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RESEARCH ARTICLE

NON-PHARMACOLOGICAL TREATMENT OF COGNITIVE IMPAIRMENT- AN OVERVIEW

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Abstract

Background: With increasing proportion of geriatric population, late-life co-morbidities including dementias, heart disease, arthritis and cancers are also increasing steadily. Cognitive impairment, mainly affecting the geriatric population, is condition when a person has trouble remembering, learning new things, concentrating or making decisions that affect their everyday life, and is often considered a precursor to more serious diseases such as depression/dementia/Alzheimer's disease. As per World health Organization (WHO), globally more than 55 million people live with dementia and annually 10 million new cases are added into this pool. Alzheimer's Disease International estimated that world-wide 75% people with dementia remains undiagnosed and this can be as high as 90% in LMICs.

Methods: The literature search utilized PubMed, Google scholar, and ResearchGate databases, with a period limit of January 2018 till November 2022.

Discussion: Non pharmacological interventions (physical exercise, cognitive training, diet, meditation) have significant effect on the brain health (cognitive status) of the elderlies having cognitive impairment.

Conclusions: Cognitive impairment being a complex disorder with multiple risk factor, a multimodal strategy will bring out maximum beneficial effect. Such modalities are safe, economical and simple which can be easily adapted by senior citizens and thus should be publicized to promote healthy ageing.

Introduction:-

Population ageing is a world-wide phenomenon, with 1 in every 6 people in the world over 65 years old(1). This group is also the most vulnerable to disease and disability**.** Ageing affects physical health as well as deterioration in mental health and functioning abilities. With ageing the risk of chronic co-morbidities such as dementias, heart disease, arthritis and cancer increases and are labelled as the nation's leading drivers of morbidity, disability, death and economic burden(2).

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The preliminary study documenting a decline in memory was conducted by Willoughby in 1929. Cognitive disability or dementia, is a condition when a person has trouble remembering, learning new things, concentrating or making decisions that affect their everyday life, and is often considered a precursor to more serious diseases such as depression/dementia/Alzheimer's disease**.** Common signs include memory loss, frequently asking the same questions, having trouble exercising judgment, changes in mood, vision problems to name a few. Decline in cognitive function is a trait of ageing and predictor of mortality. Alzheimer's Disease International estimated that globally 75% of people with dementia are undiagnosed and this may be as high as 90% in Low and Middle Income Countries (LMICs)(3). As per WHO, more than 55 million people live with dementia, with 10 million new cases occurring annually(4).

At present there are no pharmacological treatments proven to slow or cure progression of cognitive impairment (CI) to dementia(5). Nonetheless, there are evidences that lifestyle modifications including diet, exercise and cognitive stimulation may be effective. Understanding scope of interventions targeting the modifiable factors, including non-pharmacological modalities is the need of hour to control this silent epidemic. With this background, this review is being conducted to know about the different non-pharmacological treatment modalities and their scope.

Literature search

A thorough literature search on PubMed, google scholar and ResearchGate databases was done and non-pharmacological randomized controlled trial studies done among cognitively impaired individuals to improve their cognitive status as the primary outcome in the last 5 years were included in this review.

Observations:-

Summarized results are shown in Table 1 on different non-pharmacological treatment methods.

Table 1:- Non-pharmacological Randomized Controlled Trial (RCT) Studies:

Authors	Study design	Country	Sample	Intervention	Results
Song D et al. (2019)(6)	RCT	China	120	Moderate intensity aerobic exercise program	Participants in the intervention group had a significant improvement in cognitive function (β= 1.895; 95% CI=1.421, 2.368; p < 0.001) & health-related quality of life (β= 0.605; 95% CI= 0.295, 0.914; p < 0.001).
Mahendran R et al. (2018)(7)	RCT	Singapore	68	Art therapy (AT) and music reminiscence	In the AT arm, neurocognitive domains improved as compared to the control arm at 3 months interval (mean difference (d) = 0.40; 90% CI 0.126, 0.679) and were sustained at 9 months (d = 0.31; 90% CI 0.068, 0.548).
Fonte et al. (2019)(8)	RCT	Italy	87	Cognitive treatment and physical treatment	No change in MMSE score at after intervention and at 3 month follow up in intervention group while control showed decline in MCI -11.8%, AD: -16.2%.
Peng et al. (2019)(9)	RCT	China	140	Cognitive training	The overall MoCA score in the intervention group improved (19.77±2.24 to 21.09±2.20) at 6 month follow up. Significant effect

					was noted between time and cognitive training.
Rosenberg et al. (2018)(10)	RCT	Finland	1260	Multi-domain lifestyle intervention (nutrition, exercise, cognitive training & management of vascular risk factors)	Significant effect on the primary cognitive outcome (change in total score) (p=0.030) and secondary cognitive outcome including executive functioning (p=0.039) and processing speed (p=0.029) in the intervention group.
Xue B et al. (2021)(11)	RCT	China	72	Game training	Significant improvement was seen in MoCA scoring in the intervention group (p<0.05). Scores of four entries (Naming, Attention, Language and delayed recall) were significantly higher in the intervention group (p<0.05).
Straubmeier et al. (2017)(12)	RCT	Germany	362	MAKS therapy	Intervention group had better MMSE and ETAM scores than the control group (Cohen's d, 0.26 and 0.21 respectively, p=0.012) at 6 month follow up.
Innes et al. (2021)(13)	RCT	USA	60	Meditation program Music listening	At 3 month follow up participants in both the groups showed significant improvement from baseline characteristics in both memory and cognitive function (p<0.004).
Giuli et al. (2016)(14)	RCT	Italy	321	Cognitive training	Subjects with AD showed significant effect on ADAS score (p<0.001) as well as on functional status measured by IADL (p=0.002)
Li et al. (2021)(15)	RCT	China	90	Multi-component exercise training	Intervention significantly improves the physical function and cognitive function of elderlies with MCI. Average PPT score increases from 11.36±2.69 to 11.88±2.40 at 3 monthly follow up. Average score of MoCA increased from 21.52±2.05 to 23.48±1.47 at 3 months. The score of MMSE showed similar trend as well.
Bisbe et al. (2019)(16)	RCT	Spain	36	Choreographed exercise	Statistically significant greater benefits in verbal recognition memory wereseen in choreography group (mean difference=1.03, p

