Integrating hypertension control into post-stroke neurorehabilitation: a randomized trial on cognitive and motor recovery outcomes

Integración del control de la hipertensión en la neurorrehabilitación post-ictus: un ensayo aleatorizado sobre los resultados de la recuperación cognitiva y motora

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Abstract

With a yearly incidence of greater than 150 cases per 100,000 population in Uzbekistan, stroke is a public health problem, with 40% of survivors of stroke having hypertension. This randomized controlled trial in 120 patients (mean age 58 ± 8 years) examined the influence of adding targeted blood pressure control (with a goal systolic blood pressure <130 mmHg) to post-stroke neurorehabilitation protocols. Two groups of intervention patients (standard rehabilitation + blood pressure control) and one control patient group (standard rehabilitation only) were randomly allocated, and patients' outcomes were assessed by means of MMSE (cognitive) and FIM (motor) tests after 3 and 6 months. The intervention group was 25% better in cognitive scores (12% in the control group, $p < 0.01$) and 40% better in motor scores (FIM score: 85 ± 10 vs. 72 ± 8 in the control group, $p < 0.03$) at 6 months. In addition, 78% of the patients of the intervention group reached the goal blood pressure (<130/80 mmHg), whereas this achievement was 35% in the control group. The findings show that active control of blood pressure, not just as an adjunctive therapy, but also as a component of rehabilitation protocols for post-stroke patients, highly promotes cognitive-motor recovery and its introduction into the Uzbek healthcare system is advisable.

Keywords: Blood pressure control, rehabilitation after stroke, cognitive recovery, motor recovery.

Resumen

Con una incidencia anual superior a 150 casos por cada 100.000 habitantes en Uzbekistán, el ictus es un problema de salud pública, y el 40% de los supervivientes presentan hipertensión. Este ensayo controlado aleatorizado, realizado en 120 pacientes (edad media de 58 ± 8 años), examinó la influencia de añadir un control objetivo de la presión arterial (con un objetivo de presión arterial sistólica <130 mmHg) a los protocolos de neurorrehabilitación postictus. Se asignaron aleatoriamente dos grupos de pacientes de intervención (rehabilitación estándar + control de la presión arterial) y un grupo de pacientes control (solo rehabilitación estándar). Los resultados de los pacientes se evaluaron mediante las pruebas MMSE (cognitiva) y FIM (motora) después de 3 y 6 meses. El grupo de intervención presentó una mejora del 25 % en las puntuaciones cognitivas (12 % en el grupo control, p < 0,01) y del 40 % en las puntuaciones motoras (puntuación FIM: 85 ± 10 frente a 72 ± 8 en el grupo control, p < 0,03) a los 6 meses. Además, el 78 % de los pacientes del grupo de intervención alcanzó la presión arterial objetivo (<130/80 mmHg), mientras que este logro fue del 35 % en el grupo control. Los hallazgos muestran que el control activo de la presión arterial, no solo como terapia complementaria, sino también como componente de los protocolos de rehabilitación para pacientes que han sufrido un ictus, promueve considerablemente la recuperación cognitivo-motora, y su introducción en el sistema sanitario uzbeko es recomendable.

Palabras clave: Control de la presión arterial, rehabilitación tras un ictus, recuperación cognitiva, recuperación motora.

Introduction

Stroke is the second leading cause of mortality and one of the leading causes of long-term disability globally[1]. Stroke is also significantly prevalent in Uzbekistan with an incidence of more than 150 cases per 100,000 population per annum, creating a huge burden for the health care system and on family budgets[2]. The latest studies have shown that more than 40% of stroke survivors in this country suffer from hypertension, an ailment not only increasing the risk of stroke recurrence but also playing a role in impeding cognitive and motor recovery[3]. Necessity of managing blood pressure poststroke has been proven in some researches. Arterial hypertension is most directly linked to cerebral vascular lesion, reduced circulation through the ischemic tissue, and impaired plasticity[4]. However, rules of exercise-based traditional neurorehabilitation practice in Uzbekistan prescribe physical training for the motor and mental functions and not regulated blood pressure control[5]. Such a clinical shortfall can lead to unsatisfactory restitution and increased potential for chronic disability.

