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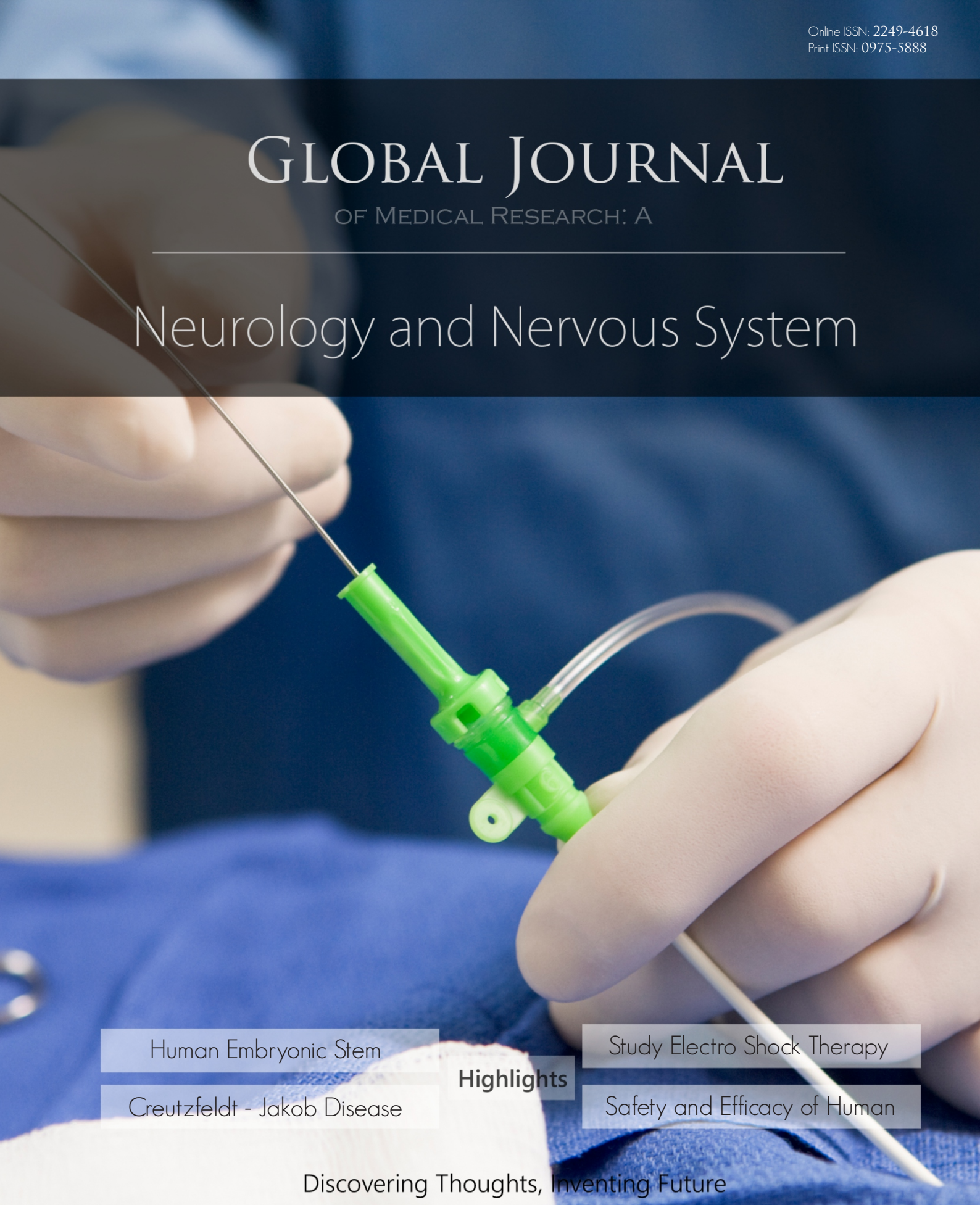

Human Embryonic Stem

Creutzfeldt - Jakob Disease

Highlights

Study Electro Shock Therapy

Safety and Efficacy of Human

Discovering Thoughts, Inventing Future

VOLUME 15 ISSUE 2 VERSION 1.0

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Safety and Efficacy of Human Embryonic Stem Cells for the Treatment of Cerebrovascular Accident: A Case Series

By Dr. Geeta Shroff & Dr. J.K. Barthakur

Abstract- *Background:* To evaluate the efficacy and safety of hESC therapy on 22 patients with CVA.

Materials and methods: The present study included patients with CVA and was conducted between 29 Dec 2004 and 03 Oct 2011 at a single site in New Delhi, India. The study consisted of six treatment phases (T1, T2, T3, T4, T5, and T6), each phase separated by a gap phase. Patients were evaluated for improvement on the basis of European Stroke Scale (ESS) at baseline and at the end of each treatment period. The ESS scores ranged from 0 (minimum score) to 100 (maximum score).

Results: A total of 22 patients were included and all received intensive dosing with hESCs in T1. Eight patients returned for T2, 6 patients for T3, 4 patients for T4, and only 2 patients each for T5 and T6. Median ESS scores increased from baseline through all the treatment periods indicating improvement in the condition of patients. All affected patients showed an improvement in gait (22 patients); speech (15 patients); level of consciousness (2 patients); comprehension and gaze (1 patient each) by at least one point at the end of T6. In addition, patients showed improvement in walking, balance (sitting and standing), and spasticity after receiving hESC therapy. Overall, 11 patients (50%) experienced adverse events (AEs) during the study. No serious adverse events (SAEs) and deaths were reported.

Keywords: *cerebrovascular accident, hESC therapy.*

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Conclusion: All the patients showed improved cognitive skills and regained their functional ability. No severe AEs or SAEs were reported during the study. hESC therapy was well tolerated among all the patients included in the study.

Keywords: cerebrovascular accident, hESC therapy.

I. Introduction

Cerebrovascular accident (CVA) or stroke may result from multiple reasons including thrombus formation in the atherosclerotic cerebral blood vessels, hemorrhage due to rupture of a blood vessel (resulting from aneurysm), or due to a travelling clot which may block blood flow to a particular area in the brain [1]. CVA is one of the leading causes of mortality globally [2]. According to the World Health Organization (WHO), 15 million people suffer from stroke, of which 5 million die, and 5 million experience permanent disabilities as a result of stroke every year [3].

Several risk factors contribute to the occurrence of CVA. The Reasons for Geographic And Racial Differences in Stroke (REGARDS) study showed that smoking, poor diet, lack of physical activity, body mass index of more than 30 kg/m^2, high blood pressure, high total cholesterol, and high fasting blood glucose are the risk factors that may contribute to CVA [4]. In addition, the REGARDS study also showed that the cognitive skills of patients with stroke are compromised. Das et al demonstrated that the incidence of stroke related deaths is higher among the elderly [5].

There are multiple aspects of CVA treatment which begin from the time of first attack. The American Heart Association/American Stroke Association (AHA/ASA) encourages education on stroke management to enhance early stroke detection and pre-hospital stroke management [6]. Effective neuroprotection can be achieved by initiating treatment of stroke within hours of injury [7]. Tissue plasminogen activator (tPA), anticoagulants, antiplatelet agents, vasodilators, neuroprotective agents, and surgical interventions are conventional therapeutic agents available for the management of stroke [8]. However; the use of these agents is considered helpful within few hours of stroke attack. Most patients with CVA continue to live a compromised life due to decreased quality of life (QoL), impaired cognitive skills, and several psychological symptoms [9, 10].

Previous research has shown that stem cell therapy may help restore the neurological functions among patients with CVA. Bone marrow derived stem cells have demonstrated participation in neurogenesis and angiogenesis resulting in restoration of normal function [7]. Intracerebral transplantation of the neuronal stem cells in patients with stroke showed stable motor function even six months after transplantation [7]. Lindvall et al showed improved forelimb performance after transplantation of neuronal stem cells in stroke affected rodents [11]. Huang et al showed decrease in oxygen glucose deprivation and decrease in the rate of apoptosis via interlukin-6 and vascular endothelial growth factor signaling pathways after transplantation of mesenchymal stem cells (MSCs) [12].

