SCSICON 2017-18

SCSI
STEM CELL SOCIETY (INDIA)

SCSICON 2017-18

4th Annual Conference of

Stem Cell Society (India)

28th and 29th April 2018

India Habitat Centre, New Delhi (India)

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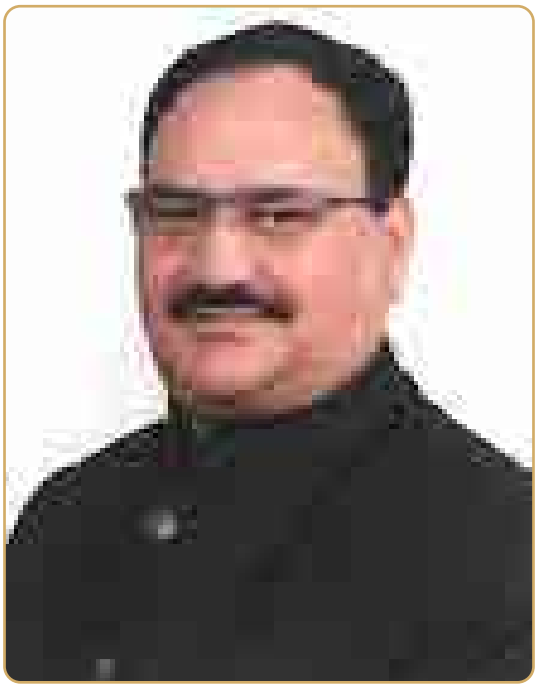

A Message from
Shri Jagat Prakash Nadda
Minister of Health & Family Welfare
Government of India

जगत प्रकाश नड्डा
Jagat Prakash Nadda

स्वास्थ्य एवं परिवार कल्याण मंत्री
भारत सरकार
Minister of Health & Family Welfare
Government of India

MESSAGE

It gives me great pleasure to know that Stem Cell Society is organizing its Third Annual Conference at New Delhi on 11th – 12th June 2016.

Stem Cell therapy is the latest and most promising development in the world medical sciences. Many incurable diseases that have no definitive treatments at present can be helped with Stem Cell Therapy. Recent scientific publications worldwide and from India as well show that in killer diseases like Duchenne muscular dystrophy and Motor neuron disease lives can be saved, that limb amputations can be prevented in ischemic limb diseases, that children with autism and cerebral palsy can be integrated back into mainstream society though improvements in their mental and physical states, that paralysed patients of Spinal cord injury and brain injury can be lifted out of wheelchairs, that our elder citizen suffering from osteoarthritis can be given relief and that lifestyle diseases such as diabetes and ischemic cardiac disorders can also be helped.

It is a matter of pride for us that India is playing a leadership role in this field with many of our doctors doing pioneering work and helping thousands of patients. The work of these doctors in Stem Cell Therapy is in alignment with the Government of India's and our Honourable Prime Minister Shri Narendra Modi's Vision of "Make in India" and "Skill India". I wish the Conference all success and hope that the deliberations of this Conference create greater awareness amongst the medical community about this field so that eventually the ordinary citizen of the country suffering from incurable diseases can benefit from Stem Cell Therapy.

(Jagat Prakash Nadda)

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A Message from
Dr. G. N. Singh
Drugs Controller General (India)
Directorate General of Health Services
Central Drug Standard Control Organisation

Dr. G. N. Singh
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DIRECTORATE GENERAL OF HEALTH SERVICES
CENTRAL DRUGS STANDARD CONTROL ORGANIZATION
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MESSAGE

I am glad that the Stem Cell Society is organizing its Third Annual Conference in New Delhi on 11-12 June 2016. I had pleasant memories of the 2015 Annual conference where I had inaugurated the first issue of the Indian Journal of Stem Cell Therapy.

A lot of developments have happened on the regulatory framework on Stem Cell during the last one year globally including in USA, Japan and Korea etc. Regulators world over are realizing that safer stem cell therapies for older as well as newer clinical indications should be more easily available to patients needing them and are modifying their regulations accordingly. In our country, we are in the process of revisiting the Drugs and Cosmetics Act 1940 and rules 1945 with respect to Stem Cell.

The importance of Stem Cell therapy lies in the fact that it is able to treat diseases that were earlier considered incurable and for which there was no hope. These include some severely debilitating neurological, pediatric, orthopedic, cardiac, endocrine and other conditions.

I hope the Conference will provide a vital platform for discussion and knowledge dissemination to all the Society members. I wish the event a grand success and I convey my best wishes to the organizers.

(Dr. G. N. Singh)

Welcome Message From Organizing Committee of SCSICON 2017-18

Dear friends & colleagues,

We welcome you all to the 4th Annual Conference of Stem Cell Society (India).

Dr. B S Rajput
Organizing Chairman

Dr. Ajay Lekhi
Organizing Co-Chairman

Dr. Rohit Kulkarni
Vice President &
Organizing Secretary

Dr. Alok Sharma
President
Stem Cell Society (India)

