Transcranial Direct Current Stimulation Technique: A Need of Bangladesh for Stroke Management

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Abstract Stroke has been considered as one of the leading cause of death worldwide. It results in reduced excitability, deregulated plastic modifications, and formation of aberrant connections and, these factors hinder recovery from stroke. Transcranial direct current stimulation (tDCS) is a promising technique for the treatment of a wide range of neurological disorders including stroke. Its application could improve the condition of patients having neurological disorders by making functional connections and maintaining existing pathways. In Bangladesh, stroke remains the third leading cause of death with 0.3% prevalence. The number of disability-adjusted life years lost for stroke is 485 per 10000 people, which depicts great economic burden of this disease in the future. Thus, introduction of new technologies such as tDCS in the treatment of stroke will not only improve conditions of stroke patients but also reduce economic burden of this disease in Bangladesh.

Keywords Transcranial Direct Current Stimulation, Stroke, Bangladesh

1. Introduction

Stroke, the second leading cause of death worldwide, is considered to affect at least one sixth of all people at least once in their life [1]. Moreover, this is the third most common cause of disability in adults. About one third of patients who survive 6 months after stroke attack become dependent on others [2]. Although mortality rate due to stroke has decreased, the incidence is increasing and, is estimated to reach 23 million cases by 2030 [3]. Patients suffering from ischemic stroke require constant monitoring in intensive care units (ICU) at hospitals.

Due to stroke, cells deprive of their nutrient supply, thus resulting in immediate cells death and brain damage and, this impairment is not only confined to the brain but may also result in alteration in inflammatory immune response. Suppression of systemic immunity may increase the stroke

patients' susceptibility to infections. For instance, pneumonia and urinary tract infections are the most common post stroke complications in patients [4].

1.1. Risk Factors for Stroke

Factors that seem to increase the risk of stroke attack are diabetes, high blood pressure as it increases a person's stroke risk by four to six times, smoking, lack of physical activity, obesity, old age, gender, high cholesterol levels, atrial fibrillation, thrombophilia, migraine with aura, heredity (family history), and prior stroke or heart attack [5]. The chances of occurring of stroke double after 55 years of age; however, it can happen at any age even in children. African-Americans have higher risks of stroke than Caucasians [6], which can be attributed to higher risks of high blood pressure, diabetes, and obesity in black people. Women have more stroke attacks and deaths due to this disease. The factors which pose stroke risks for females include pregnancy, use of birth control pills, history of preeclampsia/eclampsia or gestational diabetes, smoking, and post-menopausal hormone therapy [7]. Transient ischemic attacks (TIA) that produce stroke-like symptoms but no lasting damage are regarded as warning strokes [8]. The risk of stroke following TIA is 4% within the first 2 days, 6% within 7 days, 8% within 30 days and 9% within 90 days [9].

Limited data is available about stroke incidences from Bangladesh. However, few hospital studies have indicated high stroke prevalence in males and in age group above 70 years [10]. Number of patients having ischaemic stroke is higher than that of having hemorrhagic stroke. The main risk factors observed in stroke patients include hypertension which is the main risk factor followed by heart diseases, diabetes mellitus, obesity, hyperlipidemia, prior stroke attack, cigarette smoking, alcohol consumption, and oral contraception use. Moreover, some of the patients had multiple risk factors [10, 11]. Interestingly, several nontraditional risk factors, for instance, water-pipe use, **desi** (country-made) ghee (a class of clarified butter), chewable

tobacco, and infectious causes of stroke are under investigated. Moreover, there is still need to know exactly about the happening of stroke incidences and to gather findings of existing stroke risk factors in Bangladesh.

1.2. Symptoms of Stroke

The symptoms linked with stroke are numbness or weakness in the arm, leg or face, particularly on one side of the body, dizziness, loss of balance, lack of coordination, difficulty in walking, seeing, speaking or understanding speech, and sudden severe headache with no known cause. Even symptoms of stroke may disappear after few hours of stroke. However, it does not guarantee that stroke attack will not occur again. Thus, in case of above-mentioned symptoms, one should immediately go for medical assistance to minimize risk of brain damage and, to avoid progression of stroke to other areas of brain [12].

1.3. Consequences of Stroke

Patients with stroke have a wide range of impairments and a broad spectrum of symptom severity. Stroke can result in several neurological disorders and even can lead to death if remains undiagnosed and untreated promptly. Generally, stroke causes damage to local areas of the brain, however bleeding and increase in intracranial pressure in the brain can harm whole brain, which may lead to severe conditions [13]. Swallowing is another problem faced by patients after stroke, which may lead to choking if food enters the airways [14].