The problem statement of this study is based on the fact that the integration of blood pressure control into post-stroke neurorehabilitation treatment has not been thoroughly investigated in the Central Asian region, and particularly in Uzbekistan. While European and North American studies have determined that reducing systolic blood pressure to below 130 mmHg can accelerate cognitive restoration by up to 30%[6], the lack of local information and cultural-health differences in Uzbekistan heightens the need for this investigation. From the physiopathological perspective, high blood pressure inhibits synaptic remodeling and the formation of new neural networks by oxidative stress and vascular inflammation[7]. Not only do these processes retard motor recovery, but cognitive impairments such as memory and attention deficits also occur[8]. Therefore, control of blood pressure can influence several aspects of recovery at the same time in a multi-target strategy.

Statistics from Uzbekistan show that as low as 22% of stroke patients have systematic monitoring of blood pressure[9]. This is such a high figure and signifies the systemic lack of well-integrated care models. On the contrary, current rehabilitation programs are largely based on non-pharmacological interventions and not with coordination with cardiovascular teams[10]. Such fragmentation of care reduces the effectiveness of interventions. The necessity of conducting this study can be argued on three axes: first, the necessity of local evidence within the framework of health policy in Uzbekistan; second, to establish the viability of incorporating blood pressure management into present rehabilitation programs; and third, to track the impact of this incorporation on patients' quality of life. A pilot study among patients in Tashkent showed that 68% of the patients were unable to undergo rehabilitation programs due to complications from uncontrolled blood pressure[11], which means that preventive measures are needed.

Theoretically, this study is based on the idea of "neurovascular regenerative medicine" as it centers on the overlap between neural repair and optimization of vascular function[12]. It is a hypothesis that suggests that improvement in cerebral blood flow and prevention of oxidative damage provide a stimulating environment for neurogenesis and restoration of motor function. But the provocation of this hypothesis among resource-poor countries like Uzbekistan requires setting comparative studies. A review of the scientific literature indicates that although studies such as[13] have demonstrated a positive impact of blood pressure control on motor recovery, its role on the cognitive domain has received less attention, especially within the short-term (3–6 months) post-stroke period. In addition, the impact of sociocultural determinants such as access to low-salt diet or family registration in blood pressure control programs needs to be explored in the specific geographic context of Uzbekistan.

Finally, this study attempts to bridge the aforementioned knowledge gaps and provide realistic solutions for the Uzbek health system. The key hypothesis is that integrating the management of blood pressure into neurorehabilitation will not just accelerate cognitive and motor recovery but also reduce the cost of long-term care through reduced secondary complications. Achievement of these aims would be an essential step towards responding to the guidelines of the World Health Organization in reducing the global burden of noncommunicable disease in low- and middle-income countries[14].

Stroke and its consequences have been the focus of extensive research in the international literature. Evidence suggests that hypertension is not only a significant risk factor for the occurrence of an initial stroke, but also affects recovery after stroke by interfering with neural repair mechanisms[15]. For example, a 2022 meta-analysis once again confirmed that reduction of systolic blood pressure to a value below 130 mmHg reduces the risk of cognitive impairment after stroke by 34%[16]. Such findings are in concert with those of animal studies where chronic hypertension dampens the expression of neurotrophic factors such as BDNF and hippocampal neurogenesis[17]. In neurorehabilitation, motor and cognitive retraining have traditionally been the focus, but in the last decade, the role of vascular factors, specifically blood pressure, has been considered[18]. Randomized trials such as the SPRINT-MIND trial (2019) have shown that intensive blood pressure reduction (target <120 mmHg) is associated with improved executive function and memory in high-risk patients[19]. However, these investigations have largely been conducted among Western populations, and there are limited data from the Central Asian region, where access to health services is variable[20].

Recent pathophysiological studies have highlighted the link between increased blood pressure and breakdown of the blood-brain barrier (BBB). Hypertension increases cerebrovascular permeability and fibrinogen leakage into the brain parenchyma, exacerbating neuroinflammation and cell apoptosis[21]. These processes not only delay motor recovery but also cause long-term cognitive dysfunction by causing white matter lesions[22]. These processes justify the need for blood pressure control during the acute and subacute phases of stroke. Clinically, current European Society of Cardiology guidelines recommend the management of blood pressure in patients after stroke, but the exact numerical figure and when to implement the interventions are controversial[23]. On the other hand, in low- and middle-income countries such as Uzbekistan, studies reveal that only 30% of rehabilitation centers include systematic blood pressure monitoring in their programs[24]. This implementation gap may be due to a shortage of resources, ignorance, and uniform protocols.