SCIENTIFIC PROGRAMME

DAY 1 - 28TH APRIL 2018

8:30 am	**Registration**	
Session 1: Workshops and Demonstration		
9:00 am-10:00 am	Dr. Deepali Bharadwaj	**Cosmetology Workshop**: Combination of PRP and Fillers for Facial Rejuvenation
10:00 am- 11:30 am	Dr. B.S. Rajput, Dr. Rohit Kulkarni, Dr. Alok Sharma	Bone Marrow Extraction and Processing **Workshop**
11:30 am- 11:45 am	**Tea Break**	
Session 2: Guest Lectures- Stem cell therapy in Gynaecology and Cord blood banking		
Chairpersons: Dr. Sandeep Shrivastava, Dr. Roopam Jain, and Dr. Vivek Mahajan		
11:45 pm-12:10 pm	Dr. Jyoti Malik	Role of PRP in thin endometrium
12:10 pm- 12:35 pm	Dr. Rohit Kulkarni	Significance of Cord blood banking in current scenario
12:35 pm- 1:00 pm	Dr. Mini Chaturvedi	Newer Indication of use of Cord blood and Cord tissue
1:00 pm- 1:25 pm	Dr. Vikas Verma	How to collect, transport and process cord blood and cord tissue
1:25 pm- 2:00 pm	**Lunch Break**	
Session 3: Guest Lectures- Stem cell therapy in Other Clinical Disorders		
Chairpersons: Dr. Jyoti Malik, Dr. Priya Darshi and Dr. Sachin Kandhari		
2:00 pm-2:25 pm	Dr. Rajneesh Verma	Role of iPSC in Oncology
2:25 pm-2:50 pm	Dr. Shashi Pal Sadana	Treating joint instability with chemical regenerative therapy. Adjuvant for cellular regenerative therapy in managing unresolved chronic pain. A retrospective study
2:50 pm-3:15 pm	Dr. Sandeep Shrivastava	PRP : A Future for Wound Management.
3:15 pm- 3:40 pm	Dr. Vikram Pabreja	Treatment of hypothyroidism with intrathyroidal injection of autologous PRP
3:40 pm- 4:00 pm	**Tea Break**	
Session 4: Guest Lectures-Stem cell therapy in Orthopaedic conditions		
Chairpersons: Dr. Mini Chaturvedi, Dr. R.N. Shrivastava and Dr. Vikram Pabreja		
4:00 pm - 4:25 pm	Dr. Subramanya Rao	Stem cell Therapy in Osteoarthritis knee joint and Role of PRP in Orthopaedics
4:25 pm - 4:50 pm	Dr. Roopam Jain	Role of autologous PRP in Osteoarthritis patients-A randomized controlled trial
4:50 pm - 5:15 pm	Dr. Priya Darshi	Role of PRP in Osteoarthritic Knee Joint
Session 5: Free Papers		
5:15 pm - 6:00 pm	Free papers by Young Achievers	

SCIENTIFIC PROGRAMME

DAY 2 - 29TH APRIL 2018

Session 1: Guest Lectures- Stem cell therapy in Orthopedic Disorders		
Chairpersons: Dr. Shivinder Deol, Dr. Anant Bagul and Dr. Kaushik Deb		
9:00 am-9:25 am	Dr. Hemangi Sane	Role of Stem Cell therapy in ALS
9:25 am-9:50 am	Dr. Ajai Singh	Role of stem cell transplantation in pediatric orthopedic conditions
9:50 am- 10:15 am	Dr. B.S Rajput	Role of Bone marrow derived mesenchymal cells in osteoarthritis
10:15 am-10:40 am	Dr. Siddharth	BMAC for bone defects: What does the evidence say?
10:40 am- 11:05 am	Dr. Vivek Mahajan	Role of Bone Marrow Mononuclear cells in cartilage regeneration
11:05 am- 11:30 am	**Tea Break**	
11:30 am -12:00 noon	**Inauguration**	
12:00 noon-1:00 pm	**Panel Discussion:** Regulations for stem cell therapy **Participants:** Dr. S. Eswara Reddy, Drugs Controller General (India), Dr. R.K. Vats, Additional Secretary & DG (CGHS), Ministry of Health and Family Welfare, Dr. Alok Sharma, President Stem Cell Society (India) **Moderators**: Dr. B.S. Rajput, Dr. Rohit Kulkarni	
1:00 pm- 1:30 pm	**Lunch Break**	
Session 2: Keynote Talks		
Chairpersons: Dr. Rohit Kulkarni, Dr. B.S. Rajput and Dr. Mini Chaturvedi		
1:30 noon- 1:55 pm	Dr. Alok Sharma	Guidelines, Regulations and Ethics of stem cell therapy. The urgent need for change in India
1:55 pm -2:20 pm	Dr. Rajneesh Verma	iPSC technology moving from lab to clinical applications
2:20 pm -2:45 pm	Dr. Shivinder Deol	Efficacy of Hypoxic ischemic cells in neurological indications
Session 3: Guest Lectures-Stem cell therapy in Neurological Disorders		
Chairpersons: Dr. Alok Sharma, Dr. Kanchan Mishra and Dr. Surya Kant		
2:45 pm- 3:10 pm	Dr. Nandini Gokulchandran	Role of BMMNCs in Neurodevelopmental Disorder
3:10 pm- 3:35 pm	Dr. Anant Bagul	Role of Stem cell therapy in DMD
3:35 pm- 4:00 pm	Dr. Sachin Kandhari	Role of Stem cells and epidural stimulation in spinal cord injury
4:00 pm-4:15 pm	**Tea Break**	
Session 4: Guest Lectures-Stem cell therapy in Pulmonology and Other Clinical Disorders		
Chairpersons: Dr. Nandini Gokulchandran, Dr. Ajai Singh and Dr. Vikas Verma		
4:15 pm- 4:40 pm	Dr. Surya Kant	Role of Mesenchymal cells in Interstitial Lung Disease (ILD)
4:40 pm- 5:05 pm	Prof. Rajendra Prasad	MDR, XDR AND TDR -TB : Where are we and what is way forward?
5:05 pm- 5:30 pm	Dr. Kaushik Deb	Cellular immunotherapy in cancer
5:30 pm-6:30 pm		Discussion and passing of resolution from the Stem Cell Society (India) to the government on the regulations for stem cell therapy in India

Effect Of Bone Marrow Derived Autologous Stem Cell Transplantation On Cerebral Metabolism of A 20-year-old Autistic Patient

Dr Anant Bagul
Universal Hospital, Pune

Abstract

Autism is a neurodevelopmental disorder characterized by clinically significant impairment in social, occupational and other important areas of normal functioning. The autistic brain shows altered neurochemical metabolism, such as decreased glucose uptake, increased concentrations of lactate and reduced concentrations of N-acetyl-aspartate. Besides behavioral therapies and medications for autism-associated conditions such as seizures and gastrointestinal distress, there are no U.S. FDA approved pharmacological therapies to treat Autism's core pathology. Stem cell transplantation is a promising option as it targets the core developmental abnormality in the brain through tissue regeneration. Here, we have studied the effect of autologous bone marrow derived stem cell (BMSC) transplantation on the cerebral metabolism of a 20-year-old autistic female patient who was given a total of three intrathecal infusions with 10 X 107 BMSC in each infusion. FDG-PET scan performed six months post-treatment showed significant increase in brain metabolism, evidenced by increased uptake of fluorodeoxyglucose (18F-FDG) by the parenchymal cells of the temporal and parietal lobe compared to the scan performed before intervention. There was a remarkable improvement in her eye contact, social judgment and communication skills. Her IQ increased from 52 to 80 and her Childhood Autism Rate Scale score shifted from above to below 30. There were no adverse effects of any sort and betterment in the girl's condition could be demonstrated by her scores on the Quality Of Life Scale.

