CHAPTER 18

Post-polio syndrome

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Objectives

The aim was to revise the existing EFNS task force document, with regard to a common definition of PPS, and evaluation of the existing evidence for the effectiveness and safety of therapeutic interventions. By this revision, clinical guidelines for management of PPS are provided.

Background

Many previous polio patients experience new muscle weakness, fatigue, myalgia and joint pain, and cold intolerance, and develop new atrophy several years after acute paralytic poliomyelitis. The first case of new atrophy and weakness many years after acute paralytic polio was first described in 1875 by Raymond [1, 2].

The term post-polio syndrome (PPS) was introduced by Halstead in 1985 [3]. In general, PPS has been interpreted as a condition with new muscle weakness or fatigability in persons with a confirmed history of acute paralytic polio, usually occurring several decades after the acute illness.

As PPS is reckoned to be a chronic disease, the EFNS task force on post-polio syndrome recommends that the criteria published by March of Dimes (MoD) in 2000 [4] should be regarded as universal criteria for PPS.

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1 Prior paralytic poliomyelitis with evidence of motor neuron loss, as confirmed by history of the acute paralytic illness, signs of residual weakness, and atrophy of muscles on neurological examination, and signs of denervation on electromyography (EMG).
2 A period of partial or complete functional recovery after acute paralytic poliomyelitis, followed by an interval (usually 15 years of more) of stable neurologic function.
3 Gradual or sudden onset of progressive and persistent muscle weakness or abnormal muscle fatigability (decreased endurance), with or without generalized fatigue, muscle atrophy, or muscle and joint pain. (Sudden onset may follow a period of inactivity, or trauma, or surgery.) Less commonly, symptoms attributed to PPS include new problems with swallowing or breathing.
4 Symptoms persist for at least 1 year.
5 Exclusion of other neurologic, medical, and orthopaedic problems as causes of symptoms.
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[3, 5–12]. A history of previous paralytic polio seems to increase long-term mortality [13].

Deterioration of the neuromuscular function, overuse of motor units, the general ageing process, and inflammatory changes in the central nervous system and serum, have all been proposed as possible explanations for the new symptoms [14–17]. However, the underlying mechanisms are not fully elucidated, and we cannot conclude

which underlying factors are causing PPS. Regarding the clinical course, there is increasing evidence that the decline in muscle strength is slow with modest effect on functional tasks [18, 19]. Generalized fatigue is a common complaint among PPS patients, and not well understood, although both neuromuscular decline and increased levels of inflammatory cytokines indicate that fatigue in PPS should be reckoned as a physical entity [16, 20]. From a clinical point of view it should be emphasized that comorbidity could cause PPS- mimicking conditions, requiring other investigations and treatments [10, 21–23].

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 [5, 10, 24–28]. In many population-based studies, terms such as '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% [5, 29–31].

With regard to symptomatic treatment and clinical purposes, the difference between stable muscle weakness after polio and PPS seems as yet rather irrelevant. Still, it would be of great benefit to have a consensus on the term PPS for research and when evidence-based therapeutic interventions have become available. The MoD criteria are based on the principle of exclusion of other causes for new deterioration, where PPS is characterized with new muscle weakness or abnormal muscle fatigability, and persistence of symptoms for at least 1 year. 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.

Many patients report a sense of weakening in the muscles before it is detectable by clinical examination, although dynamometric muscle strength evaluation and computed tomography (CT) imaging may be helpful [32, 33]. 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.

Role of clinical neurophysiology

Clinical neurophysiology is used for four main reasons. First, to establish typical lower motor neuron involvement (neurogenic EMG findings, normal findings of the sensory and motor nerves except for parameters reflecting muscle atrophy). Second, 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 revised. Third, to find concomitant nerve or muscle disorders, such as entrapments and radiculopathies. Fourth, to assess the degree of motor neuron loss. This cannot be quantified clinically, since 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 [15].

In longitudinal studies with macro EMG, a continuous loss of neurons is demonstrated with exaggerated speed compared to normal age-dependent degeneration[34]. New weakness appears when the compensatory mechanisms are no longer sufficient, and occurs when macro motor unit potential (MUP) exceeds 20 times the normal size [34].

Search strategy

MEDLINE via Pubmed, EMBASE, ISI, and Cochrane were searched with time limits 1966 until 2004. Search terms were post-polio syndrome, postpoliomyelitis, PPMA, PPMD, poliomyelitis, in combination with management, therapy, treatment, medicaments, physiotherapy, and intervention.

