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Research Article

Intracarotid Platelet Rich Plasma In Sub-Acute Ischemic Stroke Cases (From 5th To 21st Post Stroke Day) - Pilot Study In 6 Cases Gives No Effect

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Abstract

Background: Tissue Plasminogen Activator (tPA) showed a level 1 benefit in acute stroke (within 4.5 hours). But for more than 4.5 hours cases (if they fail to qualify for clot retrievers within 12 hours), autologous Intracarotid/Intraarterial Platelet rich plasma (PRP) is used here to provide growth factors at the cyton level to maintain and restore the raw materials for the synaptic flow.

Aims/Study Design: PRP provides growth factors at the cyton level are the basis of the

authors' hypothesis to treat sub-acute stroke cases from 5th day to 21st day. Pilot study on 6 cases prospective study.

Materials and Methods: The human population included 6 sub-acute ischemic stroke patients from 5th to 21st post stroke day. The mean time for superfusion was 8 days post-stroke. Pre- and post PRP status was monitored by NIHSS, MRI-DWI and ALTENS.

Results: After 2 hours of PRP, the mean change in the NIHSS score was no change in NIHSS, ALTENS or MRI-DWI in LACS, PACS, TACS or POCS.

Conclusions: PRP alone via intracarotid do not cause improvement in neurological deficit in these 6 cases.

Keywords: Brain Infarcts; Intracarotid Platelet Rich Plasma; Nihss; Mri-Dwi; Altens

Introduction

Acute stroke should be treated with rTPA as recommended by NINDS and Indian study too but within 4.5 hours [1-3]. For > 4.5 hours of ischemic stroke cases if they qualify for clot retriever then that treatment modality is being used now a days that too within 12 hours in few selected cases, it may go upto 24 hours. But what will be the fate of those patients who arrive clinicians after this critical time window of 12 hours be it developed or developing country [4].

We have proved Intra-arterial Sodium Nitroprusside (IASNP) as treatment modality for sub-acute stroke cases from 5th to 21st post stroke day first in rats [5] then in humans [6]. In our publications [5,6] on IASNP alone in sub-acute ischemic stroke cases (from 5th to 21st post stroke day), we have pointed out that there was a decrease of power after 24 hours of IASNP always in nearly each case. Then after vigorous search of literature we didn't find any remedy for it. We attended many conferences including Regenerative medicine conferences and stem cell conferences in India. We came across the Platelet Rich Plasma extraction technique [7] which provided multiple growth factors contained in platelets' Alpha granules of platelets are having Brain-derived neurotrophic factor (BDNF), a major neurotrophin and vascular endothelial growth factor (VEGF) in large quantities. BDNF and VEGF can both be found in the brain,

their ability to cross the blood brain barrier is not straightforward. BDNF can cross the BBB, but its transport may be limited and influenced by factors like the specific region of the brain and the presence of other molecules. Infarct causes disturbed BBB is well documented in many publications in rats and in humans too. VEGF's ability to cross the BBB is also complex, with some studies suggesting it can cross under certain conditions or via specific mechanisms. BDNF is in maximum concentration in platelets of humans, VEGF is in moderate concentration in platelets. BDNF is having larger structural unit (27 KDA) which cannot effectively penetrate through the BBB (BBB permeates only those molecules which are less than 20 DA) [8-12].

Now we want to use some autologous blood product which can provide ample amount of growth factor at the cyton level without the use of IASNP.

With this hypothesis we injected PRP alone in Carotid artery to provide BDNF and VEGF for raw material for neurotransmitters to be used at synapses.

Aim

To give PRP in sub-acute ischemic stroke cases from 5th to 21st post stroke day.

Materials and Methods

This is a pilot study in 6 cases between Oct-2024 and Jan-2025, treated at Advance Neuro and General Hospital Lucknow prospectively. Potential benefits and significant risks, specifically uneasiness, vomiting, retching, diaphoresis, apprehension, restlessness, perspiration, muscle twitching, palpitation, dizziness and abdominal pain and possible hypotension were discussed with all patients and/or their families. Written and video consent were obtained from relatives of patients for PRP injection and NIHSS score, ALTENS, MRI with DWI brain and Video-recordings of pre- and post-injection phases.