Keywords: Autism, cerebral metabolism, bone marrow derived stem cell infusion

Role of Stem Cell Therapy In Duchenne Muscular Dystrophy (DMD).

Dr Anant Bagul
Universal Hospital, Pune

Abstract:

Duchenne muscular dystrophy (DMD) is the most common and serious form of muscular dystrophy. One out of every 3500 boys is born with the disorder, and it is invariably fatal. Until recently, there was little hope that the widespread muscle degeneration that accompanies this disease could be combated.

However, stem cell therapy now offers that hope. Like other degenerative disorders, DMD is the result of loss of cells that are needed for correct functioning of the body. In the case of DMD, a vital muscle protein is mutated, and its absence leads to progressive degeneration of essentially all the muscles in the body.

To begin to approach a therapy for this condition, we must provide a new supply of stem cells that carry the missing protein that is lacking in DMD. These cells must be delivered to the body in such a way that they will engraft in the muscles and produce new, healthy muscle tissue on an ongoing basis.

Patients who were clinically and pathologically diagnosed with Duchenne muscular dystrophy were transplanted with stem cells by intravenous infusion, in combination with multi-point intramuscular injection. They were followed up for 12 months after cell transplantation. Results showed that clinical symptoms significantly improved, daily living activity and muscle strength were enhanced,. These pieces of evidence suggest that stem cell transplantation can be considered as a new regimen for Duchenne muscular dystrophy.

In order to make this process into something that could be used in the clinic, we will develop standard procedures for making and testing the cells, to ensure that they are effective and safe. In this way, this project could lead to a new stem cell therapy that could improve the clinical condition of DMD patients. If we have success with DMD, similar methods could be used to treat other degenerative disorders, and perhaps even some of the degeneration that occurs during normal aging.

Key Words: stem cells; Duchenne muscular dystrophy; case report; dystrophin; muscular force; activities of daily living.

Role of Bone Marrow Derived Mesenchymal Stem Cells In The Management of OA Knee

Dr B.S. Rajput
Consultant orthopaedic and stem cell transplant surgeon
Criticare hospital and research centre, Juhu, Mumbai, India

Abstract:

Osteo arthritis Knee is one of the commonest diseases of the joints and a leading cause of chronic disability, especially in the aged population. The pathogenesis of OA knee has been linked to biomechanical and biochemical changes in joint cartilage, e.g. inability to withstand normal mechanical stress, limited nutrients and oxygen supply, inadequate synthesis of extracellular matrix components, increased synthesis of proteinases and overall apoptosis of chondrocytes. Synovial inflammation is a response of synovial macrophages to cartilage debris and catabolic mediators entering the synovial cavity which limits the cartilage repair. Current nonsurgical treatment options for OA knee focus on shortterm relief of symptoms like physical therapy, activity modification, bracing, oral medications, and intra−articular use of steroids.

Although these may be effective in providing some relief of pain, allare short-term measures. Intra−articular injection of Hyaluronic acid (HA) is effective in patients with less-severe OA, but pain relief is limited to a few months only. Since hyaluronic Acid does not slow down the progression of the disease process, the surgical option becomes inevitable. Autologous biologic therapies are also promising with early data showing that platelet rich plasma (PRP) injection for OA knee may be of benefit for patients with mild to moderate osteoarthritis. Two recent trials of HA versus PRP injections for OA knee demonstrated the superiority of PRP. However, PRP is less effective for patients with more severe OA. Regenerative medicine has gained researcher's and clinician's interest as an alternative of surgical treatment for OA knee. The use of autologous BM−MNCs in OA knee to decrease symptoms with the slowing down of underlying disease process is quite promising. The composition of these nucleated cells is diverse including Mesenchymal Stem Cells (MSCs), Hematopoietic StemCells (HSCs), Monocyte Precursor cells, Macrophages, T cells, B cells, Dendritic Antigen Presenting Cells, Natural Killer Cells and Neutrophils. The action of these cells, both in isolation and synergistically, once introduced into the arthritic joint may help in improving the pain and functions by replenishing damaged joint structures and slowing down of catabolic immune responses, thus alleviating the symptoms and progression of the disease.

Early clinical studies using both isolated mesenchymal stem cells and bone marrow aspirate concentrate to treat osteoarthritis have been encouraging. Stem cell treatments could potentially be a safe, less invasive, and nonsurgical treatment for OA knee.

Adult Human Stem Cells in Regenerative Medicine

Dr Kanchan Mishra, (Ph.D.-SGPGIMS, India; PDF -TMIN, Tokyo, Japan)
(Assistant Director R&D & HOD Operations of SmartStem)
NABH Accredited Regional Blood Transfusion Centre
Surat (Gujarat), India

Abstract:

Stem cells are self-renewing cells that can differentiate into specialized cell type(s). Pluripotent stem cells, i.e. embryonic stem cells (ESC) or induced pluripotent stem cells (iPSC) differentiate into cells of all three embryonic lineages. Multipotent stem cells, like hematopoietic stem cells (HSC), can develop into multiple specialized cells in a specific tissue. Unipotent cells differentiate only into one cell type, like e.g. satellite cells of skeletal muscle. There are many examples of successful clinical applications of stem cells. Over million patients worldwide have benefited from bone marrow transplantations performed for treatment of leukemias, anemias or immunodeficiencies. Skin stem cells are used to heal severe burns, while limbal stem cells can regenerate the damaged cornea. Pluripotent stem cells, especially the patient-specific iPSC, have a tremendous therapeutic potential, but their clinical application will require overcoming numerous drawbacks. Therefore, the use of adult stem cells, which are multipotent or unipotent, can be at present a more achievable strategy. Noteworthy, some studies ascribed particular adult stem cells as pluripotent. However, despite efforts, the postulated pluripotency of such events like "spore-like cells", "very small embryonic-like stem cells" or "multipotent adult progenitor cells" have not been confirmed in stringent independent studies. Also plasticity of the bone marrow-derived cells which were suggested to differentiate e.g. into cardiomyocytes, has not been positively verified, and their therapeutic effect, if observed, results rather from the paracrine activity. Here in SCSI conference Iwill be discuss the examples of recent studies on adult stem cells in the light of current understanding of stem cell biology.

