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Review Article

Cold PRP is Cutting-Edge Therapy in Nerve Regeneration in the Field of SNHL

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Abstract

Definition of SNHL → SNHL (Sensorineural Hearing Loss) is a type of hearing loss in which the root cause lies in the inner ear or sensory organ, or the vestibulocochlear (cranial nerve VIII) nerve.

It consists of damage to the cochlea or auditory nerve.

It is the most common type of hearing loss in adults, approximately 90% of hearing loss [1].

Keywords: SNHL; Cold PRP; B.P.S.T Point; Blood Group; Tinnitus

Description

Cold PRP

Cold PRP is a concentrated solution of plasma and platelets prepared from patient's own blood (or from a 1st degree relative with homologous blood group) prepared and handled till infusion at temperature between 2 to 8°C. It is used in medical treatment to accelerate tissue healing and nerve regeneration.

Method of cold PRP preparation

PRP is prepared from patient's blood (preferably) drawn at the time of intratympanic instillation.

- An 18G needle is used to draw venous blood in order to avoid mechanical trauma to platelets. The blood drawn is added with an anticoagulant such as citrate dextrose to prevent platelet activation.
- 12 ml blood is required for 1 ml PRP.
- Centrifusion of blood is done 1st as a (soft spin), i.e. 1500 RPM for 5 minutes in cold PRP at -10°C.
- Transfer the supernatant plasma containing platelets into another sterile tube (without anticoagulant).
- Centrifuge tube at a higher speed (a hard spin), i.e. 3000 RPM for 5 minutes, to obtain platelet concentrate.
- Lower 1/3 is PRP, and upper 2/3 is platelet-poor plasma.
  - 1/3rd PRP + 1/4th PP = 30 lacs platelets/cumm At the bottom of the tube are platelet pellets.
  - Take bottom sediments (rich plasma) with pipette.
  - Take take the PRP with 18 no. needle via syringe (sample ready to inject).
- Intratympanic injection of PRP is done with 18 no. needle in adults and 27 no. needle in children [1].

Activation of PRP

PRP can be activated exogenously by thrombin, calcium chloride, or mechanical trauma **[2].**

Indication

Moderate to severe SNHL (Sensorineural Hearing Loss).

Contraindication

- Active infection
- Immune deficiency
- Platelet dysfunction

- Low platelet count
- Cancer
- Chronic liver disease
- Hemodynamic instability
- Hypofibrinogenemia Ischemic disorders
- Sepsis [1].

Safety →

As per study done by Aslan., *et al*. prolonged use of L- PRP (Leukocyte -Platelet Rich Plasma) in the middle ear is safe for the middle ear mucosa. No evidence of malignancy seen [3].

Review

Pathophysiology of SNHL →

- Whenever there is damage to the pathway for sound impulses from hair cells of the inner ear to auditory nerve or brain, it will result into SNHL (Sensorineural Hearing Loss), a heterogenous disorder.
- Various causes of SNHL Includes congenital abnormalities, infections, noise exposure, and age-related degeneration.
- The underlying mechanism involves disruption of hair cell function, the auditory nerve, or both.

Mechanism of action of PRP →

PRP has the potential to deliver a high concentration of growth factors to the target tissue by virtue of the contents within the alpha and dense granules of platelets, which plays a role in:

- Collagen synthesis
- Cytokine activity
- Anti-inflammatory effects
- Angiogenesis promotion
- Apoptosis inhibition

Alpha granules contain various fundamental growth factors:

- Platelet-Derived Growth Factors (PDGFaa, PDGFbb, and PDGFab)
- Transforming growth factor beta (isoforms TGFβ1 and TGFβ2)
- Insuline like Growth factors (IGF1, IGF2) Epithelial growth factor (EGF)
- Vascular endothelial growth factor (VEGF), Basic fibroblast growth factor (FGF)
- These modulate cell proliferation, cellular migration, differentiation, angiogenesis, and hemostasis.

The dense granules contain bioactive agents including:

- Serotonin, Histamine, Dopamine, Calcium, Adenosine
- These can increase membrane permeability and modulate inflammatory processes.

