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EFNS TASK FORCE/CME ARTICLE

EFNS guideline on diagnosis and management of post-polio syndrome. Report of an EFNS task force

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Post-polio syndrome (PPS) is characterized by new or increased muscular weakness, atrophy, muscle pain and fatigue several years after acute polio. The aim of the article is to prepare diagnostic criteria for PPS, and to evaluate the existing evidence for therapeutic interventions. The Medline, EMBASE and ISI databases were searched. Consensus in the group was reached after discussion by e-mail. We recommend Halstead's definition of PPS from 1991 as diagnostic criteria. Supervised, aerobic muscular training, both isokinetic and isometric, is a safe and effective way to prevent further decline for patients with moderate weakness (Level B). Muscular training can also improve muscular fatigue, muscle weakness and pain. Training in a warm climate and non-swimming water exercises are particularly useful (Level B). Respiratory muscle training can improve pulmonary function. Recognition of respiratory impairment and early introduction of non-invasive ventilatory aids prevent or delay further respiratory decline and the need for invasive respiratory aid (Level C). Group training, regular follow-up and patient education are useful for the patients' mental status and well-being. Weight loss, adjustment and introduction of properly fitted assistive devices should be considered (good practice points). A small number of controlled studies of potential-specific treatments for PPS have been completed, but no definitive therapeutic effect has been reported for the agents evaluated (pyridostigmine, corticosteroids, amantadine). Future randomized trials should particularly address the treatment of pain, which is commonly reported by PPS patients. There is also a need for studies evaluating the long-term effects of muscular training.

Objectives

The aim was to develop a common definition of post-polio syndrome (PPS) and evaluate the existing evidence for the clinical effectiveness of therapeutic interventions and on this basis provide clinical guidelines for management of PPS.

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Background

Many previous polio patients experience new muscle weakness, new atrophy, fatigue, muscular and joint pain and cold intolerance several years after acute paralytic poliomyelitis. A case of new atrophy and weakness many years after acute paralytic polio was first described in 1875 by Raymond [1].

The term post-polio syndrome was introduced by Halstead in 1985 to cover medical, orthopaedic and psychological problems possibly or indirectly related to the long-term disability occurring many years after the acute episode. The criteria for PPS were as following.

1 Confirmed history of polio.
2 Partial or fairly complete neurological and functional recovery after the acute episode.
3 Period of at least 15 years with neurological and functional stability.

4 Two or more of the following health problems occurring after the stable period: extensive fatigue, muscle and/or joint pain, new weakness in muscles previously affected or unaffected, new muscle atrophy, functional loss, cold intolerance.
5 No other medical explanation found [2].

Halstead revized these criteria in 1991 and added 'gradual or abrupt onset of new neurogenic weakness' as a necessary criterion for PPS, with or without other co-existing symptoms [3].

Dalakas redefined and narrowed the use of PPS in 1995. He combined the criteria for post-polio muscular atrophy (PPMA), i.e. new muscular atrophy at least 15 years after the acute infection, and the following symptoms: fatigue and decreased endurance, increase in skeletal deformities and pain in joints [4]. A third term, post-polio muscular dysfunction (PPMD), was introduced in 1996 with the following criteria.

1 History of paralytic polio; confirmed or not confirmed; partial or fairly complete functional recovery.
2 After a period of functional stability of at least 15 years development of new muscle dysfunction: muscle weakness, muscle atrophy, muscle pain and fatigue.
3 Neurological examination compatible with prior polio: lower motor neurone lesion; decreased or absent tendon reflexes; no sensory loss; compatible findings on electromyography (EMG) and/or magnetic resonance imaging [5].

The symptoms reported for PPS are the same from all parts of the world. Muscle weakness, atrophy, generalized fatigue, post-exercise fatigue, muscle pain, fasciculations, cramps, cold intolerance and joint pain dominate [2,6–13]. A history of previous paralytic polio seems to increase long-term mortality [14].

The prevalence of PPS has been reported from 15% to 80% of all patients with previous polio depending on the criteria applied and population studied [4,6,11,15–18]. In many population-based studies, terms like 'late onset polio symptoms' have been used instead of PPS. Hospital-based studies use the term PPS, but in these studies it is always debatable whether the patient material is representative. Exact prevalence of PPS is therefore difficult to establish. For European populations, one Dutch study reported a prevalence of late onset polio symptoms of 46%, one study from Edinburgh reported a prevalence of more than 60%, in Estonia a prevalence of 52% has been reported, Norway 60% and Denmark 63% [6,12,19,20].