MDR and XDR TB: Where Are We and What Is Way Forward

Dr Rajendra Prasad, Dr Saurav Pandey
Director Medical Education And Head Department Of Pulmonary Medicine Eras
Lucknow Medical College And Hospital Lucknow

Abstract:

Tuberculosis occurs worldwide and remains an important cause of morbidity and mortality in many countries including India. There were an estimated 10.4 million new cases of tuberculosis causing death to 1.7 million people globally in 2016. Of which there were an estimated 2.8 million new cases in India and 0.48 million people died in India due to tuberculosis in 2016. It is a cause for concern as India stands first in terms Of absolute number of cases..In India, it is estimated that the prevalence of MDR-TB among new and previously treated patients was 2.5% and 16% respectively. It is estimated that 1470,000 cases of MDR-TB/RR-TB emerge every year of which 79,000 were among notified cases of TB in 2016. Out of 79000 MDR –TB/RR-TB cases, only 28876(36%) were diagnosed, 26988(34%) were started on treatment and treatment success rate was only 46%5. since 2011, there have been rising instances of Extensively drug resistant tuberculosis(XDR-TB) in India. XDR-TB has been reported in all regions of the world and it has become a serious emerging threat to global public health especially in countries with a high prevalence of Human Immunodeficiency Virus (HIV). 6.2 % of MDR-TB cases were found to have XDR-TB. To date, a cumulative total of 124 countries have confirmed at least one case of XDR-TB5as treatment of mdr and xdrtbis expensive, lenthy and toxic . a new treatment like stem cell theraphy can be explore to manage such type of patient.

iPSC Technology Moving From Lab To Clinical Applications

Rajneesh Verma 1, 2, Ratchanont Guy Suprakob 1, 2, Naoshi Sugimoto1, Koji Eto1 and Yamanaka1
Department of Clinical Applications,
1Centre for iPS Research and Applications (CIRA), Kyoto, Japan.
2 Bio Cell Innovations, Bangkok, Thailand.
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Abstract:

Stem cells are still a relatively new discovery, as the first stem cells were discovered in human cord blood in 1978, the first mouse embryonic stem cells were derived in 1981, and it was not until 2006 that induced Pluripotent Stem (iPS) Cells were produced for the first time.

Since the discovery of iPS cells, a large and thriving research product market has grown into existence, largely because the cells are completely noncontroversial and can be generated directly from adult cells. Today, the number of iPS cells products sold worldwide is growing at an annual rate of 14.7%. In addition, 22% of all stem cell researchers now self-report having used iPS cells within a research project.

It is clear that iPS cells represent a lucrative product market, but methods for commercializing this cell type are still being explored, as clinical studies investigating iPS cells continue to increase in number. At this time, nearly all clinical studies involving iPS cells are for the creation and evaluation of iPS cell lines from specific patient populations, in order to determine if these cell lines could be a good model for a disease of interest in that patient population.

However, the first clinical study involving transplant of iPS cells into humans began in August 2014 to investigate the use of iPS cells in treating patients with macular degeneration. This clinical study is now underway at the Riken Center in Japan.

Sickle cell disease and thalassemia are genetic disorders caused by errors in the genes for haemoglobin, and are inherited, and usually both parents must pass on an abnormal gene in order for a child to have the disease. The body reacts by destroying red blood cells, causing anemia and when this happens, the resulting diseases are serious and, at times, fatal.

Medications that increase fetal haemoglobin (HbF) in both disease have greatly improved life for patients suffering from these diseases; however, safer and more effective drugs are still being sought. Stem cell (adult)transplantation can be used to treat both illnesses, but it has many limitations.

Recently, we established expandable erythroblast cell lines (imERYPCs) from hiPSC as a cryopreservable cell source for ex vivo production of erythrocytes. The manufactured iPSC-erythrocytes were fetal type erythrocytes bearing HbF. This method can produce erythrocytes in pathogen-free condition and independent of donors for stable supply with no risk of transfusion-related infections. Regarding tumorigenicity, enucleated erythrocytes pose no risk and contaminating nucleated cells can be separated by size and specific weight and further irradiated without affecting the structure and function of erythrocytes.

Through generation of platelets from iPSC derived megakaryocytes celll lines, our lab have found that the optimal turbulent flow condition is important to induce the release of enucleated platelets from megakaryocytes. By using a novel flow concept bioreactor, platelet yield from megakarycytes and their quality dramatically improved, which was suggested to occur through the regulation of acetylation-deacetylation of tubulins by HDAC family proteins. Considering that HDAC family molecules also regulate acetylationdeacetylation of cytoskeletal proteins such as tubulins in erythrocyte enucleation, these findings suggest that erythroblasts may also require optimal physical condition for their enucleation.

Based on these preliminary ideas, several approach will be taken to achieve efficient generation of enucleate HbF type erythrocytes. First, settings in this novel reactor will be test to find an optimal flow condition for efficient and viable generation of iPSC-erythrocytes. We will also profile the expression of HDAC family proteins in maturing erythrocytes and how they correspond in various flow conditions. The function of HDAC family proteins will also be assessed through HDAC inhibitors and gene silencing procedures to find improved condition for enuclaeation. Furthermore, high throughput drug screening using the imERYPCs will be performed to identify biochemical substances that can enhance erythropoiesis ex vivo.