Mean age of our patients were 50 years (range 45-55). Out of the 6 patients who were given PRP, 4 were males and 2 were females. Co-morbid-illnesses in form of hypertension, diabetes, hypercholesterolemia were present in all 6 patients. There was no history of prior stroke in any patient. Mean-blood-pressure at admission was 184/110 and mean-maximum-pretreatment was 152/100 mmHg. 2 of 6 patients were smokers. Detailed blood-pressure monitoring was performed.

Variables recorded: time of symptom onset, arrival time, NIHSS score, ALTENS, MRI and Video-recordings of pre- and post-injection phases. Extensive-neurological examination including Baseline NIHSS was performed in all patients. Other parameters noted were demographic profile, stroke risk factors, ECG-examination, baseline CT-scan findings / MRI- study, platelet-aggregation-activity monitoring (bleeding-time), PT/PC/APTT and INR level.

Patient's venous blood samples 15 ml in 4 test tubes is taken and placed them upright in the test tube, waited for half an hour [1]. Do the multiple spins in an appropriate centrifugation machine and get the plasma then add calcium gluconate at the ratio of 1:10 in it and do one more spin so that activated PRP is ready to use. Around 12 ml of double dose PRP is prepared [2].

Patients received pretreatment for nausea in form of ondansetron HCl (32.0 mg IV push) 15 minutes before treatment. Meticulous photoprotection, sterile technique was observed for all aspects of delivery of medication as well as its formulation. Patients were hydrated and PRP was given via 20 G Viggo at the ipsilateral carotid artery of MRI DWI indicating hyperintensity at the dose of 0.01 mg/kg body weight up to a maximum of 12 ml. We waited for 2 hours for the recovery. NIHSS scores were recorded at baseline, 2-h, 24-hrs, 7-days, and 2-months. The mRS was recorded at 2 months.

Heparin/aspirin/clopidogrel/Antihypertensives were given during hospital stay. High- protein (arginine-rich) diets were started as was in our previous human studies.

Using Oxford stroke classification (BAMFORD's classification), LACS(LACUNAR- STROKE) was found in 2/6 patients, PACS (PARTIAL-ANTERIOR-CIRCULATION- SYNDROME) was found in 2/6, TACS (TOTAL-ANTERIOR-CIRCULATION-STROKE) was found in 1/6 and POCS (POSTERIOR-CIRCULATION-SYNDROME) was found in 1/6.

Mean time of INTRACAROTID-PRP injection was 8 days (range 6-10) after stroke onset. Mean length of hospitalization was 7 days. The MEAN BASELINE NIHSS SCORE was 28 (range 24-30). Pre and post PRP clinical examination, NIHSS was video recorded. ALTENS and MRI-DWI were performed in each case.

Results

We obtained telephonic or clinic follow-up with patients and caregivers in cases for next three months and assessed mRS scale.

For analysis based on NIHSS GRADING: NIHSS 24-30 (6/6) 6 patients were of LACS / PACS / TACS / POCS and with NIHSS at 24 (1/6) and 30 (5/6) respectively. PRP was given on mean 8th post stroke day respectively and after 2 hours, after 24 hours was same. Then after one week, 21 days and after 3 months at same in all cases. The ALTENS study was at same level in all cases. The modified RANKIN SCORE (mRS) was 4 after 3 months.

Even ALTENS and MRI-DWI done in these cases has not produced any change either after 2 hours, after 24 hours was same. Then after one week, 21 days and after 3 months at same in all cases. The ALTENS study was at same level in all cases. Alone PRP has been given in these cases but has not produced any results either in clinically NIHSS score, MRI-DWI or ALTENS examinations after 2 hours, after 24 hours was same. Then after one week, 21 days and after 3 months at same in all cases.

Discussion

NINDS study gave a brain salvaging time of 4.5 hours and clot retriever can be used within 12 hours in some selected cases only. PRP is used here directly in ipsilateral carotid artery to get physiological recovery after 5th day to 21st day cases of sub-acute ischemic stroke cases.

The PRP will deliver raw material (BDNF and VEGF) to the stroke ischemic areas and thus to the cyton and that area will give positive results later on. None of our patients developed any form of intracerebral hemorrhage (as found in the NINDS study), which suggests a good safety profile for PRP.

2 cases with LACS out of 6 cases having baseline NIHSS-scores of 30, PRP was given on 10th post stroke day. After 2 hours of NIHSS remained at 30 and after 24 hours NIHSS remained at 30 so he showed no improvement. Then after a week NIHSS was at 26 and after 21 days it came to be at 26 which continued at 3 months. In MRI DWI there was no change noticed from pre PRP then post PRP for 1 week. Even ALTENS done immediately after 2 hours showed no improvement from 5 - 6 mAmp to 5 - 6 mAmp. The modified RANKIN SCORE (mRS) was 4 after 3 months of follow up. Video recordings also showed no improvements at 2 hours, 24 hours, 7 days, slight improvement at 3 weeks and 3 months that also coincided with the MRI- DWI and NIHSS clinical scoring findings.