For symptomatic treatment and clinical purposes, the difference between stable muscle weakness after polio and PPS often remains insignificant. Still, it would be of great benefit to have a consensus on the term PPS, both for clinical use and for research. All three definitions are based on the principle of exclusion of other causes for new deterioration and new symptoms. Halstead claimed that two different symptoms, like joint pain and cold intolerance, were sufficient for a diagnosis of PPS, but later redefined and included new neurogenic muscle weakness as an obligatory criterion for the diagnosis. Dalakas proposed an even more focused neuromuscular approach where new atrophy was the cornerstone. Many patients report a sense of weakening in the muscles before it is detectable by clinical examination as new atrophy. These findings can be confirmed by isometric muscle strength evaluation and computer tomography imaging ([21,22], unpublished observation). Atrophy is the end stage of new neuromuscular deterioration and by using this as a necessary criterion, patients in an earlier stage of neuromuscular deterioration will be excluded.

We suggest that the criteria for PPS used within European Federation of Neurological Societies (EFNS) and Europe should be based on the Halstead's definition from 1991 with emphasis on the new muscle weakness. The diagnosis of PPS is an exclusion diagnosis with no test or analysis specific for PPS, and the role of the investigation is to rule out every other possible cause for the new symptoms and clinical deterioration [4,23].

Role of clinical neurophysiology

Clinical neurophysiology is used for four main reasons. First, to establish typical lower motor neuron involvement (neurogenic EMG findings, normal sensory findings and normal motor findings except for parameters reflecting muscle atrophy). Secondly, to exclude other causes. This is part of the PPS definition, and it is not uncommon to find patients in whom the initial diagnosis of polio must be revized. Thirdly, to find concomitant nerve or muscle disorders, such as entrapments and radiculopathies. Fourthly, to assess the degree of motor neuron loss. This cannot be quantified clinically, as loss of neurones may be completely masked by compensatory nerve sprouting and muscle fibre hypertrophy. Macro EMG studies have shown that loss of up to 50% of neurons may be compatible with a normal clinical picture [24].

In longitudinal studies with macro EMG, a continuous loss of neurons is demonstrated with exaggerated speed compared with normal age-dependent degeneration [25]. New weakness appears when the compensatory mechanisms are no longer sufficient, and occurs when Macro MUP exceeds 20 times normal size [25].

Search strategy

Medline via Pubmed, EMBASE, ISI and the Cochrane Library were searched from 1966 to 2004. Search terms

were PPS/post-poliomyelitis/PPMA/PPMD/poliomyelitis in combination with management, therapy, treatment, medicaments, physiotherapy and intervention.

No meta-analyses of interventions for PPS were found when searching the databases.

Data were classified according to their scientific level of evidence as class I–IV [26]. Recommendations are given as level A–C according to the scheme for EFNS guidelines. When only class IV evidence was available but consensus could be reached the task force gives our recommendations as good practice points [26]. Consensus was reached mainly through e-mail correspondence.

A questionnaire about diagnosis, management and care of post-polio patients was answered by the group members from The Netherlands, Norway, Poland, Sweden and UK.

Results

National surveys

None of the countries represented in this task force had formal national guidelines for PPS, for diagnosis or treatment. Diagnostic criteria applied were those of Halstead (Sweden), Borg (the Netherlands) and Dalakas (Norway). There were no national competence centres in any of the countries. Medical specialities involved were mainly physical medicine and rehabilitation, neurology, clinical neurophysiology, respiratory medicine and orthopaedics. Neurologists were involved in diagnosis whereas rehabilitation physicians were involved in long-term management and care. In UK, PPS patients were mainly taken care of by their general practitioners with less contact with the secondary level of the health service.

Therapeutic interventions

Acetylcholinesterase inhibitors, steroids and amantadine
The effect of pyridostigmine in PPS has been investigated in four studies with particular emphasis on fatigue, muscular strength and quality of life. Two open pilot studies indicated a positive effect on fatigue [27,28], but this was not confirmed in two double-blinded randomized-controlled trials using a daily dose of 180 mg pyridostigmine [29,30]. Horemans *et al.* reported a significant improvement in walking performance, but the difference in quadriceps strength was not significant as reported by Trojan *et al.* Hence, there is evidence at Class I that pyridostigmine is not effective in the management of fatigue and muscular strength in PPS. There are two randomized placebo-controlled studies investigating the effect of high-dose prednisolone (80 mg daily) and amantandine (200 mg daily) on muscular weakness and fatigue (prednisone) and fatigue (amantadine) [31,32]. They included a small number of patients, 17 and 23 respectively, and only Stein *et al.* included statistical power calculations. There was no significant effect on muscular strength or fatigue in any of these Class I studies.