We expect to achieve (>90%) efficient production of enucleated erythrocytes by novel flow concept bioreactor and will identify the crucial factors which affect the stable yield and enucleation of erythrocytes. I believe this will be a robust and efficient way to produce enucleated erythrocytes with HbF type for anemic patients with the sickle cell and thalassemia, which will also provide resistant to malaria parasite invasion.

PRP : A Future for Wound Management

Author: Dr Sandeep Shrivastava ; MS , DNB , Ph.D
Professor Orthopaedics
Director - Centre for Autologous Platelet Biotechnological Interventions ,
Affiliation: Datta Meghe Institute of Medical Sciences , Wardha , INDIA.

Abstract:

The management of wounds has been a huge challenge; particularly those which are complex in nature and associated with severe infections , necrosis , exposed bones, tendons, implants, non healing chronic ulcer etc. The resources spent for treating these wounds are huge. They need multiple surgeries, judicious antibiotic management and intricate local dressings. This involve substantial cost and and further morbidities. Despite the reconstructions, many a times the normalisation of skin is not possible; for example in the sole and heel. The Prolong Antibiotics intake , puts patients to further risks and side effects. Evolvement of Antimicrobial resistance is also a huge concern. In MRSA positive cases the cost, intensity and risk increases many fold. The local dressings assisted by devices such as Vacuum / negative pressure ; chemically impregnated dressings etc need meticulous care and may not succeed in such cases.

This work is dedicated to evolve a solution which can lead to predictable wound healing in all such cases with minimum of surgical intervention ; drugs such antibiotics and analgesics; and simplified local care. The Regenerative Medicinal Products getting evolved includes three key biological human cell products - Stem cells; Mesenchymal Stem Cells and Platelets, particularly Platelet Rich Plasma(PRP).Out of these the first two needs a state of art laboratory and equipments to meet the purpose and are mostly not into clinical practices, yet. The platelets offers a huge window of opportunity particularly in terms of their availability and ease of preparing PRP. The Platelet seems to have the potential for shaping up as “Regenerative & Repair” solution for complex wounds and many more. The ease, safety and accessibility of PRP is an outstanding leverage for regenerative medicine; to be tested for developing solutions which could be free of Drugs, Devices and may be surgical interventions, preserving the tissues which are not dead yet.

This study is embarked on this discovery of very exciting option of Regeneration of tissues and consolidation of reparative process by biotechnological intervention with PRP, tissue engineering the skin over the wounds, as they are assisted to heal such defects. At the Dept. of Orthopaedics, J.N.Medical College, Wardha The Project PRP_ Biotechnological Intervention was started in 2012 and after 5 years of different observations of usage of PRP in wounds , we developed a technique now called as “STARS Technique” - “Sandeep's technique for Assisted Regeneration of Skin”. This involves use of autologous PRP as the Mono-therapy and mainstay treatment for almost all wounds including the above described complex wounds. Its basically infiltration of PRP followed by Moist Saline dressings. A pilot case based prospective interventional study involving 200 Patients is now completed and in this address we intend to share disclosures related to the clinical outcomes of this technique with focus to keep it with in the reach of every doctor, its experience and its future role as regenerative medicine .

The STARS technique is a very simple protocol , developed scientifically step by step, through animal studies, standardisations of laboratory preparations, clinical case based observations and needful adoptions, till desirable results are obtained.

The results are excellent with complete control of infections , a predictable healing in almost all cases including bed sores, diabetic sores, complex wounds involving bones , tendons and near necrotic flaps and tissues. The results in the last group of near necrosis / gangrenous situation is a quantum jump in the history of mankind , where in reversal/ restriction of damage has been achieved perhaps for the first time , restricting the morbidity to the minimum. We have been able to salvage limbs which were referred for amputations.

This is the beginning of new era in Wound Management by propagation from “Reconstruction to Regeneration”, opening up the huge potentials for furtherance of Modern Medicine through Stem cells and Cellular therapy.

Biography of Author:

Dr. Sandeep Shrivastva is the Director of Centre of Autologous Platelet Biotechnological interventions, at Datta Meghe Institute of Medical Sciences, Wardha India.

He is Professor of Orthopaedics having done his MS, DNB and Ph.D.

He is also Chief Executive Officer, Hospitals. and Ex DEAN of JNMC.

In the field of Regenerative Medicine, he has pioneered the wound management with PRP, by developing the clinical Protocol of “Sandeep's Technique for Assisted Regeneration of Skin (STARS Therapy) . His work is widely published and presented across the World. He has 2 books, 63 Publications and 75 presentations, including Orations , Key note addresses and guest lectures.

He also has 6 copyright & is inventor for H_COIN - a research outcome measurement tool, “Pre- Yell” - an emergency response Application., Self assertive learning (SAL), Academic appraisal program (AcAP). and “Early Research Exposure Model” (ERE Model).

Treating joint instability with chemical regenerative therapy. Adjuvant for cellular regenerative therapy in managing unresolved chronic pain. A retrospective study

Dr Shashi Pal Sadana MS (ortho)
Sadana fracture centre, Rambagh, Agra (UP) India

Abstract

Introduction – Management of chronic pain has always been a tricky and tedious job for orthopedic surgeons. Most of the time degenerative disorders of ligaments, tendons and cartilages are responsible for these. It has become a clinical necessity to develop the novel therapeutic approaches to accelerate regeneration of these tissues and halt progression of degeneration. In our study we evaluated the effect of local regenerative injection therapies (RIT) in patients of unresolved chronic pain.

- **Aim & Objectives -** Outcome of 161 patients of unresolved chronic pain in different regions viz knee joint area; low back area, shoulder joint area, and ankle joint area were investigated undergoing local regenerative injection therapies.

- **Materials & Methods -** On average, 20 months following their last RIT session {Chemical regenerative injection therapy only/or with Platelet rich plasma (PRP) therapy or Mesenchymal stem cells} , Patients were contacted and asked numerous questions in regard to their levels of pain and a variety of physical and psychological symptoms, as well as activities of daily living, before and after their last RIT.