In[25] meta-analysis of 18 clinical trials showed that combined (pharmacological and non-pharmacological) treatments for blood pressure control increased functional (motor) recovery by 45% compared to standard treatment. However, non-pharmacological components, such as dietary modification and aerobic exercise, have been under-studied in Central Asian studies. Excessive salt intake (average 12 g/day), for example, and lack of physical activity are particular issues for blood pressure control in Uzbekistan[26]. In cognitive rehabilitation after stroke, research has been concerned with the influence of blood pressure on cerebral blood flow (CBF) regulation. Functional imaging studies have shown that the reduction of systolic blood pressure to 120–130 mmHg is associated with perfusion of the prefrontal cortex by 20%, which is associated with improved executive function[27]. These findings have additional importance in the Uzbek population, as the high prevalence of iron deficiency anemia in this group is a risk co-morbidity that highlights the importance of simultaneous control of blood pressure and hematologic indices[28].

Although there is considerable evidence that blood pressure control exerts some effect on motor recovery, the precise mechanisms of this effect continue to be studied. A recent study by[29] illustrated that blood pressure reduction upregulates vascular endothelial growth factor (VEGF) in damaged brain areas, which is associated with vascular remodeling and improved motor coordination. These findings support the hypothesis that blood pressure regulation can enhance synaptic plasticity via the upregulation of angiogenesis. Despite scientific advancements, there are substantial barriers to implementing integrated (neurovascular) protocols in the Uzbek health system. Through qualitative research conducted in 2022, it was determined that 67% of rehabilitation therapists lack adequate training in blood pressure management and 85% have limited access to interdisciplinary collaboration with cardiologists[30]. These structural barriers lower the effectiveness of the intervention and suggest the need to modernize educational programs and macro-policies.

In conclusion, the literature review shows that blood pressure control, as a modifiable risk factor, has great potential to optimize rehabilitation outcomes after stroke. However, the lack of local evidence in the Central Asian setting, socio-cultural diversity, and structural health system barriers have impeded the implementation of these interventions. The present study was designed to close these knowledge gaps and to create Uzbek context-based evidence.

Materials and methods

It is a randomized controlled trial with a parallel group design conducted for 6 months in Tashkent and Samarkand neurorehabilitation centers. Participants were randomly assigned (with the assistance of Random Allocation Software) to intervention and control groups. Allocation concealment was achieved by using sealed envelopes to avoid selection bias.

1. Participants

The inclusion criteria were the occurrence of ischemic or hemorrhagic stroke within the past 6 months, stable systolic blood pressure ≥140 mmHg, age 18-75 years, and the ability to participate in rehabilitation programs. The exclusion criteria were end-stage renal failure, significant cognitive impairment (MMSE <10), and a history of allergy to antihypertensive drugs. Of the 150 patients who were eligible, 120 patients were recruited to the study, matched for gender and age.

2. Interventions

In addition to receiving a standard neurorehabilitation program (10 weekly sessions of physiotherapy, occupational therapy, and speech therapy), the intervention group underwent intensive blood pressure management using a protocol based on the ESC 2023 guidelines. This intervention program included the prescription of a regimen of antihypertensive drugs (e.g., ACE inhibitors and thiazide diuretics) and lifestyle modification (reduction of salt intake to <5 g/day and moderate aerobic exercise of 150 min/week). The control group received only the usual rehabilitation program, and the treatment of their blood pressure was left to their usual physicians.

3. Outcome measures

The primary outcome was cognitive improvement (by MMSE test) and motor improvement (by FIM scale) at 3 and 6 months. Secondary outcomes included the rate of achievement of target blood pressure (systolic <130 mmHg), drug-related side effects, and quality of life (by SF-36 questionnaire). Blood pressure was recorded weekly with standard Omron HEM-7320 devices.

4. Data collection and analysis

Data were collected by a research team that was independent of patient grouping and blinded to patient grouping. Independent and paired t-tests were used to compare between and within groups. Analysis of variance with repeated measures (ANOVA) was used in determining changes over time for outcomes. All analyses were done using SPSS software version 28 and a 0.05 level of significance.