Degranulation of these organelles results in the release of pre-packaged growth factors, many of which have short half-lives.

Therefore, greater effectiveness may result if they are activated at or just before application.

PRP has 3–5 times the concentration of platelets normally found in wounds, and the resulting growth factor release following activation can further Stimulate cell proliferation And differentiation towards tissue regeneration [2].

Application of PRP for nerve regeneration →

- Recovery in facial nerve paresis (idiopathic or post-operative)
- Recovery in vocal cord paresis or palsy
- Improved hearing in SNHL

Protocol for PRP Injection

Checklist →

Various studies done at various centers to see PRP role in SNHL has shown significance of wide bore needle, temp. maintenance for PRP, role of platelet count but no study has shown role of IgF1, Blood group significance to increase the efficacy of PRP in SNHL.

At our Centre we follow these following protocols to improve the result of PRP.

1. Protocol before PRP injection.

- Quadrivalent Flu Vaccine ↠ in order to avoid recurrent cold/flu to patient.
- Blood Grouping (Study done at our center have shown slow improvement in blood group O [6]) ↠ CHILD MOTHER FATHER ↠ In case PRP sample can't be taken from child, it is preferable to take sample from mother or father with whom the blood group matches.
- Platelet Count of ↠ CHILD, MOTHER, FATHER is done ↠ Should be more than > 1.5 Lakh (The higher the platelet count the more likely it is to stimulate nerve regeneration). As the higher the platelet count the more the growth factors released after activation.

- Serum IgF1, done for↠ CHILD, MOTHER, FATHER ↠ IgF1 is a growth factor preset in plasma and plays a significant role in neural development, recovery from neuronal injury, neuronal survival and neurite outgrowth following crush injury. It contributes to improve nerve regeneration including proliferation, mobilization, mycharian and shwan cell axon interaction [7-9].
- HRCT Temporal Bone ↠ To see bony cochlear morphology.
- MRI For Cochlear Nerve ↠ To See status of cochlear nerve.
- BERA Test/PTA ↠ to record the hearing status of patient pre-treatment.

2. Protocol doing PRP injection

- Wide bore needle venipuncture
- Temperature
- LP Needle
- BPST Point

Clinical evidence of nerve regeneration and cold PRP →

Local PRP administration increases the regenerative axon diameter and the regenerative axon number at the distal portion.

- Similarly, KucukL., *et al*. demonstrated positive effects of platelet-rich plasma on sciatic nerve in case of sciatic nerve injury model in rats [4]
- PRP accelerated Schwann cell proliferation in vivo, as concluded by Ikumi A., *et al*. (study done in rabbit model) for the effect of PRP on peripheral nerve regeneration [5].
- Administration of high viscosity PRP to the tympanic cavity in humans to study prophylactic or therapeutic effect on SNHL or tinnitus was done in United States in 2017 and it was found that the hearing threshold levels improved after administration of high viscosity PRP to the tympanic cavity.

Combination therapies

- **PRP + GF:** In patient with low IGF-1 levels, GF (growth factors) is added to L-PRP to enhance the action of L-PRP for nerve regeneration. Also, in patients with blood group O, IGF-1 level is in general found to be low as per our study. In these patients, GF is added to L-PRP.
- **PRP + Calcium:** Calcium is added to PRP to activate platelets in L-PRP.

Limitations

- PRP needs to be stored between 2°C to 8°C.
- Platelet count of the patient undergoing PRP therapy should be > 1.5 lakh for better results.
- Small child < 6 kg weight, whose venipumcture is difficult [6].

Conclusion

- Advantage of Cold PRP is to prevent release of various growth factors way before the intratympanic injection of PRP.
- The additional advantage of using growth factors in PRP is in patients with low serum IGF-1 level and is most commonly observed in O blood group.
- Platelet count is crucial in PRP as it directly impacts the concentration of various growth factors within the PRP for good results of PRP we recommend platelet count > 1.5 lakh.
- Wide bore needle is used for venepuncture in order to avoid trauma and hence activation of platelets.

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