- **Results -** The results of this study showed that patients had a statistically significant decline in their level of pain, stiffness, crunching sensation, and improvement in their range of motion with RIT. More than 82% showed improvements in walking ability, medication usage, anxiety, depression, and overall disability. Though study was subjective but we were able to gather some special radiographic and sonographic evidences showing improvement in parameters.

- **Conclusion -** In this study, patients with unresolved chronic pain, treated with regenerative therapies, showed improvements in many clinically relevant parameters and overall quality of life. Degenerative disorders of joints are not merely degeneration of cartilage but degeneration of soft tissues surrounding is also there so efforts to regenerate stabilizing tissue of joints should always be considered in managing degenerative disorders of joints.

Efficacy of Hypoxic Allogeneic MSC in Clinical Applications

Dr Shashi Pal Sadana MS (ortho)
Sadana fracture centre, Rambagh, Agra (UP) India

Abstract

Human tissue oxygen tension (tPO2) varies in different organs & tissues from 2-7% at 21% FIO2. Placenta & embryo tPO2 is 1-2%. Several studies have shown that stem cell (SC) niches in different tissues exist under hypoxic conditions, which promotes the dedifferentiated state. Even small amounts of shift in tPO2 stimulates differentiation. Most cell cultures in vivo are done at normoxic condition (20% O2 tension), potentially resulting in smaller cell expansion, lower VEGF, angiogenesis & potency. Stemedica has patented method of culturing cells under hypoxic conditions of 3-5% O2. This promotes greater cell expansion up to 30-fold in a study of BM-MSC over normoxic conditions, higher release of VEGF & growth factors, & angiogenesis. The SC are fully characterized with less than 1% of cells exhibiting HLA-DR, thereby removing risk of rejection or transfusion reactions.

Results CT: Phase I/II study completed on Ischemic Stroke showed no serious side effects (SAE) & significant improvement on all measured scales. Phase II study completed on Heart Failure showed no SAE & improvement in all scales with statistical significance in 6-min walk, reduction NK cells. Study published in Circulation journal. Phase II/III study on Ac Myocardial Infarction completed in KZ showed no SAE & statistical improvement on all scales. MSC have been commercially approved by KZ Ministry of Health as New Drug for AMI Aug 2017.

A new global study is planned to study the effects of MSC in diabetes: A PHASE II/III, MULTI-CENTER, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO ASSESS THE EFFICACY OF A SINGLE IV DOSE OF MSC TO SUBJECTS WITH DIABETES MELLITUS TYPE 2". 114 subjects will be enrolled & randomized 1:1. Inclusion Criteria include: Males & females 18-75 yr, T2DM of minimum 1-yr duration, with poor glycemic control with HBA1C of 8.0-11.0% (inclusive), on any combo meds & or insulin.

“Treatment of hypothyroidism with intrathyroidal injection of Autologous PRP"

Dr Vikram Pabreja

Abstract

Background

Hypothyroidism is a global health issue, with a staggering 200 million people suffering around the world. Hypothyroidism can occur due to iodine deficiency or autoimmune conditions as Hashimoto s thyroiditis. This study excluded post surgical and drug induced hypothyroidism. Further this study is to expand the literature on role of intrathyroidal injection of autologous PRP in treating hypothyroidism.

Methods

This study was carried out to investigate the effects of intrathyroidal injection of autologous PRP under ultrasound guidance in patients with hypothyroidism, subclinical hypothyroidism and autoimmune thyroiditis. 27 patients were selected from age group of 20-70yrs. All patients held oral thyroxine prior to intrathyroidal injection. 20ml peripheral venous blood was withdrawn after pharmacologic intervention with iv omega 3 fatty acids and ascorbic acid without preservative. Further it was centrifuged to yield 10ml of PRP. PRP was tested for microbial contamination before injection. 5ml PRP was injected in each lobe of thyroid. The patients were followed up for a period of 1year with 1month, 3month, 6 month and 1 year interval. Thyroid function test, free T3, free T4, TSH, anti TPO, anti TBG antibody tests were assessed along with Ultrasound of thyroid gland.

Results

A positive response to intra thyroidal injection of autologous PRP was observed in more than 90% of cases after 1month of injection. No adverse event were found during 1year follow up with significant decrease in serum TSH , anti TPO and anti TBG antibody values. Patients reported less lethargy , less musculoskeletal pains , better sleep and no weight gain from baseline. All measurements were statistically significant.

Thin endometrium and PRP : A case study and analysis

Dr Jyoti Malik (IVF specialist & Lap surgeon) MBBS, DGO, DNB, MNAMS, FICS.

Abstract

Endometrial thickness plays a vital role in the process of implantation. Endometrium is the lining of uterine cavity and undergoes changes according to the cyclic patterns of estrogen & progesterone hormones.Endometrial thickness and morphology is very important for successful implantation of embryo. Endometrial thickness has high specificity and sensitivity in predicting pregnancy outcomes.A minimum thickness of 7mm is essential for proliferative phase for successful implantation to occur. Endometrium is best assessed on endovaginal scans where thickness and endometrial pattern are studied .Other parameters like endometrial volume and doppler USG for uterine and endometrial flows is done by 3D/4D USG

Causes of thin Endometrium:-

1. **Iatrogenic**- Due to over jealous D&C myomectomy where cavity of got opened or caesarian section where placental bits had to be removed by curettage but, if the basalis layer has been damaged, the endometrium will not be able to regrow.(1)

2. **Inflammatory**:-

   - Tuberculosis
   - Pelvic Inflammatory Disease
   - Sexual transmitted diseases.

3. **Low Estrogen Level -** Due to use of clomiphene citrate, prolonged O.C use or in the conditions of hypogonadotrophic hypogonadism.

4. **Systemic causes-** Hypertension, Diabetic mellitus, Epilepsy, Substance abuse like smoking.

5. Inadequate blood flow.

6. Idiopathic.

Treatments available for improving thin Endometrial Lining :-

1. **Low dose aspirin -** It increases the uterine blood flow by decreasing the impedance to blood flow by decrease in pulsatility index of Uterine arteries

2. **Pentoxyphylin & tocopherol -** Tocopherol (Vit-E) is a potential antioxidant & scavenges reactive oxygen species.Pentoxyphylin is vasodilator and reduces blood viscosity by inhibiting platelet aggregation.