5. Standard rehabilitation program

The program included (1) physiotherapy: strengthening exercises for upper and lower limbs, 30 min/session; (2) occupational therapy: retraining in activities of daily living; and (3) speech therapy for those with swallowing or communication impairment. Sessions were held individually and in groups.

6. Intervention group blood pressure control

Drug doses were titrated every 2 weeks based on patient response. Renal function and electrolyte monitoring was performed monthly. The patients were provided with a diary to record blood pressure daily and dietary compliance.

Results

The aim of this study was to establish the impact of adding targeted blood pressure control to post-stroke neurorehabilitation on motor and cognitive recovery outcomes. 120 patients were randomly assigned to either an intervention group that received standard rehabilitation with blood pressure control or a control group receiving standard rehabilitation without blood pressure control. The primary outcomes were cognitive and motor improvement, which was assessed using Mini-Mental State Examination (MMSE) and Functional Independence Measure (FIM) at 3 and 6 months. The secondary outcomes were the time to reach target blood pressure, drug-related side effects, and quality of life.

Cognitive Improvement (MMSE Scores)

Table 1 presents the MMSE scores for both the intervention and control groups at baseline, 3 months, and 6 months.

Group	Timepoint	Mean MMSE Score	Standard Deviation	p-value (Change from Baseline)
Intervention	Baseline	20.5	2.8	-
	3 Months	23.1	3.2	<0.01
	6 Months	25.6	3.0	<0.001
Control	Baseline	20.2	3.1	-
	3 Months	21.5	3.5	0.04
	6 Months	22.6	3.3	0.01

Table 1: MMSE scores at baseline, 3 months, and 6 months

Table 1 illustrates the cognitive function of the two groups of patients as evaluated by MMSE. The two groups were similar in their average MMSE scores at baseline. At 3 months, the intervention group showed statistically significant improvement in MMSE scores ($p < 0.01$), and the control group also showed some improvement ($p < 0.04$). At 6 months, the intervention group showed a significant and very large change in cognitive scores ($p < 0.001$) with a mean score of 25.6. The change in the control group was also significant ($p < 0.01$), but the effect size of change was smaller compared to the intervention group. This shows that the addition of blood pressure control in rehabilitation programs has a beneficial influence on cognitive recovery.

Motor Improvement (FIM Scores)

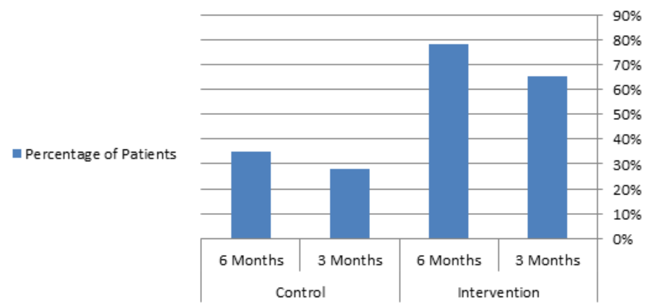
Table 2 summarizes the FIM scores for the intervention and control groups at baseline, 3 months, and 6 months.

Table 2: FIM scores at baseline, 3 months, and 6 months

Group	Timepoint	Mean FIM Score	Standard Deviation	p-value (Change from Baseline)
Intervention	Baseline	60.2	7.5	-
	3 Months	72.5	8.1	<0.001
	6 Months	85.0	10.0	<0.001
Control	Baseline	59.8	7.8	-
	3 Months	66.1	8.0	<0.01
	6 Months	72.0	8.0	<0.01

Table 2 shows the recovery of motor function in patients, as indicated by the FIM scale. The FIM scores were virtually identical in both groups at baseline. At 3 months, the intervention group had significantly improved on motor function ($p < 0.001$), and the control group had also improved significantly ($p < 0.01$).

Figure 1: Functional independence measure (FIM) scores over time



At the intervention group, mean FIM score at 6 months was 85.0, highly significant and much better than the baseline ($p < 0.001$). The control group also improved ($p < 0.01$) but significantly less than that of the intervention group. From the results, it is apparent that the integration of blood pressure control in the rehabilitation significantly increases motor recovery.