Although several studies evaluating the effect of stem cells in the treatment of CVA are available, the evaluation of human embryonic stem cells (hESCs) is less explored. In the present study, we aimed to evaluate the efficacy and safety of hESC therapy on 22 patients with CVA.

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II. Materials and Methods

a) Study Characteristics

The present single cohort study included patients with CVA and was conducted between 29 Dec 2004 and 03 Oct 2011 at a single site in New Delhi, India. This study evaluated the safety and efficacy of hESC therapy in patients with CVA.

The study protocol was approved by the Independent Institutional Ethics Committee. The institutional committee for stem cell research and therapy at our institute reported the clinical study to the National Apex Body and the Indian Council of Medical Research (ICMR). The study was conducted in accordance to the Declaration of Helsinki [7]. A written informed assent/consent was obtained from the patients/parents or legal guardians prior to the treatment.

b) Inclusion and Exclusion Criteria

Patients who approached our institute with a documented diagnosis of CVA and those who were willing to provide a written informed consent were included.

Patients who had previously received any other form of stem cell therapy simultaneously or less than a year of receiving hESC and patients who were not willing to provide a written informed consent were excluded. Pregnant and lactating women were also excluded.

c) Removal of Patients from Therapy

The patients who willingly wanted to discontinue the study were removed from therapy. Death of the patient or adverse events (AE) which were not related to hESC therapy led to discontinuation from the study.

Cell Culture, Preparation, and Transplantation

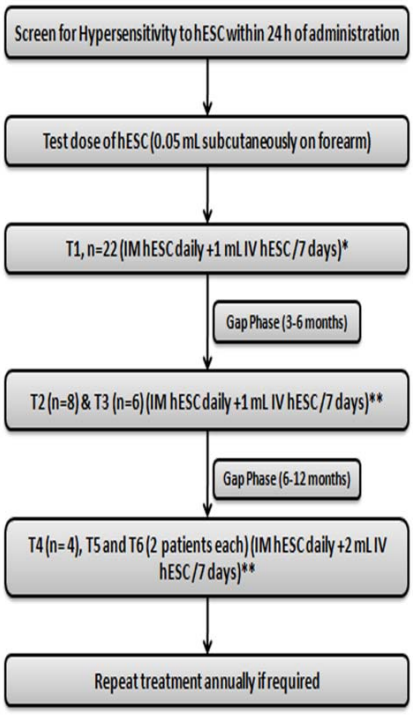
The hESCs were derived from a primary cell line of pre-embryonic cell through two secondary cell lines derived by directed neuronal and non-neuronal differentiation of primary cell. The detailed cell culture technique has been described elsewhere (detailed compositions comprising human embryonic stem cells and their derivatives, methods of use, and methods of preparation is available at http://patentscope.wipo.int/search/en/WO2007141657). The cells have been characterized and are chromosomally stable [13].

Study Design

The study consisted of six treatment phases (T1, T2, T3, T4, T5, and T6), each phase separated by a gap phase. After the patients were diagnosed with CVA, the dosage and schedule of hESC was administered according to a protocol (Fig 1). The treatment schedule for each patient was individualized and modified as per the ongoing process of patient evaluation. Each patient was administered 0.05 mL hESCs subcutaneously to observe any hypersensitivity, pain or inflammation reactions at the site of injection for 24 hr. If the patient did not show any sign of hypersensitivity reactions 24 hr after the administration of test dose, the patient started to receive intensive dosing.

In T1, 0.25 mL hESCs were administered twice daily for 8 weeks. During T1, patients also received intravenous (IV) infusion of hESCs in 100 mL of normal saline which was repeated every 10 days and a priming dose of hESC by one of the supplemental routes by rotation (caudal injection, deep spinal injection, branchial plexus injection, and epidural route) for 5-14 days. hESCs were administered through the caudal route to ensure they reach the spinal fluid and regenerate the spinal cord and allow deep muscles to repair.

At the end of T1, the patients were discharged from the hospital and instructed to return for T2 and T3 which lasted for 4 weeks, each with a gap phase of 3 to 6 months in-between. During T2 and T3, the patients received 0.25 mL of hESC intramuscularly (IM), 1 mL of hESC every 10 days intravenously, and 1 dose of hESC every 7 days by supplemental routes by rotation as in T1. In addition to hESC therapy, all patients received physiotherapy and occupational therapy. The detailed treatment plan is illustrated in Figure 1.



*Caudal/BPI route if required + deep spinal muscle injection weekly (treatment period: 8 weeks
**Additional dosing by caudal route + deep spinal muscle injection weekly (treatment period: 4 weeks)

d) Efficacy and Safety Evaluation

The efficacy variable included assessment of European Stroke Scale (ESS) in each patient at baseline and at the end of each treatment period [14]. This scoring system assessed the functional disability of the patients and the prognosis of the patients suffering from CVA.

The ESS scores ranged from 0 (minimum score) to 100 (maximum score) and evaluated the patients on 14 parameters including consciousness, comprehension, speech, visual field, gaze, facial movement, arm in outstretched position, arm raising, extension of wrist, fingers, leg maintained in position, leg flexing, dorsiflexion of foot and gait. Each parameter of evaluation has different scores based on the extent to which the patient is affected. A completely normal patient would score 100 and a maximally affected person would score 0 on the ESS scale. In addition to ESS scores, we also analyzed improvement in other important parameters which are usually compromised in stroke patients scores developed in-house. These scores were used to assess the improvement in walking, balance (sitting and standing) and spasticity.

All AEs were documented during the study. In addition, the severity (1-mild; 2-moderate; 3-severe), seriousness, duration, nature of treatment or intervention to manage the event, and the outcome of the AE including the causality in the opinion of the investigator were documented.

e) Statistical Analysis

Intention to treat (ITT) population consisted of all patients who had received at least one test dose followed by intensive doses. The population included in the safety analysis was excluded from the efficacy evaluation. Only patients for whom all data was available were included in the statistical analysis. Patients with missing data were excluded. All demographic data of the patients was analyzed with descriptive statistics. The summary statistics of median, minimum and maximum values were presented. The AEs were summarized using number of patients (n), percentage (%) and system organ class (SOC) and preferred term (PT) for each study period and overall study period. A p value of less than 0.05 was considered to be statistically significant (5% level of significance). Statistical analysis was performed using software SPSS version 19 (IBM Corporation, Armonk, NY).

III. Results

a) Here Study Patients

A total of 22 patients were included in the study and all patients received intensive dosing with hESCs. Most of the patients included were males (63.6%) with a mean age of 61.8 yr. All the 22 patients received hESC during T1, 8 patients returned for T2, 6 patients returned for T3, 4 patients returned for T4, and only 2 patients each returned for T5 and T6. Of the 22 patients, 14 patients had received treatment only once, 2 patients each received 2, 3, 4, and 6 treatment phases.

Efficacy Evaluation

b) ESS Scores

Median ESS scores increased from baseline through all the treatment periods indicating improvement in the condition of patients. The change in ESS scores at each treatment phase and the change from baseline are summarized in Table 1. At baseline, the median ESS score for the affected 22 patients was 61 (24, 86). At the end of T1, the ESS score increased to 74 (42, 93). Eight patients returned for T2 and the ESS score at the end of this period was 67 (52, 92) for these patients. For T3, 6 patients returned and the ESS score was 67 (66, 79) at the end of this period. The ESS score at the end of T4 was 70 (66, 79) and 4 patients received hESC therapy in this period. A total of 2 patients each returned for T5 and T6 and the ESS scores at the end of these periods were 74 (72, 76) and 81 (76, 85), respectively. The change in the ESS score of each patient per treatment phase is presented in Table 2.