In the present revised document, the database search was supplied with the years 2004–2009.

No meta-analyses of intervention for PPS were found when searching the databases, but one Cochrane review is being prepared [35]. Data were classified according to their scientific level of evidence as Class I–IV [36]. 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 (GPP)[36]. Consensus was reached mainly through email 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 the United Kingdom in the first version; this has not been repeated in this revision.

Results

Therapeutic interventions

Acetylcholinesterase inhibitors, steroids, amantadine, modafinil, lamotrigine, coenzyme Q10, intravenous immunoglobulin (IVIg)

The effect of acetylcholinesterase inhibitors in PPS has been investigated in four studies with particular emphasis on fatigue, muscular strength, and quality of life. One open pilot study indicated a positive effect on fatigue [37, 38], but this was not confirmed in two double-blinded randomized controlled trials using a daily dose of 180 mg pyridostigmine [39, 40]. 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. One randomized study explored the effect on fatigue of 400 mg modafinil daily in PPS [41]. Modafinil was not superior to placebo, and there is Class I evidence that modafinil is not effective on fatigue 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) [42, 43]. 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.

Lamotrigine has been tried in an open study (15 patients treated with 50–100 mg lamotrigine daily), where a positive effect on quality of life (Nottingham Health Profile), pain (VAS), and fatigue (FSS) was found after 2 and 4 weeks [44]. A double-blinded randomized study is needed to confirm this finding. In a randomized double-blinded pilot study of coenzyme Q10 (200 mg daily) including 14 patients, no additional effect to resistance muscle training was found [45].

Several reports of increased levels of inflammatory markers in serum and CSF in PPS have raised the question whether immunological changes could be a part of the pathophysiology in PPS [16, 17, 46]. These findings have also presented a rationale for investigating immune-modulating therapies in PPS. Intravenous immunoglobulin (IVIg) has been tried in three therapeutic intervention studies. Gonzalez *et al.* performed a multicentre double-blinded randomized study including 135 patients where the primary endpoints were muscle strength in a preselected muscle group and quality of life measured with the SF-36 scale. The patients were treated with either placebo or 90 g IvIg, repeated after 3 months. A significant difference on muscle strength was found, but no significant effect on the SF-36 on pain, balance, or sleep quality[47]. Farbu *et al.* performed a double-blinded randomized study with 20 patients with the primary endpoints muscle strength (isometric), pain (VAS), and fatigue (FSS) after 3 months [48]. The patients were treated with one dose of IvIg (2 g/kg body weight). A significant effect was found on pain, but not on muscle strength or fatigue. One open study with 14 patients explored the effect of 90 mg IvIg on muscle strength, physical ability measured by walking test, and quality of life (SF-36) [49]. There was a positive effect on quality of life, but not on muscle strength or physical ability. These studies indicate that IvIg could have a modest therapeutic benefit in PPS, but they include a small number of patients, the results are diverging according to which symptoms improving after treatment, and the IvIg has not been compared with other therapies like specific training programmes. There is also a remaining question about the appropriate dose of IvIg and therapeutic interval. Hence, IvIg can at present not be recommended as standard treatment in PPS, despite two Class 1 studies [50].

Muscular training

It has been claimed that muscular overuse and training may worsen the symptoms in patients with residual weakness after paralytic polio, and even provoke a further loss of muscular strength.[51]. Many post-polio patients have been advised to avoid muscular overuse and intensive training [4, 52]. Studies of morphology and oxidative capacity in the tibialis anterior muscle indicate a high muscular activity due to gait and weight bearing [53, 54]. 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 [55]. This indicates a more pronounced denervation-reinnervation process in the tibialis muscle, which may be due to 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 to absence of training or less muscular activity. On the contrary, patients who reported regular physical activity had fewer symptoms and a higher functional level than physically inactive patients [11, 56]. One randomized controlled trial reported significant improvement in muscular strength after a 12-week training programme with isometric contraction of hand muscles [57]. Non-randomized trials with training programmes lasting from 6 weeks to 6 months involving both isokinetic, isometric, and endurance muscular training have shown a significant increase in both isokinetic and isometric muscle strength [58–61]. Oncu *et al.* found that both time-limited hospital and home exercise programmes improved fatigue and quality of life in the short term [62]. No complications or side effects were reported. Hence, there is evidence at Class II and III that supervised training programmes increase muscle strength and can improve quality of life and relieve fatigue in patients with post-polio syndrome. Two follow-up open studies of multidisciplinary rehabilitation report a positive effect on fatigue and physical capacity up to 1 year after the intervention [63, 64]. This is promising, but long-term effects (several 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 cycle [65] (Class I). Aerobic training in upper extremities had a beneficial effect on oxygen consumption, minute ventilation, power, and exercise time [66] (Class II). Aerobic walking exercises can help to economize movements and increase endurance without improvement in cardiovascular fitness [67]. 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 PPS patients in general. Most of the participating patients in these studies younger than 60 years, and the effect of exercise programmes older patients 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 [68]. Significant improvement was found only for the two groups with exercise (Class II). The endpoints in this study were combinations of several symptoms. Further studies are needed to identify improvement on particular symptoms before conclusions are drawn regarding 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 [69]. 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 wellbeing in a controlled but not randomized study (Class III) [70]. A qualitative interview study (Class IV) indicated a positive effect on the self-confidence when performing group training in water [71].