3. **Sildenafil -**Acts by CGMP mediated pathway. Cochran review 2014 concluded that there was not enough evidence to support the use of vasodilator to improve clinical pregnancy rates in infertile women.

4. **L-Arginine -** An amino acid is a Precursor to nitric oxide. Nitric oxide increases blood flow by causing dilatation of uterine arteries.Takasaki et al (2010) found significant effect endometrial thickness in six out of nine patients who were given L-Arginine.

5. **Estrogen -** Vaginal Estrogen improves the endometrial thickening and uterine blood supply acting on systemic & local levels together (Fanchin R 2001).

6. **G-CSF -** Is a type of Colony stimulating factor which plays an important role in stimulating endometrial mesenchymal stem like cells Adult stem cells have been identified in the human endometrium which is highly regenerative.Many trials are in favor of using G-CSF though more RCT are still needed.

7. **Endometrial scratching -** Endometrial injury induces inflammatory reactions which favors implantation .recent cochrane review which included nine RCT suggest benefit from endometrial scratching for the endometrial receptivity.

PRP :-

PRP is autologous blood plasma, enriched with platelets 4-5 time more than the circulating blood.The platelets on activation releases various growth factors from alpha granules ,such as vascular endothelial growth factor(VEGF),Epidermal growth factor (EGF),Platelet derived growth factor (PDGF),Transforming growth factor(TGF),and cytokines.

Method of preparing PRP

1. Take 10 ml or 50 ml tube as per the need.

2. Add 1.5 ml anticoagulant (ACD-A) solution and 8.5 ml blood or 5 ml anti coagulant and 45 ml blood.

3. Mix well and centrifuge for 15 min at 3000 RPM.

4. The blood was divided into three layers: red blood cells at the bottom , cellular plasma in the supernatant and a Buffy coat layer between them.

5. The plasma layer and Buffy coat were collected to another tube and re-centrifuged at 1800 RPM for 5 min to get platelet pellet.

6. The resulting pellet of platelets was mixed with 1 ml of supernatant and then 0.5-1 ml of PRP was obtained

This will make 7-10 times concentration of platelets in the final prepration compared to blood which will give appropriate quantities of growth factors.

Stem cell :-

Regenerative potential of stem cell has been studied, in various studies in animal models, and has shown to improve endometrial thickness .The use of stem cell is still preliminary and more research and trials are needed before it can be applied into clinical practice.

Case study :-

In our study at J J Institute of medical sciences ,Bahadurgarh ,Haryana.8 Infertility cases were taken between age group 37 to 44 and all these women were for Oocyte donation-IVF. 3 patients were 37 to 40 years age group and 5 patients were between 41 to 44 years of age. Their endometrial thickness varied from 4.0mm to 6.4 mm. All the 8 women were treated with PRP and 5 patients were treated with PRP + G-CSF before oocyte donation.The result of the study was was successful endometrial development up to 7mm in 75% (6 out of 8) of the cases and positive clinical pregnancy was obtained in 37.5% (3 out of 8) of the cases.

The study hence supports that PRP therapy and G-CSF administration have substantial encouraging clinical impact on the treatment of infertility, specifically in the patients having thin endometrium.

Decellularizedamniotic membrane activated PRP - A Stable Dressing Material

Jivita Kshirsagar, Ravi Kshirsagar, Shashikant Desai, and Meghnad Joshi

Abstract

Applications of amniotic membrane for burn wounds is 100 year old technique. It can be used as biological dressing for burn injury which is simple, and cheap compared to allograft and xenograft. One of the limitations in using these dressings is stability and some time acute graft rejection. Additionally,direct application of amnion has greater risk of infection. Decellularization is an effective method to lower the risk of graft rejection and infections. The bioreactor assembly with multiple cassettes was designed for decellurization of multiple amnions with different cell types simultaneously in single run. A detergent-based protocol was modified to remove all cellular components from amnion and diminish the DNA content to render it non-immunogenic. Decellularization process was carried out (n=10) by detergent based protocol. Decellularized amnion samples were analysedby different histological techniques, DNA quantification, mechanical testing and scanning electron microscopy (SEM). Histological analysis showed complete removal of cellular components and the histoarchitecture of scaffold remained intact. Amnion scaffold activated with platelet rich plasma (PRP) supported better adherence to the wound than amnion alone. Only single application showed good healing. In vivo assessment of activated amnion revealed stable dressing. It has good promising outcome. At day 7, histologically the wounds treated with activated amnion were almost closed without scarring and showed well differentiated epidermis, proliferation of keratinocytes, hair follicles and basement membrane as compared to controls and silver nitrate gel dressings in a mouse *(Mus musculus)*. Cryopreservation had no adverse effect on the mechanical properties of the amnion scaffold. Cryopreservation of decellularized amnion by Dulbecco's modified eagle medium (DMEM) was expected to prepare off-the-shelf skin substitutes and preserve them to be immediately available upon request of patients' needs.

Keywords: Burn wound, bioreactor, scaffold, activated PRP, cryopreservation

Dr Akshat Vijay

Abstract

Introduction: Osteonecrosis of the femoral head (ONFH) is a disease with a wide-ranging etiology and poorly understood pathogenesis seen commonly in young patients. Various head-preserving procedures have been used to avert the need for total hip replacement. We carried out a prospective study on treatment of AVN of the femoral head with thorough debridement, bone grafting and bone marrow mononuclear cells implantation.

Materials & Methods: We use drills, curettes, broaches under image intensifier to perform a thorough debridement of all necrotic lesion, pack autogenous cortical and cancellous bone which were harvested from the ipsilateral iliac crest tightly into the femoral head, implant bone-marrow mononuclear cells containing mesenchymal stem cells into the necrotic lesion. The study included 15 patients (20 hips, 10 males, 5 females, mean age 35 years, range 23-58 years) with stage II-III ONFH according to the association research circulation osseous classification.