Table 1 : Change in ESS Scores from Baseline to Each Treatment Period

Treatment Period	N	End Period Score Median (Min, Max)	Change from Baseline Median (Min, Max)
Baseline	22	61 (24, 96)	-
T1	22	74 (42, 93)	14 (0, 20)
T2	8	67 (52, 92)	22 (3, 38)
T3	6	67 (66, 79)	24 (3, 42)
T4	4	70 (66, 79)	22 (3, 42)
T5	2	74 (72, 76)	14 (8, 19)
T6	2	81 (76, 82)	20 (19, 21)

Table 2 : ESS of all Patients per Treatment Phase

Sl.No	Age	Baseline	T1	T2	T3	T4	T5	T6
1	25	64	78	-	-	-	-	-
2	32	64	64	67	67	67	72	85
3	41	73	79	-	-	-	-	-
4	42	52	64	67	71	79	-	-
5	56	66	77	-	-	-	-	-
6	56	50	64	66	79	-	-	-
7	57	52	72	-	-	-	-	-

8	57	68	80	-	-	-	-	-
9	58	40	56	75	-	-	-	-
10	60	30	50	64	66	-	-	-
11	62	52	72	-	-	-	-	-
12	66	86	93	-	-	-	-	-
13	67	60	76	-	-	-	-	-
14	68	70	78	-	-	-	-	-
15	69	24	42	52	66	66	-	-
16	70	62	76	-	-	-	-	-
17	72	54	72	92	-	-	-	-
8	74	75	86	-	-	-	-	-
19	79	58	74	-	-	-	-	-
20	82	57	64	64	67	73	76	76
21	82	63	73	-	-	-	-	-
22	85	61	77	-	-	-	-	-

Maintenance of leg position was affected in all the 22 patients who were included in the study. Of these, 19 showed improvement by at least one level during the study. The other parameters which were affected and their improvement by at least one level during the study period are summarized in Table 3. Of the many parameters, all affected patients showed an improvement by at least one level at the end of T6 in gait (22 patients; 100%); speech (15 patients; 100%); level of consciousness (2 patients; 100%); comprehension and gaze (1 patient each; 100%).

Table 3 : Number of Patients Showing Improvement in ESS Scores by At least 1 Point

Parameter	Number of Patients Affected at Baseline	Number of Patients Showing Improvement by at least 1 level n (%)
Leg maintain position	22	19 (86.4)
Leg flexion	22	20 (90.9)
Gait	22	22 (100)
Arm outstretched position	21	19 (86.4)
Arm raising	21	20 (95.2)
Fingers	21	12 (57.1)
Foot Dorsiflexion	21	16 (76.2)
Wrist Extension	20	14 (70)
Speech	15	15 (100)
Facial movements	11	10 (90.9)
Level of consciousness	2	2 (100)
Visual field	2	1 (50)
Comprehension	1	1 (100)
Gaze	1	1 (100)

All the 22 patients included in the present study had problem walking before receiving hESC therapy. However; after receiving hESC therapy an improvement in walking by at least one level occurred in a total of 21 patients. Of the 21 patients who had affected balance while standing, 20 patients showed an improvement by at least one level after receiving hESC therapy. In addition, all the affected patients showed improvement in balance while sitting (20 patients); and spasticity (17 patients).

In addition to the ESS scores of the patients, all patients were evaluated for recovery using single photon emission computerized tomography (SPECT) scan and magnetic resonance imaging (MRI). At the end of therapy (T6) most patients showed improved perfusion on SPECT scan. (Fig 2)

c) Safety Evaluation

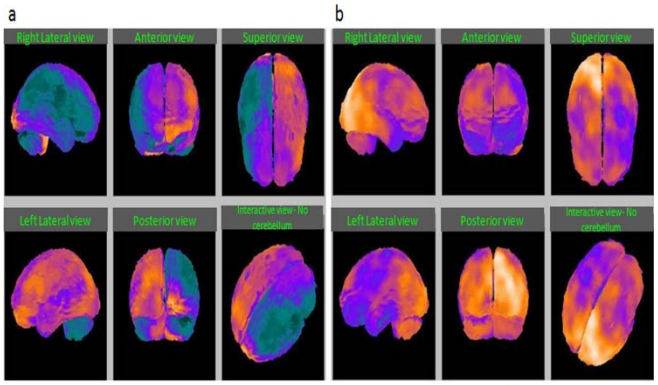
Overall, 4 patients experienced 11 AEs during the entire duration of the study. Of these, 3 patients experienced AEs in T1 and 1 patient experienced AEs in T2. However, no AEs were reported in T3, T4, T5 and T6. The most commonly experienced AEs included weakness/dizziness (3 patients, 27.3%); pain in shoulder, wrist, and joint (2 patients, 18.2%); constipation; fever; anxiety; blurred vision; diarrhea; and acidity (1 patient each, 9.1%). Of all the AEs experienced by the patients, 45% were mild and 55% were moderate in intensity. All AEs reported during the study period resolved within 48 hr. No serious adverse events (SAEs) and deaths were reported during the study (Table 4).

Table 4 : Adverse Events Reported during the Study Period

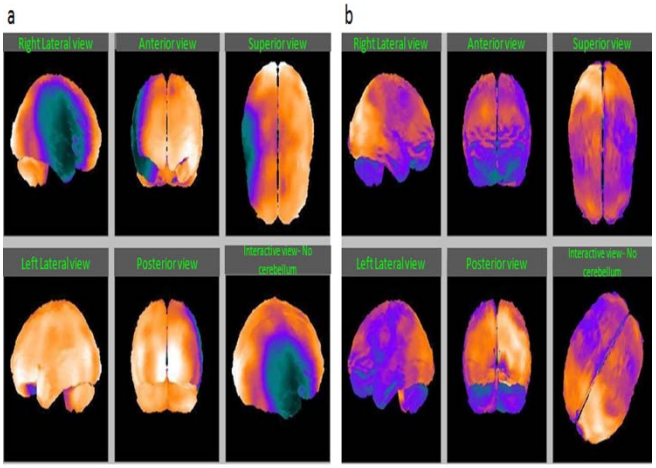
Adverse Event	Number of Events (%)
Weakness/dizziness	3 (27.3)
Pain (shoulder, wrist, and joint)	2 (18.2)
Constipation	1 (9.1)
Fever	1 (9.1)
Anxiety	1 (9.1)
Blurred Vision	1 (9.1)
Diarrhea	1 (9.1)
Acidity	1 (9.1)

IV. Discussion

The present study has shown promising results among the patients with CVA after treatment with hESC therapy. Most of the patients included had difficulty in maintaining leg position, leg flexion, gait, arm outstretched position, raising of arms and fingers, foot dorsiflexion, wrist extension, and experienced difficulty in speech. However, these patients demonstrated an improvement in their condition after receiving hESC therapy. After receiving hESC therapy, an improvement by at least one level was noted in gait (22 patients); speech (15 patients); level of consciousness (2 patients); comprehension and gaze (1 patient each),. Improvement in these parameters showed a better QoL among most patients included in the present study. The patients who received hESC therapy at the early stages of CVA showed a better improvement in most aspects as compared with patients who received hESC therapy at later stages of CVA. SPECT scan done after the therapy showed normal perfusion as compared with SPECT scan done before the therapy. (Figure 2 and Fig 3).



SPECT images reconstructed in transaxial, sagittal and coronal axis shows diffuse hypoperfusion globally with relative sparing of the cerebellum



SPECT images reconstructed in transaxial, sagittal and coronal axis shows normal hyperfusion

Kondziolka et al evaluated the effect of neuronal stem cells on patients with stroke using ESS scores and found that mean total ESS scores of patients increased from 69.3 at baseline to 74.4 at 6 months. In addition, this study demonstrated an improvement in functional deficits among patients with stroke [15]. However, the results of our study showed an improvement in both functional and motor deficits using hESCs.

