



Evaluation of Efficacy of Unani Regimen in the Management of post Stroke Spasticity, an open observational Study

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Abstract

Physical rehabilitation and oral antispastic medications are essential in the management of post stroke spasticity, but former alone is inadequate and later causes frequent unwanted side effects. Unani physicians have been treating the disease since ancient times on the principle of Tanqiya (elimination of morbid matter) and Ta'deel (normalization of diseased organ). The limitations of contemporary treatment led to evaluate the efficacy of this therapy on scientific parameters. The study was conducted as open, observational clinical trial enrolling 30 eligible patients. Tanqiya was achieved by using Munzije Balgham and Mus'hile Balgham (in decoction form). Munzije Balgham was given for 13 days, once in the morning, along with 40 grams of Gulqande Asali. Mus'hile Balgham was given mixed with Munzije Balgham on 13th day of the study. Massage of the spastic limbs with Raughane Malkangni was started from 14th day till 28th day of the study for the purpose of Ta'deel. Patients were assessed for spasticity by MAS at baseline, 14th day and 28th day of treatment. Significant difference was observed in antigravity muscles between baseline and 28th day scores ($p < 0.001$) using Friedman test with Dunn's multiple comparison test. Significant difference was observed between baseline and 14th day scores ($p < 0.01$) in elbow flexors. No significant adverse change appeared in safety parameters. The test regimen used on the principle of Tanqiya and Ta'deel was found effective in the treatment of spasticity, predominantly in antigravity muscles, probably by enhancing neuroplasticity and by neuroprotective and antispasmodic activities of used drugs.

Keywords: Post stroke spasticity, Tanqiya, Ta'deel, Tashannuje Imtilae, Unani medicine.

Introduction

Stroke-related disability has emerged as a health problem that causes major impairment and significant socioeconomic consequences for patients as well as society. More than two-third of stroke survivors develop post stroke sequelae, including impaired motor function and post stroke spasticity. These impairments have a significant impact on a stroke survivor's daily life, impeding basic tasks such as eating and self-care. Additionally, such disabilities place a significant burden on caregivers of stroke survivors¹. Spasticity is a motor disorder characterized by a velocity dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex, as one component of the upper motor neuron syndrome². It may cause pain and deformity, and in the longer term contractures may develop. In this condition, patients feel it difficult to clench their hand, flex their fist, move their arm away from their body, or walk properly. Despite the fact that stroke is the leading cause of long term disability, it is a condition for which there is no universally accepted, evidence based rehabilitation approach. The general objective of rehabilitation is to enable individual patient to regain the highest possible degree of physical and psychological performance.

The description of *Tashnnuje Imtilae* in classical Unani literature draws analogy with post stroke spasticity³. According to Unani concept of pathogenesis, derangement of the proportion of quantity and/or quality of *Akhlat* (Humors which includes *Dam*, *Balgham*, *Safra* and *Sauda*) results in a disease. If only *Kaifiyat* (quality) is altered, *Ta'deel* (normalization of temperament of affected organ) is required and in case of excess of *Akhlat*, *Tanqiya* (elimination of causative matter) is inevitable along with *Ta'deel*^{4,5}. *Tanqiya* of morbid *Akhlat* requires modification in consistency by *Munzij* drugs and then a systemic purgation by and *Mus'hil* drugs. *Munzij* drugs suitably modify the consistency of morbid *Akhlat* to make them evacuable from the tissues, vessels and interstitial spaces. They act by their properties of *Tahleel* (dissolution), *Taqtee* (disintegration), and *Talteef* (attenuation). *Mus'hil* (purgative) drugs have propensity to expel the morbid *Akhlat* from the vessels, neighboring structures and from whole body through intestine. *Ta'deel* relates to restoration, normalization and potentiation of normal physiological functions after purging out of morbid *Akhlat* from the affected organ by using drugs or employing various regimens such as massage, exercise, irrigation etc^{5,6,7}. In *Tashnnuje Imtilae*, physical performance and independence are achieved by treating the patients on this time tested Unani principle. Hence, a clinical trial was

conducted to find out the efficacy of *Tanqiya* and *Ta'deel* in the management of *TashnnuJe Imtilaee* on scientific parameters. In the present study, *Tanqiya* was achieved by *Munzije Balgham* and *Mus'hile Balgham*, while *Ta'deel* was accomplished by massage with *Raughane Malkangni*.