					value=0.003).
Bademli et al. (2018)(17)	RCT	Turkey	60	Physical activity program	Mean MMSE score among experimental group was higher ($p<0.05$). Also, mean PQSI score in the experiment group increases post-intervention (after 20 weeks).

Discussion:-

Prevalence of dementia is remarkably is increasing, with population ageing. With no cure and only symptomatic treatment with limited adequacy is available. Knowledge and awareness regarding life-style related interventions promoting brain-health is still sparse.

Non-pharmacological treatment options are:

It is considered a safer with less side-effects and cost-effective treatment modality mainly influencing cognition, mood and other behavioral and psychological symptoms(5).

Physical exercise

Physical exercise is a low cost, low risk and readily available investigation and has been researched generously because of its well-known effects on rain health. As per systematic review conducted by **Song et al. (2018)**(18) on 11 studies physical exercise (aerobics as well as resistance training) has significant effect on cognitive function.**Song et al.** in their study tested 16-week aerobic stepping exercise programamong 60 elderly individuals with mild cognitive impairment. Cognitive function was assessed using MoCA. Participants in the intervention group showed significant improvement in their MoCA score as compared to the control group ($\beta=1.895$, 95% CI=1.421-2.368, $p<0.001$). Among the subdomains, results were significant for memory ($\beta=0.913$, $p<0.001$), executive function ($\beta=0.405$, $p<0.001$), attention ($\beta=0.252$, $p<0.003$), language ($\beta=0.155$, $p<0.005$) and visuospatial ability ($\beta=0.177$, $p=0.003$)(6).

Bademli et al.among 30 participants with MCI in the experimental group conducted 20-week Physical Activity Program. It included warming activities, rhythmic exercises, cool-down exercises and 40 min walking. After the intervention, mean MMSE score in the experimental group was higher than that of the control group, with statistically significant difference ($p<0.05$)(17).

Multi-component exercise training includes motor and physical components. **Li et al.** studied the effect of multi-component exercise training among 42 elderlies with MCI and reported significant effect of intervention on the cognitive function of the intervention group (MMSE, MoCA and three subdomains- visual-spatial, attention and delayed memory) ($p<0.05$)(15).

Similarly,**Fonte et al.** reported that maximum change in scores was seen in MCI patients as compared to AD patients inclining towards better benefit in latter group(8).

RCT conducted by **Bisbe et al.** studied the effect of choreographed exercise in comparison to the physical therapy. The choreography group showed significantly greater benefits in verbal recognition ($p<0.003$). With reference to balance, participants in the physical therapy group showed better performance(16).

Cognitive training

Giuli et al. in their study 'The Mind project'gave cognitive training which included learning strategies for orientation, memory, categorization and clustering. Intervention group presents significant effect in auditory verbal short-term memory ($p<0.001$), visuospatial short-term memory ($p<0.01$), learning and memory of word pairs ($p<0.01$) and selective attentive processes ($p<0.001$)(14).

Peng et al. reported significant effect of intervention(time and cognitive training) on total MoCA score after three and six months ($p<0.001$)(9).

Straubmeier et al. studied the effect of MAKS therapy (warm-up session followed by sensorimotor activation and then cognitive activation). After six months of training, significantly better results were noted for cognitive and ADL abilities in the intervention group(12).

Other therapies

The famousFINGER trial studied the effect of multi-domain lifestyle intervention focusing mainly on nutrition, exercise, cognitive training and management of vascular risk factors and reported significant effect of intervention on the primary cognitive outcome (change in overall cognitive performance) ($p=0.030$) as well as on executive functioning and processing speed ($p=0.039$ and 0.029 respectively)(10).

Innes et al. studied the effect of meditation and musicon participants with subjective cognitive decline. At three months into the intervention, participants in both the groups (meditation and music) showed significant improvement in memory and cognitive functioning. At six month assessment, four participants reported change in medication including antidepressants, analgesics and statin medication(13).

Xue et al. explored the effect of game training on cognitive functioning of individuals with mild cognitive impairment and reported that game training improved scores in particularly four subdomains- naming, attention, language and delayed recall ($p<0.05$)(11).

Conclusion:-

The aim of this article was to shed light onvarious non-pharmacological therapies being practiced among cognitively impaired individuals. This review article indicates thatnon-pharmacological treatment modalities especially physical exercise and cognitive training significantlyaffects the cognitive functions in a positive way. Cognitive impairment being a complex disorder with multiple risk factor, a multimodal strategy will bring out maximum beneficial effect. Such modalities are safe, economical and simple which can be easily adapted by senior citizens and thus should be publicized to promote healthy ageing.

Limitations

This review article included studies only from the past 5 years. Socio-demography of population differs from region to region; hence generalizability of such studies needs to be further explored.

Abbreviations:

AD: Alzheimer's Disease, CI: Cognitive Impairment, MCI: Mild Cognitive Impairment, MMSE: Mini Mental State Examination, MoCA: Montreal Cognitive Assessment, LMICs: Low and Middle Income Countries

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