CVA is third among all the leading causes of death globally [8]. The increasing incidence of stroke has led to rising healthcare costs [16]. Although treatment of patients with stroke is available with tPA, it has a narrow time window (within 3 hr of onset) [17] and several contraindications due to which it is available to less than 5% stroke patients [18]. Decreased QoL makes it extremely difficult for these patients to perform their daily activities. According to a study conducted by Kim et al, patients with stroke have decreased functional independence, social interaction and reduced QoL [19]. Most of the patients with stroke are unable to walk and maintain balance while sitting and standing. According to the stroke association patients with stroke are unable to sit or stand while maintaining balance and may also experience trouble walking [20]. In a study conducted by Weerdt et al to identify different problems associated with stroke, 25.7% patients showed lack of active movement and general mobility and 19.5% patients showed imbalanced muscle tone [21]. The ESS scores used to evaluate the improvement in most parameters

does not consider improvement in walking and balance. Therefore, we analyzed improvement in these parameters using an in-house scoring system. Most of the patients showed an improvement in walking, balance problems, and spasticity after receiving hESC therapy.

Stem cells possess self-renewal and multipotency features and have the ability to differentiate into any cell type in vivo. Of the different types of stem cells, embryonic stem cells are considered to possess the highest potential to give rise to any cell type and are referred to as pluripotent cells. Stem cells are capable of forming synaptic connections in the stroke injured brain after transplantation. Stem cells have neuroprotective properties which help reverse the damage caused by stroke [18].

Stem cell therapy is gaining more importance for the treatment of CVA. Most studies conducted to evaluate the effect of stem cell therapy suggest that stem cells have a neuroprotective effect. Chen et al demonstrated that adipose tissue-derived stem cells (ADSCs) restore brain function through several mechanisms including secretion of vascular endothelial growth factor (VEGF) for angiogenesis of the injured region, stimulation of brain repair markers and reduction of brain injury derived apoptosis [22].

A study conducted by Chang et al showed that hESC derived neural precursor cells (NPCs) migrate and survive in the infarct region and show improvement in functional deficits in rodents with ischemic stroke. This study reported that improved functional deficits may be associated with neurorestorative and neuroprotective effects of the transplanted hESC-NPCs [23]. Another study showed that hESC derived neural progenitor cells improved regenerative activities and sensory function without immune suppression when transplanted into the ischemic core and penumbra region after ischemic stroke in an animal model [24].

There are very few studies which have shown the effect of hESCs in the treatment of stroke. The difficulty in isolation of hESCs has restricted evaluation of their potential in the treatment of CVA. After being transplanted, hESCs grow in the affected area to replace the degenerated cell type. hESCs regenerate damaged cells by communicating with the damaged area and "homing" in the site of injury. This often occurs by the release of chemokines, cytokines, and growth factors from the site of injury [25]. In addition, the route of administration was selected as this shows an impact on the migration of hESCs and their ability to "home" in the damaged tissue. MSCs have also shown the influence of administration route on their potential to migrate and home at the site of injury [26]. The route of administration and the dosing schedule of hESCs play a vital role in their mechanism of action. The IM and IV routes were used to facilitate faster migration and transplantation of the hESCs to the affected area. A gap phase was included between each treatment period to facilitate the process of homing, and regeneration within the body. Adequate time intervals were maintained between each treatment period for the elucidation of maximum effect in the affected areas of the brain. Patients were treated in subsequent treatment phases after carefully monitoring the extent of improvement with MRI and SPECT scan. In the present study, we used hESCs which were isolated using a patented in-house technique for the treatment of patients (United States Granted Patent-WO 2007/141657A PCT/1B 2007 Published 13 Dec 2007). These cells do not have any xeno-product in them.

V. Conclusion

In conclusion, the results of the present study have demonstrated effective improvement in the condition of patients with CVA. Most patients showed improved cognitive skills and regained their functional ability which improved the QoL of the patients included in the study. Although AEs were reported, no patients experienced severe AEs or SAEs during the study as a result of hESC therapy. hESC therapy was well tolerated among all the patients included in the study. However; further large scale prospective studies are required for making hESC therapy available clinically for patients with CVA.

Consent Statement: A written informed assent/consent was obtained from the patients/parents or legal guardians prior to the treatment for publication of this Case report and any accompanying images.

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Conflict of Interest

The authors have no conflict of interest.

Author's contribution

GS has made substantial contributions to design, conception, and investigation of the patients. GS also reviewed and approved the final draft of the manuscript for publication. JKB has made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data.

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Creutzfeldt - Jakob Disease – A Rare Case Report

By Dr. Thomas George, Dr. Rajesh RU, Dr. Ajay Manickam & Dr. Sudipta Banerjee

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Introduction- Prion diseases are neurodegenerative diseases that have incubation period. Five prion diseases are recognized they are kuru, Creutzfeldt-Jakob disease (CJD), variant CJD, Gerstmann-straussler Scheinker syndrome (GSS) and fatal familial insomnia1. Among all these disease, CJD accounts for 90% of all prion disease. One case of CJD occurs among 1,000,000 populations per year. It is such a rare presentation. Dementia and myoclonus are the most common presenting condition of CJD. This is a rare case report of a patient who had a rare clinical presentation, and finally it was diagnosed to be a case of CJD.

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Creutzfeldt - Jakob Disease – A Rare Case Report

Dr. Thomas George [α], Dr. Rajesh RU [σ], Dr. Ajay Manickam [ρ] & Dr. Sudipta Banerjee [ω]

I. Introduction

Prion diseases are neurodegenerative diseases that have incubation period. Five prion diseases are recognized they are kuru, Creutzfeldt-Jakob disease (CJD), variant CJD, Gerstmann-straussler Scheinker syndrome (GSS) and fatal familial insomnia[1]. Among all these disease, CJD accounts for 90% of all prion disease. One case of CJD occurs among 1,000,000 populations per year. It is such a rare presentation. Dementia and myoclonus are the most common presenting condition of CJD. This is a rare case report of a patient who had a rare clinical presentation, and finally it was diagnosed to be a case of CJD.

II. Case Report

40 years old male patient presented to the Emergency department with complaints of weakness of left side of body two and half months back which was diagnosed and treated a s CVA from some private hospital. Now patient presented with complaints of right side of body along with progressive deterioration of speech and orientation. Patient also had myoclonus. He is not a known diabetic, hypertensive, asthmatic. He was on any long term medication. When patient presented to us, he was taking treatment for CVA. On examination patient was disoriented, responding to pain. Tone all four limbs spasticity present. Power could not be assessed properly. Deep tendon reflex exaggerated in all the four limbs. Superficial reflexes were present. Sensory system, cerebellar signs and gait couldn't be assessed. Spine was normal. Other system examination was within normal limits. The patient was planned for routine blood and urine examination. In complete hemogram there was mild leucocytosis. Other routine tests were within normal limits.

Lumbar puncture and CSF study was found to be within normal limits, protein value in CSF was within normal limits. CSF study for abnormal proteins could not be done. As the condition of the patient was slowly deteriorating day by day, the patient was planned for MRI scan. MRI scan was showing features of increased signal intensity in putamen and caudate nucleus (Figure 1). EEG done in this patient was showing periodic sharp wave complex (Figure 2). Hence from these findings we came to a conclusion that there are chances suggestive of CJD in this patient.