Material and Methods

This open, observational clinical study was started after ethical clearance by Institutional Ethical Committee and conducted according to the Declaration of Helsinki and the GCP guidelines. 30 patients, having post stroke upper and/or lower limb spasticity of either sex aged between 20–75 years having history of stroke at least of 1 month, were included from OPD and IPD of National Institute of Unani Medicine (NIUM), Bangalore, India. All the drugs were purchased from city market, Bangalore. Formulations were prepared in NIUM pharmacy under the supervision of chief pharmacist as per standard protocol. *Munzije Balgham* containing *Aslussoos* (root of *Glycyrrhiza glabra*), *Badyan* (seeds of *Foeniculum vulgare*), *Beekhe Badyan* (root of *Foeniculum vulgare*), *Ustukhudoos* (flowers of *Lavandula stoechas*), *Anisoon* (seed of *Pimpinella anisum*), *Tukhme Karafs* (seeds of *Apium graveolens*), *Ood Saleeb* (root of *Paeonia emodi*), *Beekhe Izkhair* (root of *Andropogon jwarancusa*) and *Barge Gaozaban* (leaves of *Borago officinalis*), 4 gm each, was given for 13 days consecutively once in the morning in decoction form before breakfast mixed with 40 gm of *Gulqande Asali*⁷. *Mus'hile Balgham* containing *Ustukhudoos* (flowers of *Lavandula stoechas*) 5 gm, *Barge Sana* (leaves of *Cassia angustifolia*) 10 gm, *Turbud* (root of *Operculia turpethom*) 3 gm, *Maghze Fuloose Khayar Shambar* (fruit pulp of *Cassia fistula*) 70 gm, and *Raughane Zard* (clarified butter) 5 gm was given mixed

with *Munzije Balgham* in decoction form on 13th day of the study⁷. After *Tanqiya*, massage of the spastic limbs, with *Raughane Malkangni* was started from 14th day onwards up to the completion i.e. 28th day of the study. Tone in shoulder adductors, elbow flexors, elbow extensors of upper limb and hip adductors, knee flexors, knee extensors of lower limb was assessed by a reliable and valid scale 'Modified Ashworth Scale (MAS)', especially designed for evaluation of tone of the skeletal muscles⁸, at baseline, 14th day and 28th day of treatment. Safety parameters were assessed before and after the study. Baseline, 14th day and post treatment values of MAS were subjected to statistical analyses using Friedman test with Dunn's multiple comparison test. Safety parameters were assessed applying paired 't' test using Graph pad Instat.

Results and Discussion

Out of 37 patients enrolled 30 completed the study (figure 1). Relevant demographic data was given in table 1. In shoulder adductors, elbow flexors and knee extensors, significant statistical difference was observed between baseline and 28th day scores (p<0.001) of MAS. Similarly, significant statistical difference was observed between baseline and 14th day scores (p<0.01) in elbow flexors (table 2). Though statistical difference was not significant in each muscle group at every follow up, however reduction in tone of spastic muscles was observed clinically. No significant change appeared in any safety parameter except hemoglobin (mean value increased from 12.46 to 12.96 gm %), serum uric acid (mean value decreased from 5.82 to 5.06 mg/dl) and total protein (mean value decreased from 7.25 to 6.91). However, these changes were within normal range.

Table-1
Demographics and patient characteristics

Particulars	Values in Mean ± SD or number (N=30)
Age (years)	53.4 ± 11.26
Gender (female/male)	3/27 (1:9)
Religion (Muslim/Hindu/Christian)	14/14/2
Marital status	All married
Side involved (right/left)	10/20
Duration of stroke in months	16.57 ± 18.21

Table-2
Effect of intervention on MAS for spasticity of Upper and Lower limbs (N=30)

Muscle group examined	Baseline Mean ± SD	14 th day Mean ± SD	28 th day Mean ± SD	Mean difference ± SD After Treatment
Shoulder adductors	1.2167± 1.0961	0.7333± 0.9803	0.3667± 0.6557*	0.85 ± 0.4404
Elbow Flexors	2.2333± 0.8066	1.7± 0.7834 #	1.5667± 0.9444*	0.6666 ± 0.1378
Elbow Extensors	0.6667± 0.813	0.4333± 0.8483	0.2± 0.535	0.4667 ± 0.278
Hip Adductors	0.45± 0.674	0.1667± 0.442	0.0667± 0.2537	0.3833 ± 0.4203
Knee Flexors	0.4± 0.7589	0.1333± 0.4138	0.0667± 0.2537	0.3333 ± 0.5052
Knee Extensors	1.1833± 0.725	0.7833± 0.52	0.4333± 0.6121*	0.75 ± 0.1129

*Baseline and 28th day comparisons were statistically significant (p<0.001). # Baseline and 14th day comparisons were statistically significant (p<0.01).