Muscular training
It has been claimed that muscular overuse and training may worsen the symptoms in PPS and even provoke a further loss of muscular strength [33]. Many post-polio patients have been advised to avoid muscular overuse and intensive training [34,35]. Studies of muscle morphology and oxidative capacity in the tibialis anterior muscle indicate a high muscular activity because of gait and weight bearing [36,37]. When followed prospectively, the macro EMG motor unit potential amplitude (MUP) in the tibialis anterior muscle was found to be increased after 5 years, whereas there was no change in the Macro MUP amplitude in the biceps brachii muscle [38]. This indicates a more pronounced denervation–reinnervation process in the tibialis muscle, which may be because of daily use and higher muscle activities in the leg muscles. However, there are no prospective studies, which show that increased muscle activity or training lead to loss of muscular strength compared with the absence of training or less muscular activity. On the contrary, patients who reported regular physical activity had less symptoms and a higher functional level than physically inactive patients [12,39]. One randomized-controlled trial reported significant improvement in muscular strength after a 12 week training programme with isometric contraction of hand muscles [40]. Non-randomized trials with training programmes lasting from 6 weeks to 7 months involving both isokinetic, isometric and endurance muscular training have shown a significant increase in both isokinetic and isometric muscle strength [41–44]. No complications or side effects were reported. Hence, there is an evidence at class II and III that supervised training programmes increasing muscle strength in patients with PPS. It should be added that the long-term effects (years) of training are not documented, and deserve prospective studies. For patients without cardiovascular disease, one randomized-controlled study reported improved cardiovascular fitness after supervised exercise programmes using ergometer cycles [45] (Class I). Aerobic training in upper extremities had beneficial effects on oxygen consumption, minute ventilation, power and exercise time [46] (Class II). Aerobic walking exercises can help economize movements and increase endurance without improvement in cardiovascular fitness [47]. Ernstoff *et al.* reported an increase in work performance by reduction of heart rate during exercises; hence, endurance training seems to improve

cardiovascular conditioning (Class IV). It is important to emphasize that most exercise studies have been executed with supervision, submaximal work load, intermittent breaks and rest periods between exercise sessions to prevent the likelihood of overuse effects. This is an important aspect for any PPS patient. With supervision, we mean that particularly skilled therapists should advise the training participants with respect to work load, exercise technique, time consumption and rest periods during performances. Most of the participating patients in these studies were below 60 years of age. The effect of exercise programmes for subjects older than 60 years is therefore less documented.

One randomized-controlled study of post-polio patients with pain, weakness and fatigue in their shoulder muscles compared the effect of exercise only, exercise in combination with lifestyle modification and lifestyle modification only [48]. All three groups improved after intervention, but a significant difference was found only for the two groups with exercise (Class II). The end-points in this study were combinations of several symptoms. Further studies are needed to identify improvement on particular symptoms before conclusions are drawn regarding the lifestyle modifications.

Treatment in a warm climate and training in water

Anecdotal reports from post-polio patients indicate a positive effect of a warm climate and of training in warm water with respect to pain and fatigue. One randomized-controlled study reported a significant reduction in pain, health-related problems and depression for both groups after completing identical training programmes in either Norway or Tenerife [49]. No significant difference in walking tests was seen. Both groups improved their walking skills, reduced their level of fatigue, depression and health-related problems. However, the effect remained significantly longer in the Tenerife group (Class I).

Dynamic non-swimming water exercises for post-polio patients have been reported to reduce pain, improve cardiovascular conditioning and increase subjective well-being in a controlled but not randomized study (Class III) [50]. A qualitative interview study (Class IV) indicated a positive effect on the self-confidence when performing group training in water [51].

Respiratory aid

Reduced pulmonary function because of weak respiratory muscles and/or chest deformities may occur in patients with previous polio [52,53]. Patients with chest deformities have an increased risk of nocturnal hypoventilation and sleep-disordered breathing [52,54,55]. The prevalence of respiratory impairment is highest amongst patients who were treated with artificial ventilation in the acute phase [52]. Shortness of breath is a common complaint in many post-polio patients, but is not necessarily related to respiratory impairment. Two hospital-based studies showed that respiratory function was normal in the majority of patients reporting shortness of breath, and cardiovascular deconditioning and being overweight were the most common cause for this symptom [11,56]. Respiratory impairment can occur without shortness of breath and can present with daytime somnolence, morning headache and fatigue [57]. There are no randomized trials evaluating the effect of respiratory aids. Reports indicate that early introduction of non-invasive respiratory aids like intermittent-positive pressure ventilation (IPPV) or biphasic-positive pressure (BIPAP) ventilators via mouthpiece or nasal application can stabilize the situation and prevent complications like chest infections, further respiratory decline and invasive ventilatory aid (tracheostomy) [54,58], and also improve exercise capacity [59] (Class IV). If invasive ventilatory aid is needed, PPS patients with a tracheostomy and mechanical home ventilation are reported to have good perceived health despite severe physical disability [60] (Class III). For patients already using intermittent respiratory aids, respiratory muscle training is useful [61] (Class IV). General precautions like stopping smoking, mobilization of secretions and cough assistance are beneficial [54].