Respiratory aid

Reduced pulmonary function due to weak respiratory muscles and/or chest deformities may occur in patients with previous polio [22, 72]. Patients with chest deformities have an increased risk of nocturnal hypoventilation and sleep-disordered breathing [22, 73, 74]. The preva-

lence of respiratory impairment is highest among patients who were treated with artificial ventilation in the acute phase [22]. Shortness of breath is a common complaint in many post-polio patients, but is not necessarily related to respiratory impairment, but rather to orthopaedic and general medication problems. 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 [10, 75]. Respiratory impairment can occur without shortness of breath and can present with daytime somnolence, morning headache, and fatigue [67]. 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 such as chest infections, further respiratory decline, and invasive ventilatory aid (tracheostomy) [73, 76], and also improve exercise capacity [77] (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 [78] (Class III). For patients already using intermittent respiratory aids, respiratory muscle training is useful [79] (Class IV). General precautions such as stopping smoking, mobilization of secretions, and cough assistance are beneficial [73].

Bulbar symptoms

Weakening of bulbar muscles causing dysphagia, weakness of voice, and vocal changes have been reported among patients with PPS [80–83]. Case reports indicate that speech therapy and laryngeal muscle training are useful for these patients (Class IV) [83].

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 [4, 6, 84, 85]. 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 (GPPs). 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 [10]. On the other hand, a recent weight gain was found to be a predictive factor for PPS [86]. Sleep disorders are common among PPS patients [10], 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 [87–89]. It is widely accepted that obesity is related to obstructive sleep apnoea, and weight control is crucial for this disorder [90]. The number of patients receiving mechanical home ventilation because of obesity-induced hypoventilation has increased [91]. 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 lightweight carbon orthoses can be useful and increase walking ability in polio patients with new pareses [92]. This has been confirmed in two other open uncontrolled studies [93, 94], and there is Class III evidence that lightweight orthoses should be preferred compared to metal braces. Biomechanical analysis of the walking pattern can lead to optimal design of orthoses and improve function in the lower limbs (Class IV) [94, 95].

Frequent periods of rest, energy conservation, and work simplification skills are thought to be useful for patients with fatigue [96].

Coming to terms with new disabilities, educational interventions

New loss of function, increase in disability, and handicap are common in post-polio patients [5, 10, 97]. This can lead to reduced wellbeing 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' [71, 98] (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) [99].

Recommendations

Level A

- Some controlled studies of potential specific medical treatments for PPS have been completed, and no definitive therapeutic effect has been reported for the agents pyridostigmine, steroids, amantadine, modafinil, and coenzyme Q10.

Level B

- Supervised 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. A prolonged effect up to one year after well-defined training programmes has been reported.
- There are no studies evaluating the effect of muscular training in patients with severe weakness and the long-term effect of such training is 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 wellbeing.
- Lightweight carbon orthoses can be more proper than metal orthoses.

Good Practice Points

- Weight loss, and adjustment and introduction of properly fitted assistive devices is helpful, but lack significant scientific evidence.

New revision of guidelines

Prospective follow-up studies evaluating 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. A potential positive effect of IvIg in PPS has been claimed in three recent studies, and follow-up studies to investigate whether IvIg could be a therapeutic option are needed.

Conflicts of interest

The authors have reported no conflicts of interests.

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