Results: The outcome was determined by changes in the Harris hip score (HHS), by progression in radiographic stages, and by the need for hip arthroplasty. The mean follow-up was 24 months (range 9-36 months). The mean HHS increased from 64 to 85 points. The overall clinical success rate is 80 %. There were no infection, femoral neck fracture or other complications.

Conclusion: Thorough debridement, autogenous bone grafting and bone-marrow mononuclear cells implantation is an effective procedure in patient with small lesion, early-stage ONFH.

KEY WORDS: Osteonecrosis, Bone grafting, Stem cells, Debridement

Stem cell therapy for type 2 diabetes mellitus

Dr Shrenik Vadiya1, M.S., Ms. Namrata Prakash Namewar2 and
Dr. Ramaswamy Velmurugan3

Abstract

Type 2 diabetes mellitus(DM) , which is characterized by the combination of relative insulin deficiency and insulin resistance. Transplantation of insulin-producing cells was once thought to be the most promising strategy for treating diabetes, but the research is still in preclinical level from the laboratory to clinical application has been obstructed due to its drawbacks. Adult stem cell therapy is designed to aid in the replacement and repair of aging and deteriorated tissues in the body. Our team uses adipose, bone marrow aspirate or umbilical cord-derived stem cells as methods of therapy. Stem cell therapy for Diabetes type 2 helps the body's natural healing process work faster and more effectively. Mesenchymal stem cells (MSCs) harbor differentiation potential, immunosuppressive properties, and anti-inflammatory effects, and they are considered an ideal candidate cell type for treatment of DM. MSC-related research has demonstrated exciting therapeutic effects in glycemic control have been translated into clinical practice. However, some critical potential problems have emerged from current clinical trials. The inclusion and exclusion criteria with strict supervision were followed before MSC transplantation to establish std protocol and develop a routine therapeutic approach for T2DM. We briefly review the molecular mechanism of MSC treatment for T2DM as well as the merits and drawbacks identified in current clinical trials. In this study, 8 patients with type 2 diabetes (T2DM) underwent autologous Mesenchymal stem cells and Adipose derived mononuclear stem cell infusion into arteries without pretreatment with any myeloablative or immune-suppressive therapy. Five of 8 (62.8%) showed normalization of their fasting glucose and the glycosylated hemoglobin (HbA1C) with significant reduction of their medication requirements. The HbA1C dropped on average 2.2 points. The three patients with diabetic complications showed improvement or stabilization and most patients reported improved energy and stamina. The durations of response varied between 6 months and 2 years. No patients had any significant adverse effects. But the patients face sudden reduction of blood sugar level leads to low sugar. We would like to share our experience and reason out the reason to get the significan results to achieve the long term benefits to the patients. The 37.2% patient were showing abnormal results which was inconclusive. The purpose of sharing this data to fellow colleagues to achieve our results to 100% benefit to all the patients and at the same time sustaining the positive effects of Stem cells in success of Cell therapy T2DM.

1 Stem cell therapist Vadodara; 2 &3 Cell biology and Biotechnologist, Century Pharmaceuticals ltd, Vadodara

Dr Sagar Kadam
Resident, Orthopedics, Fortis Hospital, Mohali

Abstract

Introduction: In osteonecrosis the success of interventions that forestall or prevent femoral head collapse and maintain hip function would represent a substantial achievement in the treatment of this disease. This study was conducted with aim to find out early results of Core Decompression and autologous bone marrow mononuclear cells instillation in femoral head osteonecrosis.

Materials & Methods: Fifty-one osteonecrotic hips in 40 patients were randomly divided into 2 treatment groups. Patients in group A (25 hips) were treated with core decompression, and those in group B (26 hips) received autologous bone marrow mononuclear cell instillation into the core tract after core decompression. Outcome between the 2 groups were compared clinically (Harris Hip score), radiographically (x-ray and magnetic resonance imaging), and by Kaplan-Meier hip survival analysis after 12 and 24 months of surgical intervention.

Results: The clinical score and mean hip survival were significantly better in group B than in group A ($P < .05$). Patients with adverse prognostic features at initial presentation, that is, poor Harris Hip score, x-ray changes, edema, and/or effusion on magnetic resonance imaging had significantly better clinical outcome and hip survival in group B than in group A

Conclusion: The additional use of bone morphogenic protein, and bone marrow stem cells may provide the opportunity to enhance the results of core decompression in AVN head of femur.

KEY WORDS- AVN, bone marrow mononuclear cells, core decompression

Dr. S. Subramanya Rao

Abstract

OSTEO ARTHRITIS KNEE JOINT

STEM CELL THERAPY

Minimally manipulated adult stem cells from bone marrow gives promising results in osteoarthritis of knee joints up to Gr 2 & Gr 3 stages especially relatively young people.

Adults stem cells harvested from bone marrow of iliac crest sent by cold chain to lab where they are minimally manipulated and sent as freeze dried cells. Two doses of 20 billion cells are injected intra articular at interval of 45 days gives good results in terms of pain & increase in cartilage thickness. Should be assisted with good physio.

Dr. S. Subramanya Rao

Abstract

PRP IN ORTHOPAEDICS

PRP has wide application in musculoskeletal conditions.

1. O.A.KNEE – In stage 1&2 O.A. knees intra articular PRP Injection gives pain relief up to 70-80%. But it should be supplemented with good physio back up & L.L.LT (Low level laser therapy) for more results.
2. Local PRP injection gives relief in various conditions like lateral / medial epicondylitis, plantar fasciitis, retrocalcaneal bursitis mild rotator cuff injuries of shoulder.
3. Wound Management-Non healing ulcer / diabetic foot hastens healing process
4. As palliative measure in osteoarthritis of hip & stage 2 AVN to reduce pain till definitive procedure are taken up.
5. Extended indications.

   Intra capsular fracture neck of femur to reduce chances of AVN, PRP into C.C.S. screw holes.
6. PVD – Peripheral vascular diseases – to save limb from amputation.

1st Annual Conference of Stem Cell Society (India) held at Renaissance Convention Centre, Powai, Mumbai on from 27 Feb-1st Mar, 2014

2nd Annual Conference of Stem Cell Society (India) held in Delhi on 31st May 2015-1 June 2015