Bulbar symptoms

Weakening of bulbar muscles causing dysphagia, weakness of voice and vocal changes have been reported amongst patients with PPS [62–65]. Case reports indicate that speech therapy and laryngeal muscle training are useful for these patients (Class IV) [65].

Weight control, assistive devices and lifestyle modifications

The importance of reducing weight, adaptation to assistive devices and modification of activities of daily living has been emphasized [35,66,67]. The scientific evidence for these recommendations is limited, but there was consensus in our group that an individual with weak muscles benefits from losing excess weight, and that proper orthoses, walking sticks and wheelchairs facilitate daily life activities (good practice points). Participating in muscle training programmes and endurance training will, in many cases, also lead to weight loss, but there is no evidence that weight reduction alone can ameliorate symptoms. Patients with BMI (body mass index) >25 which is defined as overweight did not report more symptoms than those of normal weight [11]. On the other hand, a recent weight gain was found to be a predictive factor for PPS [68]. Sleep disorders are common amongst PPS patients [11], and can be a mix of obstructive sleep

apnoea, frequency of tiredness on waking up and during the day, headache on waking up, daytime sleepiness, restless legs and hypoventilation [69–71]. It is widely accepted that obesity is related to obstructive sleep apnoea, and weight control is crucial for this disorder [72]. The number of patients receiving mechanical home ventilation because of obesity-induced hypoventilation has increased [73]. From this perspective, there is a rationale for reducing excess weight in PPS patients (Class IV).

One pilot study reported that a change from metal braces to light weight carbon orthoses can be useful and increase walking ability in polio patients with new pareses [74]. Biomechanical analysis of the walking pattern can lead to optimal design of orthoses and improve function in the lower limbs (Class IV) [75].

Frequent periods of rest, energy conservation and work simplification skills are thought to be useful for patients with fatigue [76].

Coming to terms with new disabilities, educational interventions

New loss of function, increase in disability and handicap are common in post-polio patients [6,11,77]. This can lead to reduced well-being and emotional stress. Group training with other post-polio patients, participation and regular follow-up at post-polio clinics can prevent a decline in mental status and give a more positive experience of the 'self' [51,78] (Class III). Acceptance of assistive devices, environmental support and spending more time on daily tasks can facilitate coping with home and occupational life (Class III) [79].

Recommendations

Level A

A small number of controlled studies of potential specific treatments for PPS have been completed, but no definitive therapeutic effect has been reported for the agents evaluated (pyridostigmine, steroids and amantadine).

Level B

Supervized muscular training, both isokinetic and isometric, is a safe and effective way to prevent further decline of muscle strength in slightly or moderately weak muscle groups and can even reduce symptoms of muscular fatigue, muscle weakness and pain in selected post-polio patients. There are no studies evaluating the effect of muscular training in patients with severe weakness and the long-term effects of such training are not yet explored. Precautions to avoid muscular overuse should be taken with intermittent breaks, periods of rest between series of exercises and submaximal work load.

Training in a warm climate and non-swimming water exercises are particularly useful.

Level C

Recognition of respiratory impairment and early introduction of non-invasive ventilatory aids prevent or delay further respiratory decline and the need of invasive respiratory aids.

Respiratory muscle training can improve pulmonary function.

Group training, regular follow-ups and patient education are useful for the patients' mental status and well-being.

Good practice points: weight loss, and adjustment and introduction of properly fitted assistive devices; but lack significant scientific evidence.

Time for new revision of guidelines

There are now ongoing studies evaluating the effect of immune modulating therapy in PPS [80]. The results will probably be ready within the next 2 years. A revision of these guidelines would be useful at the same time. Prospective follow-up studies evaluating the muscle strength and function during the natural course of the disorder are welcomed. Studies evaluating the effects of muscular training in patients with severe muscular weakness are needed, in addition to prospective studies evaluating the long-term effects of muscular training. Further randomized studies evaluating therapeutic interventions should be performed with particular emphasis on pain and fatigue as these are common and disabling symptoms and there is limited evidence that any intervention affects these symptoms.

Conflicts of interests

The authors have reported no conflicts of interests.

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