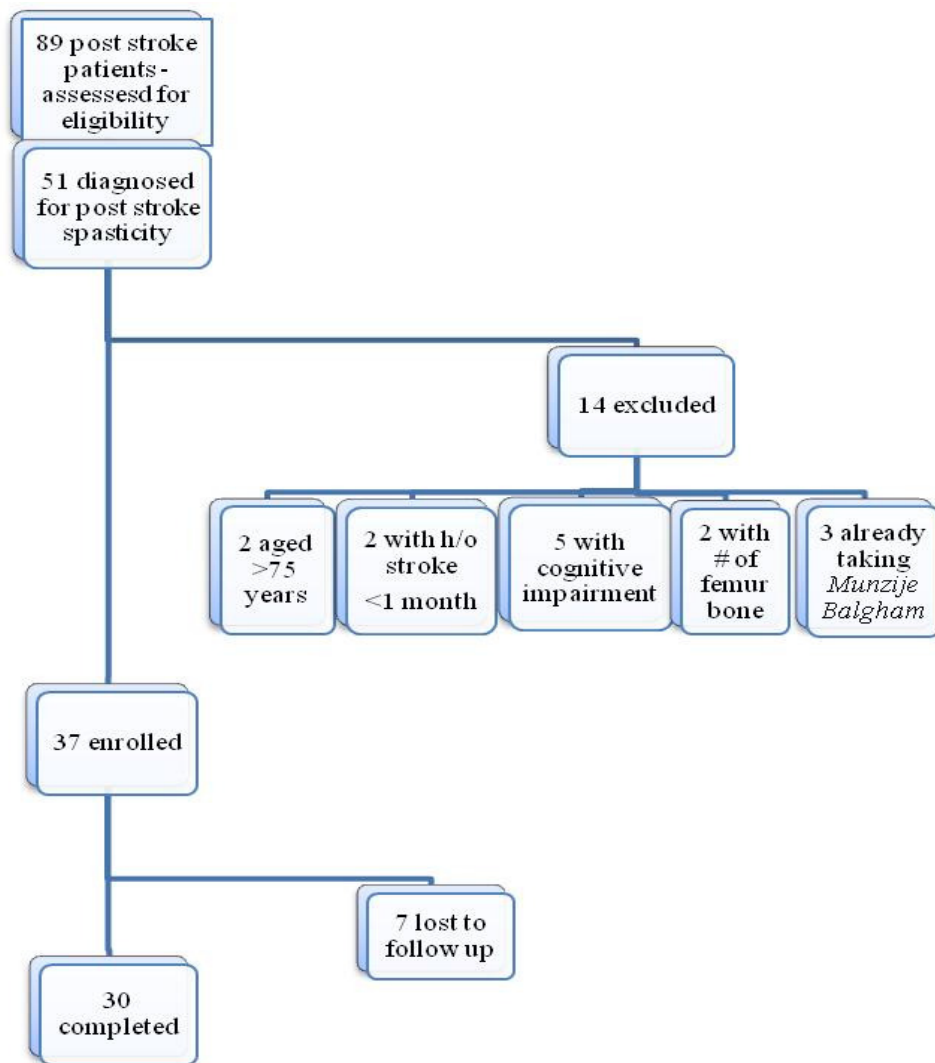


Figure-1
Study patients' flow chart

Friedman test with Dunn's multiple comparison test were used to assess the statistical differences between scores of Modified Ashworth Scale of upper and lower limb at baseline, 14th day and 28th day of treatment.

Abbreviations: ADL = Activities of Daily Living, cAMP= cyclic Adenosine Monophosphate, MAS = Modified Ashworth Scale, NIUM = National Institute of Unani Medicine

Minimal adverse effects were noted in 20% (6/30) of patients. During administration of *Munzije Balgham*, 3 patients complained of increased frequency of urine, 2 of loose motions (before administration of *Mus'hile Balgham*) and one of mild fever which subsided itself. No adverse effect was observed during administration of *Mus'hile Balgham* and massage with *Raughane Malkangni*.