In case of severe attack of stroke, patients need to admit to the hospital, and how long they will stay there, it depends upon the severity of stroke and rehabilitation of the patients. Their long stay at hospital will cause shortage of space as well as of doctors for new patients. Sometimes, this care is provided at home by family members or a nursing home. In Saudi Arabia, it takes mean 45 days for rehabilitation of stroke patients [15]. In Bangladesh, mean stay of patients at hospital is 8 days [11]. Hospital stay may also be increased if patients suffer from stroke along with other diseases such as diabetes mellitus and hypertension [16]. Stroke patients may lose their job and instead of supporting themselves and other family members, they will depend upon them. This effect can significantly be seen in those societies where joint family system is present, for instance in Bangladesh where one person is supporting his wife and children. Moreover, stroke significantly impairs quality of life of suffering persons, as depression, stress, and anxiety are common in these people. Moreover, it is difficult for them to self-care, move, and perform usual activities [17]. In Bangladesh, post stroke psychological distress (depression, anxiety, and stress) was detectable among the stroke survivors. A higher proportion of females are hypertensive after stroke [18].

1.4. Diagnosis of Stroke

Stroke can be diagnosed in different ways, for instance, by

checking of blood pressure level, as stroke can increase it significantly, electrocardiograms to check heart function, blood tests to check clotting, cholesterol, and blood sugar levels. Brain scan with computed tomography and magnetic resonance imaging (MRI) scans is another method to diagnose the stroke. Swallow test is also performed for diagnosis, as many stroke patients have difficulty in swallowing [14]. Tests used later with disease progression to determine the extent of the damage are carotid Doppler tests, chest x-rays, and echocardiograms [19, 20].

1.5. Treatment and Rehabilitation

Brain cells need constant supply of oxygen for their health and better functioning [21]. Interruption of supply only for a short period can lead to death of a person. Thus, it is vital to provide prompt attention and assistance to the affected person as soon as possible to save his life. For the recovery of stroke patient, a stroke team will create an individual rehabilitation program designed according to patient's needs. Rehabilitation treatments include physiotherapy, occupational therapy, speech and language therapy, and vision correction [22].

2. Transcranial Direct Current Stimulation

Transcranial direct current stimulation (tDCS) is a non-invasive, painless, and safe [23] brain stimulation employed in the treatment of neuropsychiatric conditions. A constant current stimulator and surface electrodes soaked in normal saline are required for tDCS. The typical target for treatment is placement of anode over the right prefrontal cortex and cathode over the left prefrontal cortex. Anodal electrodes increase excitability and cathode electrode decreases excitability. The current stimulator is the source of steady flow of 0-4 mA direct current and it constantly monitors the resistance in the system. Saline soaked electrodes applied and secured onto the scalp over desired areas [(e.g. the left or right precentral gyrus region (corresponding to C3 or C4 of the international 10-20 EEG system)] make terminal relaying currents across the scalp and via the underlying brain tissue. When switched on, the current stimulator generates a transient tingling sensation under the electrode which disappears in 30 sec to 1 min thereby making it optimal for blinding subjects (in sham-controlled studies) by turning it off after the initial sensory experience. As demonstrated in a previous work, current densities 25 mA/cm² do not damage brain tissue, thus application of 1-2 mA/cm² current is absolutely safe [24]. Although, very low density of current is administered to underlying cortex in tDCS, however previous works have demonstrated it enough for neuronal excitability shifts [25]. Even in a previous study [26], change in measures of cerebral blood flow in brain regions exposed to tDCS has been demonstrated, thus indicating changes in regional tissue

excitability through this procedure. The application of tDCS is advantageous over other stimulation methods because of its important properties, which include its ease of use, large size of electrodes, its portability making stimulation possible when and where needed, a sham mode, which allows conductance of controlled experiments and randomized controlled clinical trials. However, its poor temporal resolution and anatomical localization are its limitations. Moreover, inter-individual variation in conductivity due to differences in hair, scalp, and bone composition can hinder the current transmission to the brain.

tDCS is being administered in the treatment of stroke in different parts of the world. However, few investigations/treatments do not cite it as effective. For instance, studies carried out with post-stroke aphasia and stroke patients did not demonstrate improvement of conditions of patients using tDCS [27-29]. On the other hand, many studies have signified employment of tDCS in the treatment of patients with different neurological disorders (Table 1). The difference in response to tDCS can be ascribed to severity of neurological disorders and differences in areas of the brain that were exposed to stimulation by tDCS [30]. Studies using tDCS promise its application for manipulation of emotions regulation and decision-making in humans [31]. However, further investigations particularly involving humans are required to understand and authenticate tDCS's actions on the brain, its mechanisms, and the associated behavioral and cognitive impacts.