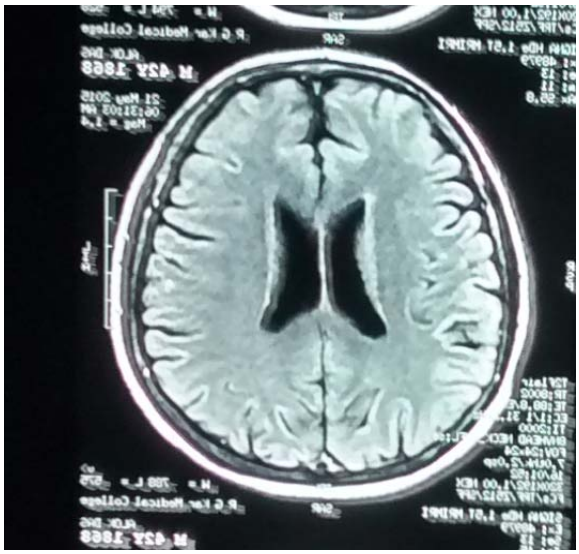

Figure 1 : Increased signal intensity in putamen and caudate nucleus

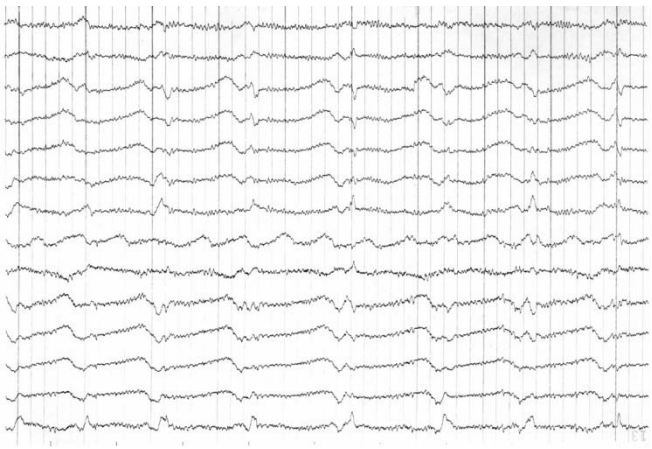

Figure 2 : EEG showing periodic sharp wave complex

III. Discussion

Rapidly progressive mental deterioration and myoclonus are the classical presentation for CJD. But in this patient, the presentation was totally confusing. The patient was having left sided weakness as the initial presentation. This was totally misleading as the earlier physician started suspecting it to be a CVA. He also started treating the patient for CVA. But slowly the general condition of the patient was deteriorating day by day. The patient was then having features of myoclonus and mental deterioration later. This is said to be a different presentation of CJD.

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Mental deterioration may be manifest as dementia, behavioural abnormalities involving higher cortical functions. With progression of age dementia becomes dominant in most patients and can advance rapidly.

Myoclonus especially provoked by startle is present in more than 90% of the patients with CJD. So whenever a patient presents with complaints of dementia and myoclonus one should have a strong suspicion of CJD. There are various subtypes of CJD described[2].

1. MM1 and MV1 variant accounts for 70% of CJD
2. VV2 ataxic variant accounts for 15% or less
3. MV2 accounts for 9 %
4. MM2 thalamic variant.

The various other differential diagnosis that we have to keep in our mind when we are suspecting CJD are parkinsonism, autoimmune disorders including Para neoplastic syndromes, sarcoidosis, infections including viral and post viral encephalitis, malignancy, toxic and metabolic encephalopathy, cerebro vascular disease, psychiatric disease. Keeping all the differential diagnosis in mind, the patient all routine and necessary investigations was done. The gold standard investigation for the diagnosis of CJD remains to be brain biopsy. Also MRI scan and EEG waves can aid in the diagnosis. All investigations clearly ruled out other possible differential diagnosis of CJD.

The MRI findings in a case with CJD will usually have abnormally increased T2 and flair signal intensity in the Globus palladius, thalamus, cerebral and cerebellar cortex[3]. EEG will provide supportive evidence but cannot be taken as confirmatory test for CJD. In this case report MRI findings suggestive of CJD was elicited also, EEG showed classical spike wave pattern. Though it is said that detection of CSF protein 14-3-3 considered as adjunctive rather than absolute test for CJD. Hence from the literature available, MRI and EEG alone was made as a tool for diagnosing CJD in this patient, as brain biopsy and CSF protein detection was very expensive could not be done.

The diagnostic criteria for CJD as described by centres of disease control and prevention outline the following criteria for probable CJD[4]

1. Progressive dementia
2. At least two of the following four features. Myoclonus, visual or cerebellar disturbance, pyramidal/extrapyramidal dysfunction, akinetic mutism
3. Atypical EEG/ CSF assay for protein 14-3-3/ MRI abnormalities in the caudate nucleus and putamen
4. Routine investigations should not suggest any other diagnosis.

In our case, all the conditions as pointed out above were present; hence the diagnosis of CJD was made.

After coming to the diagnosis of CJD, the patient was given supportive therapy. As there is no effective treatment for the prion disease, death usually occurs[5]. In this patient the condition was very rapidly progressive. The patient after the onset of initial symptom expired in a time period of two months.

IV. Conclusion

CJD is a very rare disease mean age of onset is fifth to sixth decade. Rapidly progressive mental deterioration with dementia is said to be the classical presentation of CJD. Though brain biopsy is the gold standard investigation of choice, as there is no proper treatment modality available for CJD, CDC has formulated the criteria for diagnosing CJD. When we are suspecting a diagnosis of CJD it is very important to keep in mind other common differential diagnosis. There is no treatment for CJD; death is the ultimate result for this disease.

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The Study Electro Shock Therapy (EST)

By Mehrdad Davari Agblagh Rostamkhan & Elmikarbordea zobahane Ardebil

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Abstract- Shock therapy is one of the treatment methods for psychiatric patients, which is associated with a low risk and in financial terms it also benefits the patient and the health system. Mild Electroconvulsive device, which only affects the skin (and not the nervous system), operates on the basis of classical conditioning. EST device has some morphological features including the size and much weight that causes anxiety in the patient. It also has a mechanism that can be fed with 220V. Consequently, the concentration of physician is considerably reduced and also, it causes negative effects on the patient. In behavioral therapy, reducing the patient's anxiety is a very important point that should be taken into consideration. Studying the effect of electroshock therapy on the cognitive state of patients hospitalized in the psychiatric ward showed that shortage and lack of knowledge cause fear and confusion and this, intensifies the cognitive effects that appear after the electroconvulsive therapy. Therefore, it is necessary for the nurses to provide their patients with appropriate and enough information before the implementation of this therapy. In this paper we offer a new device that consists of mild Electroconvulsive system, warning lights, warning voice, and small size and shape which has been designed on the basis of golden rate. Management system of the device is done via remote control and consequently, the patient doesn't experience any anxiety in the course of treatment, rather it increases the performance of attending physician and facilitates the treatment.

Keywords: shock therapy, wrist shock device for the elimination of harmful habits, golden rate, EST system.

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The Study Electro Shock Therapy (EST)

Mehrdad Davari Agblagh Rostamkhan [α] & Elmikarbordea zobahane Ardebil [σ]

Abstract- Shock therapy is one of the treatment methods for psychiatric patients, which is associated with a low risk and in financial terms it also benefits the patient and the health system. Mild Electroconvulsive device, which only affects the skin (and not the nervous system), operates on the basis of classical conditioning. EST device has some morphological features including the size and much weight that causes anxiety in the patient. It also has a mechanism that can be fed with 220V. Consequently, the concentration of physician is considerably reduced and also, it causes negative effects on the patient. In behavioral therapy, reducing the patient's anxiety is a very important point that should be taken into consideration. Studying the effect of electroshock therapy on the cognitive state of patients hospitalized in the psychiatric ward showed that shortage and lack of knowledge cause fear and confusion and this, intensifies the cognitive effects that appear after the electroconvulsive therapy. Therefore, it is necessary for the nurses to provide their patients with appropriate and enough information before the implementation of this therapy. In this paper we offer a new device that consists of mild Electroconvulsive system, warning lights, warning voice, and small size and shape which has been designed on the basis of golden rate[1]. Management system of the device is done via remote control and consequently, the patient doesn't experience any anxiety in the course of treatment, rather it increases the performance of attending physician and facilitates the treatment.

Keywords: shock therapy, wrist shock device for the elimination of harmful habits, golden rate, EST system.