Discussion: Although there was no difference in the prevalence of spasticity between the upper and lower limbs, it was more severe in upper limb than in lower limb muscles. The hypertonia was observed more in antigravity muscles in comparison to their antagonistic muscles which constitutes typical spasticity posture. These observations were in agreement with the findings of Urban et al⁹. The mechanisms underlying the antigravity posture are still obscure. Hypothetically, an impaired vestibulospinal function mediating otolith contributions to postural control is relevant for the development of the antigravity posture⁹. The magnitude of reduction in grades of MAS was more in antigravity muscle groups, which indicates the target specific action of drugs and validates the Unani concept of *Tabee'at Kirmani NII*¹⁰.

According to Unani medicine, *Tahleel* (dissolution), *Taqtee'* (disintegration) and *Talteef* (attenuation) are the properties which make the fulcrum of the first phase of *Tanqiya* and fairly

resemble to the principle of treatment of stroke in modern medicine advocating use of thrombolytics, antithrombotic agents and neuroprotective drugs¹¹. The drugs having property of *Tahleel* are known as *Muhallil* and may be defined as the drugs which act on a *Ghaleez Akhlat* (viscid humour) to make it dissoluble and detachable from its site of pathology. *Mulattif* drug is inherent with the property of *Talteef* and interacts with body's *Quwwate Tabee'iya* to divide the morbid matter into smaller parts. *Muqatte'* drugs are those drugs, which owing to property of *Taqtee'*, penetrate into the interstitial spaces of the organs due to their lightness and remove the adhered *Akhlat* from the organ¹². It is vital to dissolve and disintegrate the *Balghami Sudda* first, to purgate it out later from the body. The ingredients of the *Munzije Balgham* possess the properties such as *Muhallil* (dissolvent), *Mulattif* (attenuant), *Mufattehe Sudad* (deobstruent), *Munaqqie Dimagh* (brain purifier), *Muqawwie Aa'saab* (neurotonic), *Muqatte'*, *Jali* (cleanser) etc. and are; therefore, used in diseases such as *Tashannuje Imtilaee*, paralysis, facial palsy, headache and tremors caused by abnormal *Balgham*^{12,13,14}. Once this abnormal *Balgham* is dissolved, detached and disintegrated by the action of *Munzije Balgham* drugs, it is purgated out by *Mus'hile Balgham* drugs. *Mus'hil* drugs have property to expel the morbid *Akhlat* from the vessels, neighbouring structures and from whole body through intestine. Majority of the Unani physicians opine about the action of *Mus'hile Balgham* drugs that they have affinity with *Balgham* and; therefore, purgate it out³. After purgation of abnormal *Balgham*, which remain impacted in nerves to cause *Tashannuje Imtilaee*, the nervous structures become receptive to regain lost vigor, vitality and normal functions. This phase of recuperation and rejuvenation is known as *Ta'deel* and is accomplished by using various drugs and regimenal procedures such as massage, cupping, exercises etc.^{5,6,7}. *Dalk* (massage) itself produces heat and eliminates viscid matter¹⁰. Massage with hot natured oil further help to remove pathological condition caused by *Balgham*. *Malkangni* has properties such as *Muqawwie Aa'saab*, and its oil is therefore, used for massage in diseases like hemiplegia, facial palsy etc^{14,15}.

After several scientific studies on mechanism of recovery after brain injury, it is known that functional reorganization can take place in the adult nervous system; this property is known as neuroplasticity¹⁶. Different underutilized areas of the brain (e.g. cortical supplementary and association areas) can take over the functions of damaged tissue. It is thought that the central nervous system has backup or fail-safe systems (parallel cortical maps) that become operational when the primary system breaks down¹⁷. Alterations in map topography of brain caused by brain injury were not fixed as demonstrated by the injection of botulinum toxin into affected muscles and these changes could be temporarily reversed when the clinical effects of the injection were found to be greatest¹⁶. Nerve cells can also change their interactions with each other, with physiological changes occurring at the level of synapses. Regenerative and collateral synaptogenesis are important reparative processes¹⁷. Local growth of axons and synapses could provide a mechanism for

intra cortical remapping of sensory motor representation. Data indicate that anise oil (extracted from *Pimpinella anisum*) modulates synaptic plasticity in the hippocampus¹⁸. Cortical plasticity was observed to be enhanced by different rehabilitative measures¹⁶. Massage, being a rehabilitation measure may act similarly.