2 cases with PACS out of 6 cases having baseline NIHSS-scores of 24, PRP was given on 7th post stroke day. After 2 hours of NIHSS remained at 24 and after 24 hours NIHSS remained at 24, so he showed no improvement. Then after a week NIHSS was at 22 and after 21 days it came to be at 22 after 3 months at 20. In MRI DWI there was no change noticed from pre PRP then post PRP for 1 week. Even ALTENS done immediately after 2 hours showed no improvement from 6 - 7 mAmp to 6 - 7 mAmp. The modified RANKIN SCORE (mRS) was 4 after 3 months of follow up. Video recordings also showed no improvements at 2 hours, 24 hours, 7 days, slight improvement at 3 weeks and 3 months that also coincided with the MRI- DWI and NIHSS clinical scoring findings.

1 case with TACS out of 6 cases having baseline NIHSS-scores of 30, PRP was given on 6th post stroke day. After 2 hours of NIHSS remained at 30 and after 24 hours NIHSS remained at 30 so he showed no improvement. Then after a week NIHSS was at 30 and after 21 days it came to be at 30 after 3 months at 30. In MRI DWI there was no change noticed from pre PRP then post PRP for 1 week. Even ALTENS done immediately after 2 hours showed no improvement from >8 mAmp to >8 mAmp. The modified RANKIN SCORE (mRS) was 4 after 3 months of follow up. Video recordings also showed no improvements at 2 hours, 24 hours, 7 days, slight improvement at 3 weeks and 3 months that also coincided with the MRI-DWI and NIHSS clinical scoring findings.

1 case with POCS out of 6 cases having baseline NIHSS-scores of 30, PRP was given on 9th post stroke day. After 2 hours of NIHSS remained at 30 and after 24 hours NIHSS remained at 30 so he showed no improvement. Then after a week NIHSS was at 30 and after 21 days it came to be at 28 after 3 months at 26. In MRI DWI there was no change noticed from pre PRP then post PRP for 1 week. Even ALTENS done immediately after 2 hours showed no improvement from 5 - 7 mAmp to 5 - 7 mAmp. The modified RANKIN SCORE (mRS) was 4 after 3 months of follow up. Video recordings also showed no improvements at 2 hours, 24 hours, 7 days, slight improvement at 3 weeks and 3 months that also coincided with the MRI- DWI and NIHSS clinical scoring findings.

So, from these findings one can easily find out the no response was seen in sub-acute ischemic stroke cases when PRP is given alone besides it may has delivered the various growth factors at the cyton level needed for the synaptic transmissions. Even the exact etiology is unknown until now, the no effect might be due to many causes firstly it may be possible that the BBB may have been disturbed in brain insult cases which either have caused more or less permeable to the PRP, secondly the cyton functioning is hampered in these insults, thirdly the synaptic disruption and non-functionality, fourthly the axonal transport has been disturbed, fifth there might be some kind of superoxide at the level of synaptic membranes which blocked the transmission, sixth there might be some kind of destructive nitric oxide species like iNOS formation locally, seventh there might be some Magnesium surge that causes axonal and synaptic transmission blockade. The growth factors of PRP might have entered the cyton of the neurons and provided the raw material to form the various neurotransmitters needed for further synaptic activity but due to unknown reason this has not worked at all in these 6 cases.

The present study has certain limitations, such as not having fMRA (Functional MRI study) in the pre- and post-PRP injection periods with DWI, due to the non-availability of higher-end MRI at our setup. Also, in our next study we will include IASNP with PRP. We plan to conduct a broader study including all of the above investigations in the future. No patient was given blood transfusion.

Conclusions

PRP treatment is not effective modality for physiological recovery at mean of 8 days post-ischemic stroke (5th to 21st post-stroke day) cases as PRP alone has not given any benefit in terms of NIHSS score benefit clinically or MRI-DWI or ALTENS recovery pattern. In a nutshell authors concluded that it might be possible that rodents have got better results but in human beings due to more complex BBB the PRP's entry may have been restricted more thus has not produced any benefit either clinical or investigational.

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