I. Introduction

a) An introduction to the system

Nowadays with the increasing population and the problems of life that create a lot of anxieties and unconsciously affect people, in addition to physical illnesses, they cause some other mental disorders, too. One method of behavior therapy among others is making use of mild electroconvulsive which only affects the skin (not the nervous system), and works merely on the basis of classical conditioning and active conditioning. Active conditioning (which is also known as operant/ instrumental /type II conditioning or trial and error) is some kind of consonant or associative learning. In active conditioning, the animal learns to make relationship between one of its own behaviors and some kind of reward or punishment. An interesting example for making scientifically use of conditioning principles is to create "taste aversion" in jackals for the purpose of preventing them from hunting the rural animals (Gustafson et al., 1974). Conditioning "taste aversion" occurs when neutral stimulus (eating a meal) is associated with an unconditional response (becoming ill after eating). Unlike other forms of classical conditioning which require more things to form associations, this kind of conditioning, for example making use of "taste aversion", in fact is generally obtained from one thing. In one case the mutton was injected with a drug that caused nausea. After eating poisoned meat, jackals get away from the sheep instead of attacking on them [10]. And the made device also creates shock on the arms of the patient together with its continuous inappropriate behavior and consequently, an aversion is developed in patient and the device impacts on it.

Electro Shock Therapy (EST) device, whose size is large, and weighs heavy works using 220V. This device has been connected to two electrodes by some wires and it creates shock and also an alarming sound. The keys on the device have been devised in such a manner that the therapeutic doctor should stand beside the patient with his/her hand on the keys. This causes reduction in concentration of the therapeutic doctor and also leaves negative effects on curing the patient. Its another disadvantage is that it cannot be used everywhere and continuous use of the device is not appropriate for the patient.

Curing process takes place through the convulsive electric shock of the device (Electroconvulsive Therapy) using an electric current through the brain. In this approach, through two electrodes that are mounted on the scalp, an electric current with moderate intensity is passed. This electric current which is connected in less than one second, causes a wide shoot in the brain's neurons and creates a state similar to epileptic attacks. After a few minutes, and returning the consciousness, the patient forgets events that have been occurred immediately prior to the shock and after an hour or more, he/she experiences confusion. Continuation of the treatment for three to five times a week causes the patient to feel disorientation – a state that will usually and gradually be recovered after discontinuation of the treatment. Seizures cause many changes in the central and peripheral nervous system. Seizures activate autonomic nervous system. In the 1940s and 1950s, ECT was used to treat all mental disorders including schizophrenia but nowadays, based on extensive research, shock therapy is not mainly used

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[1] A positive number that in case of addition of a unit to it we will gain its square.

for patients with severe depression –those who do not respond to antidepressant drugs and commit suicide.

In designing the appearance of the device, golden ration has been used. Traditionally, this ration was known as adaptive division and its equivalent amount is about 1.618 (Phi number). One of the properties of this number is that if a unit is subtracted from it, the remainder will be equal to its own revers. This device functions similar to the electroshock (EST) device, but with more functional features; and this is more helpful and effective in curing disorders such as intellectual and practical obsessions, drug addiction, deviant and inappropriate behavioral habits. Compared with the previous one, the form and mechanism of this device has been changed for the purpose of preventing the anxiety resulting from its appearance and the mechanism that was applied for the patient by EST device, and finally in order to be effective in treatment process.

II. Done Works

By changing the human being's life from simple and primary mode into it complex state, mental disorders also like most other illnesses, is constantly rising [9]. Nausea during chemotherapy is a natural reaction for cancer patients. However, it is seen that sometimes upon entering the treatment room, these patients become nauseated. It has even been seen that at the time when children with cancer is given ice cream prior to chemotherapy, they also become conditional for ice cream at other times and even in case of not being treated with chemotherapy, they begin to vomit after they ate their ice cream [5]. Whenever an ineffective stimulus (e.g., ringing), is given to the animal together with a natural stimulus (for example: food), after sometimes the ineffective stimulus solely causes reaction (for example: Salivation) in animals. This new stimulus is called conditional stimulus; because it can cause behavior to be appeared if and only if there is another stimulus, then it will be called conditioned stimulus; because it will be able to cause the behavior when previous to it, it is along with a natural stimulant. Natural stimulant is called unconditional stimulus. Prior to being conditioned, natural stimulus or unconditional stimulus (US) causes natural or unconditional response (UR). In case of an animal that has been conditional, conditional or ineffective stimulus (CS) also causes conditional response (CR). Each time when CS and US are presented together, it will be called a Try (T). Due to the repeated attempts, the living animal is placed in the path of Acquisition (A); that is, the course during which the animal is associating the two stimuli and creating a relationship between them [5]. On the basis of the time interval of providing conditional and unconditional stimuli, three situations arise:

Simultaneous Conditioning: occurs when to stimulus are presented together and conditional stimulus remains until the beginning of the response.

Delayed Conditioning: offering the conditional stimulus a few seconds before unconditional stimulus; and conditional stimulus remains until the beginning of the response.

Trace Conditioning: offering the conditional stimulus a few seconds before unconditional stimulus; and before offering the unconditional stimulus, stimulus one is omitted.

Repeating the conditional stimulus without the unconditional one, leads to the omission of conditional response and this course has been called **Extinction** (E).

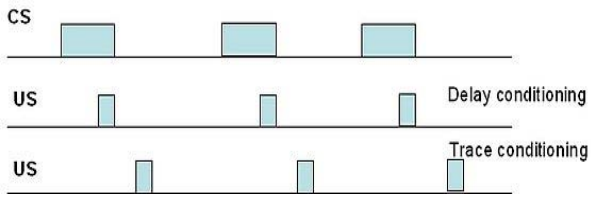

Figure 1: Comparing the Delayed Conditioning with the Trace Conditioning

In both traces of "Learning" and "Extinction", at the beginning rapid changes are occurred and gradually the rate of changes will be reduced [5]. Nausea during chemotherapy for Cancer Patients is a natural response. But it is sometimes evident that upon entering the treatment room, these patients become nauseated. It has even been seen that at the time when children with cancer is given ice cream prior to chemotherapy, they also become conditional for ice cream at other times and even in case of not being treated with chemotherapy, they begin to vomit after they ate their ice cream [5]. Sometimes, the majority of research units on ECT is weak, most of them also have negative attitudes toward treatment, awareness among households with higher education is better and also, families whose patients have more history of hospitalization and ECT, enjoy better awareness and appropriate attitude in this regard [3]. Given the widespread use of ECT, it is necessary to run the education process in these patients [7]. And in nursing cares, along with providing information, patient is encouraged to express his/her thoughts and feelings about the ECT, and by listening to the patient his / her negative beliefs and fears are studied. Then, they offered the information about the complications of this method and the familiarity of the patient with people who already experienced this treatment and/or - if the patient wishes - he/she closely observe this treatment prior to ECT [8]. Shortage and lack of knowledge, cause fear and confusion; and this intensifies the cognition of the effects after electroconvulsive therapy, therefore, it is necessary for nurses to provide the patients with appropriate and enough information prior to the

implementation of this treatment method [2]. The important point is that in dealing with patients who refer with physical symptoms, sufficient attention to individual and social factors will be effective in incidence of these symptoms. In addition, considering the other associated psychiatric Disorders and timely curing them are of great importance [1].