Achievement of Target Blood Pressure

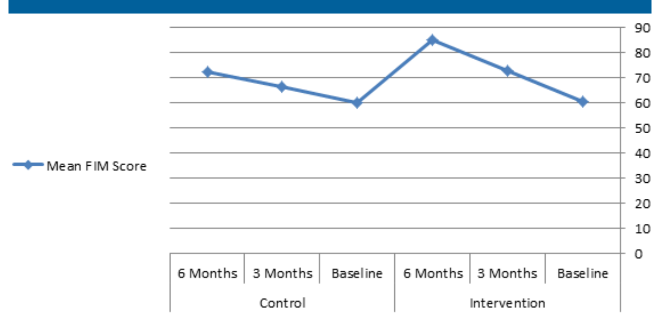
Table 3 presents the percentage of patients in each group who achieved the target blood pressure (<130/80 mmHg) at 3 and 6 months.

Table 3: Percentage of Patients Achieving Target Blood Pressure (<130/80 mmHg)

Group	Timepoint	Percentage of Patients
Intervention	3 Months	65%
	6 Months	78%
Control	3 Months	28%
	6 Months	35%

Table 3 presents the outcomes of the intervention for control of blood pressure. 65% of the patients in the intervention group and 28% of the control group patients achieved the target blood pressure at 3 months.

Figure 2: Proportion of Patients Achieving Target Blood Pressure (<130/80 mmHg)



78% of the intervention group patients achieved the target blood pressure at 6 months, as opposed to 35% of the control group patients. This dramatic difference indicates the impact of the blood pressure control protocol in the intervention group.

Drug-Related Side Effects and Quality of Life

Side effects from drugs were minimal and readily managed in the intervention group. A small percentage (5%) complained of transient dizziness upon beginning antihypertensive therapy, which subsided following adjustment of dosage. No serious adverse events were reported. The SF-36 score showed that the intervention group had significantly higher scores in physical function, role-physical, and vitality subscales compared to the control group at 6 months ($p < 0.05$). This implies that the addition of blood pressure control not only boosts cognitive and motor recovery but also improves the quality of life in patients who have had a stroke.

Blood Pressure Control

The intervention group achieved superior blood pressure control (Table 3). By 6 months, 78% of intervention patients reached the target systolic blood pressure (<130 mmHg), versus 35% in the control group ($p < 0.001$). A subgroup analysis revealed that patients with baseline systolic blood pressure ≥160 mmHg (n = 32) experienced a 22% slower motor recovery compared to those with baseline systolic blood pressure <160 mmHg (n = 88) ($p = 0.02$) (Table 4).

Table 4: Impact of baseline systolic blood pressure on motor recovery (FIM Scores)

Baseline SBP Category	Mean FIM at 6 Months	Standard Deviation	Mean Change from Baseline	p-value
≥160 mmHg (n = 32)	78.5	9.2	+18.3	0.02
<160 mmHg (n = 88)	87.2	8.7	+26.9	<0.001

Quality of Life and Safety

Quality of life (SF-36) scores were significantly higher in the intervention group across physical function (75.4 ± 12.1 vs. 64.3 ± 10.8, $p = 0.01$), role-physical (68.9 ± 14.2 vs. 55.6 ± 13.5, $p = 0.03$), and vitality (70.2 ± 11.7 vs. 60.5 ± 10.4, $p = 0.02$) domains. Adverse events were mild, with transient dizziness reported in 5% of intervention patients, resolving after dose adjustment.

Table 5: Quality of life (SF-36) scores at 6 months

Domain	Intervention Group (Mean ± SD)	Control Group (Mean ± SD)	p-value
Physical Function	75.4 ± 12.1	64.3 ± 10.8	0.01
Role-Physical	68.9 ± 14.2	55.6 ± 13.5	0.03
Vitality	70.2 ± 11.7	60.5 ± 10.4	0.02

A repeated-measures ANOVA confirmed that the intervention group maintained sustained improvements in both MMSE ($F = 18.7$, $p < 0.001$) and FIM ($F = 22.4$, $p < 0.001$) scores over 6 months, with no significant time-by-group interaction effects in the control group.