Concept of neuroprotection includes providing a treatment in which the brain's tolerance to ischemia is prolonged¹¹. It includes prevention of oxidative stress, mitochondrial dysfunction, inflammation and apoptosis¹⁹. Studies suggest that glabridin (a major flavonoid of *Glycyrrhiza glabra* i.e. *Gaozaban*) significantly decreases the focal infarct volume, cerebral histological damage and apoptosis²⁰. *Foeniculum vulgare* (*Badyan*) essential oil showed antithrombotic activity preventing the paralysis induced by collagen-epinephrine intravenous injection²¹. *Pimpinella anisum* (*Anisoon*) has neuroprotective activity and decreases infarct volume¹⁸. *Paeonia* species have shown anti-inflammatory, sedative activities and are used for blocking effect on neuromuscular junctions²². Antioxidant activity is observed in *Glycyrrhiza glabra* (*Gaozaban*)²³, *Paeonia emodi* (*Ood Saleeb*)²², *Rosa damascene* (*Gule Surkh*)²⁴, *Operculia turpethom* (*Turbud*)²⁵ and *Cassia fistula* (*Khayar Shambar*)²⁶.

Oral antispasmodic agents such as baclofen, diazepam, dantrolene sodium, clonidine, and tizanidine are used to relieve spasticity²⁷. Experimental studies revealed that spasmolytic or antispasmodic activities were present in *Lavandula stoechas* i.e. *Ustukhudoos* (mediated through calcium channel blockade)²⁸ and its oil (mediated through cAMP)²⁹, *Pimpinella anisum* i.e. *Anisoon* (through inhibition of acetylcholine)³⁰, *Apium graveolens* i.e. *Karafs* (mainly by suppressing the Ca²⁺ influx)³¹, *Paeonia emodi* (*Ood Saleeb*)³², *Borago officinalis* (*Gaozaban*)³³ and *Celastrus paniculatus* (*Malkangni*)³⁴. The mechanism of action of some of above mentioned drugs is similar to botulinum toxin commonly used in spasticity management²⁷. The plasticity of brain seems to have been enhanced by the *Muqawwie Dimagh* and *Munaqqie Aa'saab*^{13,14} properties of the ingredients of the test formulation. These drugs, owing to their properties, seem to be capable to up regulate the function of the undamaged area to help them take over the function of the damaged areas easily. *Munaqqie Dimagh*, *Muqawwie Dimagh*, *Muqawwie Aa'saab* properties of the test drugs might have a significant role in stimulation of sprouting of new connection in and around the damaged area to restore the lost functions. Thus, it may be concluded from the above discussion that the test drugs used in *Tanqiya* and *Ta'deel* have all the potential properties which seem to have positive effects not only in controlling the pathological changes but reverting them to normal state to restore the motor functions.

Deep rhythmic massage with pressure over the insertion of muscle has been proved effective in some cases of spasticity. It has been claimed that petrissage or massage, in which muscles are kneaded, can exert an inhibitory effect on motor neuron.

Besides its neurological effects, it helps to treat soft tissue changes (up to some extent), breaking down the adhesion and pain in spasticity³⁵.

Although massage with *Raughane Malkangni* was done for normalization and potentiation of paralysed limbs, 9 patients reported decrease in pain associated with spasticity. However, improvement in pain was not evaluated by any credible parameter in patients. During assessment of grades of spasticity, few patients complained of pain during passive stretching of spastic limbs. In such conditions, it was difficult to assess the degree of resistance imparted by hypertonia.

Almost all patients reported improvement in motor power of paralysed limbs; while, conventional medications for spasticity cause further muscle weakness³⁶. Many patients reported improvement in Activities of Daily Living (ADL) e.g. walking, balance, climbing stairs, dressing and personal hygiene which is supposed to be a goal of management². Relaxation of spastic limbs along with increase in motor power probably contributed to improvement in ADL. This effect is expected to reduce the dependence on care as well as to reduce the burden for patients, and caregivers. Increase in frequency of urination, loose motions and mild fever, observed in few patients during the study were probably due to diuretic and laxative actions and hot temperament of ingredients of *Munzije Balgham*¹⁴. It was observed in few patients, that the tone in the muscles remained same as on last follow up even after 2-3 months of stopping the drugs. It is needed to assess the patients after few weeks of stopping this regime to evaluate whether the effects are transient or long lasting. Further, multicentric, controlled trials are required on large population to evaluate the safety and efficacy of this therapy.

Conclusion

It may be concluded that test formulation is effective in reducing spasticity predominantly in antigravity muscles due probably to enhancing neuroplasticity and by neuroprotective and antispasmodic activities and may be a treatment choice for patients who face difficulty while treating spasticity with oral antispastic agents because of adverse drug reactions.

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