III. The Introduction of the Proposed System

a) An overall View to the System

The designed device functions similar to the electroshock (EST) device, but with more functional features; and this is more helpful and effective in disorders such as intellectual and practical obsessions, drug addiction, deviant and inappropriate behavioral habits. One of the usages of the new device is therapy with warning lights that can be an appropriate alternative for shock.

b) Properties of the Device

Figure 2 : Hemlock Wrist Device Used to Remove Harmful Habits

Modules: RF Transmitter and receiver

Resistance: 5 pieces of 330 ohms, 1 piece of 220kohms, 4 pieces of 4.7kohms, 4 pieces of 10kohms

Chemical Capacitor: 4 pieces of 3.3 micro farad, 1 piece of 47 micro farad, 1 piece of 220 micro farad

Lens Condenser: 2 pieces of 0.1 farad

Diode: 4 pieces of 41481n, 1 piece of 4001n

Light Diode: 8 pieces

Transistor: 4 pieces of 237bc

IC: 3 pieces of PT2272A-M4

*Relay:*4 pieces

Shocker: 1 piece

c) Performance of the Device

In behavioral therapy, one of the important causes of anxiety is appearance and mechanism of the device which affects the patient. In designing the new device golden ratio (Phi number) has been used; and results obtained from many scientific and psychological researches show that the most beautiful surfaces and forms from the view point of humans, are those that golden ration has been used in them [4]; and together with the reduction in size and weight for about 5 times, as it is evident in Fig. (2), and with reverse engineering and analysis of the previous device, we have designed a new circuit which is managed by remote control and is capable of being fed with battery and municipal power which is considerably an important factor in reducing the patient's anxiety. These changes are also effective important factors in increasing the concentration and speed in action of the doctor and leave positive impact on treatment process. The device has been built in a small circuit using the pieces with perfect quality and very cheap price. Therefore, the cost of the device is low and this increases the purchase possibility and using the device because of its very low price. using the device is in a manner that by referring the patient to a psychiatrist for treatment after the doctor diagnosed the disease type, for example nervous twitch(sideway jump of eye) in which the patient cannot control the nervous twitch, this device is connected to the wrist of the person and is lighted. This device includes three means for treatment such as light shock, alarming voice and alarming lights. During the conversation, and upon the recognition that the patient suffers from nervous twitch, psychiatrist pushes the key No. 1 and the red alarming light of the device is turned on. If the patient continues twitching the control key No. 2 is connected and creates an alarming voice to prevent the patient from twitching. After many alarming times, if the patient again continues the twitching, based on the doctor's recognition another light shock which is similar to a painful bite is exerted to the patient's skin; using the key No.4, the shock is increased for the purpose that associating this status (prevention) with what is considered as inappropriate or abnormal behavior (as the conditional stimulus) causes the transmission of feeling prevention and disgust to the conditioned stimulus, and in this way it creates its therapeutic effects. Therefore, avoidance conditioning, aversive therapy, and thought stopping are the most principal methods that this device uses them. The above said techniques are considered as effective means in treatment of disorders such as practical and intellectual obsessions, being addicted to narcotics, digressive and behavioral inappropriate habits and … .Also, a child who learns that assault and violence towards any of his/her brothers or sisters will follow to be punished by parents, will prevent such violence. Operant conditioning will also be activated in such cases. Of course, active conditioning through punishment has also some disadvantages; for example, the individual doesn't learn what to do and results that he/she obtains are not predictable in the same size as offering the reward. Another disadvantage is that it can be led to feeling hate about the person who acts to punish, or about the situation in which the punishment has taken place, and this leads to more destructive effects [6]. Since children are weak-minded than other people, the device has been designed in such a manner that in the first stage, the physician warns the child only through one slight shock, but in the next times since prior to each shock

one red light is turned on, physician can warn the child through only one red light or warning voice for the purpose of preventing the child from tickling and that no negative impact to be exerted to the child. One of the main difficulties in Shock Therapy is low awareness of the patients and fear and anxiety of the device. Upon increase in awareness, complete description and solving the problems the treatment can be more effective.

IV. Conclusion

In this research we studied the slight Electroshock EST device concerning the treatment manner, mechanism and the anxiety which is inserted into the patient, and came to the conclusion that creation of anxiety in patient depends on the awareness of the patient as well as the appearance and the mechanism used in the device. Also, mechanism and management of the device is one of the effective factors that impact on the performance of the doctor and leave negative effect on the process of treatment progress in patient. Consequently, in this research beside the omission of the difficulties of the previous device, a new and different device with declaration No. 139350140002002142 has been invented that has many characteristics; and through studying the previous researches and also reverse engineering of the obtained informative device helps the researcher in compiling the process of providing the new device. Unfortunately, in Iran we couldn't have an access to more papers that fully describe the electroconvulsive shock therapy method using the electroconvulsive therapy in conditioning treatment. For this reason, the researcher of this paper proposes that more researches to be done in this regard.

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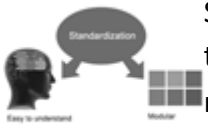

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TECHNIQUES FOR WRITING A GOOD QUALITY RESEARCH PAPER:

1. Choosing the topic: In most cases, the topic is searched by the interest of author but it can be also suggested by the guides. You can have several topics and then you can judge that in which topic or subject you are finding yourself most comfortable. This can be done by asking several questions to yourself, like Will I be able to carry our search in this area? Will I find all necessary recourses to accomplish the search? Will I be able to find all information in this field area? If the answer of these types of questions will be "Yes" then you can choose that topic. In most of the cases, you may have to conduct the surveys and have to visit several places because this field is related to Computer Science and Information Technology. Also, you may have to do a lot of work to find all rise and falls regarding the various data of that subject. Sometimes, detailed information plays a vital role, instead of short information.

2. Evaluators are human: First thing to remember that evaluators are also human being. They are not only meant for rejecting a paper. They are here to evaluate your paper. So, present your Best.

3. Think Like Evaluators: If you are in a confusion or getting demotivated that your paper will be accepted by evaluators or not, then think and try to evaluate your paper like an Evaluator. Try to understand that what an evaluator wants in your research paper and automatically you will have your answer.

4. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

5. Ask your Guides: If you are having any difficulty in your research, then do not hesitate to share your difficulty to your guide (if you have any). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work then ask the supervisor to help you with the alternative. He might also provide you the list of essential readings.

6. Use of computer is recommended: As you are doing research in the field of Computer Science, then this point is quite obvious.

7. Use right software: Always use good quality software packages. If you are not capable to judge good software then you can lose quality of your paper unknowingly. There are various software programs available to help you, which you can get through Internet.

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9. Use and get big pictures: Always use encyclopedias, Wikipedia to get pictures so that you can go into the depth.

10. Bookmarks are useful: When you read any book or magazine, you generally use bookmarks, right! It is a good habit, which helps to not to lose your continuity. You should always use bookmarks while searching on Internet also, which will make your search easier.

11. Revise what you wrote: When you write anything, always read it, summarize it and then finalize it.

12. Make all efforts: Make all efforts to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in introduction, that what is the need of a particular research paper. Polish your work by good skill of writing and always give an evaluator, what he wants.

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15. Use of direct quotes: When you do research relevant to literature, history or current affairs then use of quotes become essential but if study is relevant to science then use of quotes is not preferable.

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17. Never use online paper: If you are getting any paper on Internet, then never use it as your research paper because it might be possible that evaluator has already seen it or maybe it is outdated version.

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19. Know what you know: Always try to know, what you know by making objectives. Else, you will be confused and cannot achieve your target.

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21. Arrangement of information: Each section of the main body should start with an opening sentence and there should be a changeover at the end of the section. Give only valid and powerful arguments to your topic. You may also maintain your arguments with records.

22. Never start in last minute: Always start at right time and give enough time to research work. Leaving everything to the last minute will degrade your paper and spoil your work.

23. Multitasking in research is not good: Doing several things at the same time proves bad habit in case of research activity. Research is an area, where everything has a particular time slot. Divide your research work in parts and do particular part in particular time slot.

24. Never copy others' work: Never copy others' work and give it your name because if evaluator has seen it anywhere you will be in trouble.

25. Take proper rest and food: No matter how many hours you spend for your research activity, if you are not taking care of your health then all your efforts will be in vain. For a quality research, study is must, and this can be done by taking proper rest and food.

26. Go for seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

27. Refresh your mind after intervals: Try to give rest to your mind by listening to soft music or by sleeping in intervals. This will also improve your memory.

28. Make colleagues: Always try to make colleagues. No matter how sharper or intelligent you are, if you make colleagues you can have several ideas, which will be helpful for your research.

29. Think technically: Always think technically. If anything happens, then search its reasons, its benefits, and demerits.

30. Think and then print: When you will go to print your paper, notice that tables are not be split, headings are not detached from their descriptions, and page sequence is maintained.

31. Adding unnecessary information: Do not add unnecessary information, like, I have used MS Excel to draw graph. Do not add irrelevant and inappropriate material. These all will create superfluous. Foreign terminology and phrases are not apropos. One should NEVER take a broad view. Analogy in script is like feathers on a snake. Not at all use a large word when a very small one would be sufficient. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Amplification is a billion times of inferior quality than sarcasm.