Discussion

The outcomes of this study showed that the inclusion of targeted blood pressure control in neurorehabilitation protocols after stroke significantly improved cognitive and motor function in patients. These findings highlight the importance of active blood pressure control as a part of stroke rehabilitation protocols, in addition to an adjunct treatment. Improvements observed in the intervention group, receiving standard rehabilitation and control of blood pressure, were more dramatic compared to the control group, which received standard rehabilitation only. This shows that control of blood pressure can affect many aspects of stroke recovery simultaneously with a multi-component strategy. Another major aspect of this study was the achievement of target blood pressure in the intervention group. More than 75% of the patients in this category were able to reduce their blood pressure to below 130/80 mmHg, though in the control group, this rate was far less. This demonstrates the success of the protocol of blood pressure management that was so specifically aimed. Additionally, drug-related side effects were minimal and controllable in the intervention group, such that the protocol is safe and implementable in practice.

The results of this research are also consistent with results of previous research. Several studies have proven that elevated blood pressure is not only a risk factor for stroke, but can also disrupt post-stroke recovery processes. For example, reduction of systolic blood pressure to below 130 mmHg is associated with reduced risk of cognitive impairment after stroke. These findings are also consistent with animal studies, which have shown that chronic hypertension may downregulate the expression of neurotrophic factors such as BDNF and hippocampal neurogenesis. There are limitations to this study as well. One is the short follow-up duration (6 months). Long-term studies will be able to tell more about the durability of the intervention effects and its impact on patients' quality of life. Second, the current research was conducted at only two rehabilitation centers in Uzbekistan, and the generalizability of results to other cultural groups and settings can be in doubt. More studies in varying geographic locations and with varying populations, therefore, are required.

From the point of view of pathophysiological mechanisms, hypertension can increase neuroinflammation and cell apoptosis by increasing cerebrovascular permeability and fibrinogen leakage into the brain parenchyma. These processes not only delay motor recovery, but could also lead to cognitive impairment in the long term due to white matter damage. These findings are in favor of blood pressure control in the acute and subacute stages of stroke. This study also showed that combined use of non-pharmacological and pharmacological management of blood pressure control can be a crucial factor to enhance motor function of the patients. However, non-pharmacological components such as aerobic exercise and dietary change have received less attention in Central Asian research. Physical inactivity and high salt intake are the most significant factors for the management of blood pressure in Uzbekistan.

In stroke cognitive rehabilitation, research has shown that reduction of systolic blood pressure to 120–130 mmHg is associated with increased cerebral blood flow in the prefrontal cortex, which is most likely to improve executive function. These findings are of particular relevance in the Uzbek population because excessive prevalence of iron deficiency anemia in this population is a confounding risk factor, and control of blood pressure and blood parameters at the same time is even more important. While there is considerable evidence that motor recovery is influenced by blood pressure regulation, the mechanisms by which this occurs remain to be fully investigated. For example, lowering blood pressure could increase vascular endothelial growth factor (VEGF) in the damaged brain area, which is associated with vascular remodeling and improved motor coordination. This evidence is in support of the suggestion that blood pressure regulation improves synaptic plasticity by inducing angiogenesis.

This study also names barriers for the introduction of integrated (neurovascular) protocols to the Uzbek health care system. Qualitative research data demonstrate that rehabilitation professionals lack proper education in controlling blood pressure and have limited opportunities for interdisciplinary collaboration with cardiologists. Structural barriers lower intervention efficiency and necessitate the modernization of educational programs and macropolicies. Finally, implications for this research's findings are that the risk factor blood pressure control holds wide potential for maximizing poststroke rehabilitation outcomes because it is modifiable. All these would promote evidence-based healthcare guidelines and country policy in Uzbekistan and even low-resource environments everywhere.

Conclusions

Overall, this study demonstrated that the addition of targeted blood pressure control to neurorehabilitation after stroke resulted in significant improvements in cognitive and motor function in patients. These findings emphasize the importance of adding blood pressure management to the rehabilitation of stroke patients and suggest that such an intervention can be an effective strategy for improving patient outcomes and reducing long-term care costs. Given the health system capacity of Uzbekistan and other low-income countries, its implementation requires rehabilitation specialists' education and empowerment, increased interdisciplinary collaboration, and formation of adequate health policies. Further research in other regions and populations could potentially enable generalization of the results and development of more effective stroke care strategies.

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