Table 1. Using transcranial direct current stimulation for stroke rehabilitation

Author	Disease investigated	Improvement
Ahn YH, 2016 [45]	post-stroke dysphagia	yes
Ilić NV, 2016 [46]	stroke	yes
Darkow R, 2016 [47]	post-stroke aphasia	yes
Kirton A, 2016 [48]	perinatal stroke	yes
Valiengo LC, 2016 [49]	post-stroke depression	yes
Chang MC, 2015 [50]	subacute stroke	yes
Elsner B, 2015 [28]	post-stroke aphasia	no
Au-Yeung SS, 2014 [51]	paretic hand after stroke	yes
O'Shea J, 2014 [52]	chronic stroke	yes
Lefebvre S, 2014 [53]	chronic stroke	yes
Fusco A, 2013 [54]	subacute stroke	yes
Elsner B, 2013 [27]	stroke	no
Rossi C, 2013 [29]	acute stroke	no
Danzl MM, 2013 [55]	chronic stroke	yes
Ochi M, 2013 [56]	chronic stroke	yes

3. Human and Economic Burden of Stroke

Stroke is a costly disorder from individual to social

perspectives. It is one of the leading causes of death and disability in the world. In 2005, about 16 million first-ever strokes were registered in the world with 5.7 million deaths, which are expected to rise to 23 million first-ever strokes and 7.8 million deaths by 2030 [3]. In the United States, findings indicate 5,800,000 prevalent stroke cases. More than 780,000 first-ever or recurrent strokes are expected to occur each year [32]. In 15-country Europe, figures demonstrate 2,700,000 prevalent cases and 536,000 incident cases each year. In 48-European countries, number of deaths due to stroke is estimated at 1,239,000 per year [33]. Stroke is by no way is considered a problem of western or developed countries. About 85% of all stroke deaths are reported in low- and middle-income countries [34]. In South Asian countries including Bangladesh, 40% deaths are estimated due to stroke [35]. In Bangladesh, stroke is the third leading cause of death with 0.3% prevalence [18].

In terms of economic burden, stroke has a huge effect with about 5% of the medical costs of industrialised countries are given to disease. The long-term disorders left behind after stroke attack are hugely detrimental with respect to both hospital and other care sector costs. Previously, stroke prevalence was relatively high in the developed countries. Recently, the stroke incidence in low- and middle-income countries has exceeded that than that of high-income countries by about 20% [36]. Rapid urbanization, low physical activities, and increasing habits of smoking can further increase the risk of stroke in these countries [37].

The concerns regarding economic burden of stroke include initial hospitalization, medications, continuing medical care, productivity loss, and work limitations. Over a lifetime, the cost of an ischemic stroke in the United States is over \$140,000 including hospital admissions, rehabilitation, and long-term care and treatment for lasting disorders [38] and, direct annual stroke-related medical costs are expected to increase to \$184.13 billion by 2030 [39].

In Canada, about 62,000 strokes cases are reported per year. More than 400,000 stroke survivors are living with long-term stroke disability. The costs to the Canadian economy are \$2.7 billion a year with an average of \$27,500 being spent per stroke on acute care. Stroke sufferers spend in total 3,000,000 days in hospital per year, which is a severe drain on the economy [5].

In the United Kingdom, about 152,145 stroke cases are reported every year. Up to 13 per 100,000 children suffer with stroke. It is thought there are around 400 childhood strokes a year in the United Kingdom [40]. It is estimated that health and social care costs are approximately £4.38 billion and informal care expenses are £2.42 billion. Productivity losses (i.e., income lost) due to care, disability and death are approximately £1.33 billion, and benefit payments are approximately £841million per year, respectively. Total cost from a societal perspective is estimated to be around £9 billion a year [41].

Bangladesh is one of the poorest, least developed, low-income, and densely populated countries in the world. In

this country, prevalence of stroke is high. Limited acute stroke care i.e., thrombolysis and stroke units are available to stroke patients. Public awareness about stroke, physician training, and research facilities are inadequate. Moreover, country lacks prevention strategies at the Government level [42]. Total healthcare expenditure stands at only 3.7% of total GDP of the economy, which is less compared to developed countries. There are about 2213 hospitals with only 60 registered and trained neurologists. Neurology training programs are only offered in few hospitals [43]. This situation is dismal for Bangladeshi stroke patients as the mortality rate due to stroke is increasing. Despite major advances in the scientific understanding, technology, and management of stroke globally, Bangladesh is still suffering stroke and its aftereffects. The high number of disability-adjusted life-years lost due to stroke (485 per 10,000 people) show that stroke has severe impacts on the economy of Bangladesh. Two non-governmental organizations, BRAC and the center for the rehabilitation of the paralyzed, have taken initiative in primary stroke prevention strategies. However, the Bangladeshi Government needs to emphasize healthcare development to cope with the increasing population density and to reduce stroke risk factors and its occurrence [18].

4. Conclusions

Acute and post-discharge treatments are indispensable to avoid the natural trend of rise of human, economic, and social burden of stroke. The rising burden of stroke particularly in low- and middle-income countries leads to propose a worldwide goal for stroke: reduction of about 2% stroke cost each year is achievable following better case management and treatment. Experience of high-income countries demonstrates that about 4% annual average declines in stroke mortality is achievable [3]. Introduction of latest technologies such as tDCS in stroke management can play a significant role against stroke and its impacts, as a prognostic technique as well as a rehabilitative method [44]. In summary, the high mortality and permanent disability due to stroke coupled with costly treatments makes it crucial that better stroke management and treatment is freely accessible and implemented. tDCS can play a vital role in these improvements. Introduction of tDCS in the treatment/management of stroke in Bangladesh will not only be helpful for stroke patients but also reduce burden of government for spending a lot of money on stroke management.

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