32. Never oversimplify everything: To add material in your research paper, never go for oversimplification. This will definitely irritate the evaluator. Be more or less specific. Also too, by no means, ever use rhythmic redundancies. Contractions aren't essential and shouldn't be there used. Comparisons are as terrible as clichés. Give up ampersands and abbreviations, and so on. Remove commas, that are, not necessary. Parenthetical words however should be together with this in commas. Understatement is all the time the complete best way to put onward earth-shaking thoughts. Give a detailed literary review.

33. Report concluded results: Use concluded results. From raw data, filter the results and then conclude your studies based on measurements and observations taken. Significant figures and appropriate number of decimal places should be used. Parenthetical remarks are prohibitive. Proofread carefully at final stage. In the end give outline to your arguments. Spot out perspectives of further study of this subject. Justify your conclusion by at the bottom of them with sufficient justifications and examples.

34. After conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print to the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects in your research.

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Key points to remember:

- Submit all work in its final form.
- Write your paper in the form, which is presented in the guidelines using the template.
- Please note the criterion for grading the final paper by peer-reviewers.

Final Points:

A purpose of organizing a research paper is to let people to interpret your effort selectively. The journal requires the following sections, submitted in the order listed, each section to start on a new page.

The introduction will be compiled from reference matter and will reflect the design processes or outline of basis that direct you to make study. As you will carry out the process of study, the method and process section will be constructed as like that. The result segment will show related statistics in nearly sequential order and will direct the reviewers next to the similar intellectual paths throughout the data that you took to carry out your study. The discussion section will provide understanding of the data and projections as to the implication of the results. The use of good quality references all through the paper will give the effort trustworthiness by representing an alertness of prior workings.

Writing a research paper is not an easy job no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record keeping are the only means to make straightforward the progression.

General style:

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To make a paper clear

· Adhere to recommended page limits

Mistakes to evade

- Insertion a title at the foot of a page with the subsequent text on the next page
- Separating a table/chart or figure - impound each figure/table to a single page
- Submitting a manuscript with pages out of sequence

In every sections of your document

· Use standard writing style including articles ("a", "the," etc.)

· Keep on paying attention on the research topic of the paper

· Use paragraphs to split each significant point (excluding for the abstract)

· Align the primary line of each section

· Present your points in sound order

· Use present tense to report well accepted

· Use past tense to describe specific results

· Shun familiar wording, don't address the reviewer directly, and don't use slang, slang language, or superlatives

· Shun use of extra pictures - include only those figures essential to presenting results

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The summary should be two hundred words or less. It should briefly and clearly explain the key findings reported in the manuscript--must have precise statistics. It should not have abnormal acronyms or abbreviations. It should be logical in itself. Shun citing references at this point.

An abstract is a brief distinct paragraph summary of finished work or work in development. In a minute or less a reviewer can be taught the foundation behind the study, common approach to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Yet, use comprehensive sentences and do not let go readability for briefness. You can maintain it succinct by phrasing sentences so that they provide more than lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study, with the subsequent elements in any summary. Try to maintain the initial two items to no more than one ruling each.

- Reason of the study - theory, overall issue, purpose
- Fundamental goal
- To the point depiction of the research
- Consequences, including definite statistics - if the consequences are quantitative in nature, account quantitative data; results of any numerical analysis should be reported
- Significant conclusions or questions that track from the research(es)

Approach:

- Single section, and succinct
- As a outline of job done, it is always written in past tense
- A conceptual should situate on its own, and not submit to any other part of the paper such as a form or table
- Center on shortening results - bound background information to a verdict or two, if completely necessary
- What you account in an conceptual must be regular with what you reported in the manuscript
- Exact spelling, clearness of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else

Introduction:

The **Introduction** should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable to comprehend and calculate the purpose of your study without having to submit to other works. The basis for the study should be offered. Give most important references but shun difficult to make a comprehensive appraisal of the topic. In the introduction, describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will have no attention in your result. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here. Following approach can create a valuable beginning:

- Explain the value (significance) of the study
- Shield the model - why did you employ this particular system or method? What is its compensation? You strength remark on its appropriateness from a abstract point of vision as well as point out sensible reasons for using it.
- Present a justification. Status your particular theory (es) or aim(s), and describe the logic that led you to choose them.
- Very for a short time explain the tentative propose and how it skilled the declared objectives.

Approach:

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- Sort out your thoughts; manufacture one key point with every section. If you make the four points listed above, you will need a least of four paragraphs.

- Present surroundings information only as desirable in order hold up a situation. The reviewer does not desire to read the whole thing you know about a topic.
- Shape the theory/purpose specifically - do not take a broad view.
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This part is supposed to be the easiest to carve if you have good skills. A sound written Procedures segment allows a capable scientist to replacement your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt for the least amount of information that would permit another capable scientist to spare your outcome but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section. When a technique is used that has been well described in another object, mention the specific item describing a way but draw the basic principle while stating the situation. The purpose is to text all particular resources and broad procedures, so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step by step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

- Explain materials individually only if the study is so complex that it saves liberty this way.
- Embrace particular materials, and any tools or provisions that are not frequently found in laboratories.
- Do not take in frequently found.
- If use of a definite type of tools.
- Materials may be reported in a part section or else they may be recognized along with your measures.

Methods:

- Report the method (not particulars of each process that engaged the same methodology)
- Describe the method entirely
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures
- Simplify - details how procedures were completed not how they were exclusively performed on a particular day.
- If well known procedures were used, account the procedure by name, possibly with reference, and that's all.

Approach:

- It is embarrassed or not possible to use vigorous voice when documenting methods with no using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result when script up the methods most authors use third person passive voice.
- Use standard style in this and in every other part of the paper - avoid familiar lists, and use full sentences.

What to keep away from

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings - save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part a entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Carry on to be to the point, by means of statistics and tables, if suitable, to present consequences most efficiently.You must obviously differentiate material that would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matter should not be submitted at all except requested by the instructor.

Content

- Sum up your conclusion in text and demonstrate them, if suitable, with figures and tables.
- In manuscript, explain each of your consequences, point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation an exacting study.
- Explain results of control experiments and comprise remarks that are not accessible in a prescribed figure or table, if appropriate.
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- Not at all, take in raw data or intermediate calculations in a research manuscript.
- Do not present the similar data more than once.
- Manuscript should complement any figures or tables, not duplicate the identical information.
- Never confuse figures with tables - there is a difference.

Approach

- As forever, use past tense when you submit to your results, and put the whole thing in a reasonable order.
- Put figures and tables, appropriately numbered, in order at the end of the report
- If you desire, you may place your figures and tables properly within the text of your results part.

Figures and tables

- If you put figures and tables at the end of the details, make certain that they are visibly distinguished from any attach appendix materials, such as raw facts
- Despite of position, each figure must be numbered one after the other and complete with subtitle
- In spite of position, each table must be titled, numbered one after the other and complete with heading
- All figure and table must be adequately complete that it could situate on its own, divide from text

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The Discussion is expected the trickiest segment to write and describe. A lot of papers submitted for journal are discarded based on problems with the Discussion. There is no head of state for how long a argument should be. Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implication of the study. The purpose here is to offer an understanding of your results and hold up for all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of result should be visibly described. Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved with prospect, and let it drop at that.

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- You may propose future guidelines, such as how the experiment might be personalized to accomplish a new idea.
- Give details all of your remarks as much as possible, focus on mechanisms.
- Make a decision if the tentative design sufficiently addressed the theory, and whether or not it was correctly restricted.
- Try to present substitute explanations if sensible alternatives be present.
- One research will not counter an overall question, so maintain the large picture in mind, where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

- When you refer to information, differentiate data generated by your own studies from available information
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- Submit to generally acknowledged facts and main beliefs in present tense.

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Topics	Grades		
	A-B	**C-D**	**E-F**
Abstract	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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