used for its anti-inflammatory property but it gives a lot of side effects including weight gain, diabetes, fragile bones, and increased risk of fractures, reduced growth and suppressed immune system . Physiotherapy for DMD patients such as stretching and mobility exercises can aid in temporary muscle flexibility. However, these treatments loose effect in later stages of the disease . Therefore, the need of the hour is to develop an effective clinical intervention that is capable of arresting the disease progression and thus can save lives of hopless children.

Studies in the past have provided reliable proof about the ability of stem cells to regenerate or re-differentiate into skeletal muscles . This property of stem cells befits DMD as a perfect candidate for stem cell's regenerative effect. Since 1990s, scientists around the globe are attempting to engraft stem cells of various origins such as myoblast cells, MSCs and other types of stem cells, from a Dystrophin-positive donor to a Dystrophin-deficient muscle to facilitate normal muscle function . However the mentioned stem cells have not shown a reasonable engraftment potential owing to reasons like inefficient isolation of adequate quantity of stem cells or inappropriate mode of delivery. Therefore, an ideal stem cell population is yet to be established.

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One of the pre-requisites for a stem cell population to be considered good for DMD is to have myogenic potential. Preclinical studies have already established allogenic mesenchymal stem cells (MSCs) derived from cord tissue as naive and harmless and can be safely transplanted into small animal DMD models, without any GVHD established that (Graft versus host disease). Study by Eder Z et al. (4) showed that human umbilical cord blood (HUCB) cells were capable to differentiate into myogenic cells *in vivo* following intravenous injection into *sjl* dystrophic mice.

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Now the subject is open for suggestions and discussions

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