

Post-Polio Research at AMC Amsterdam

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The research on post-polio syndrome in Amsterdam started in 1989 and was initiated by professor Marianne de Visser, neurologist. From that time on increasing numbers of Dutch patients with post-polio syndrome came to the AMC Amsterdam. Post-polio research has continued in Amsterdam, led by Marianne de Visser, Anita Beelen and Frans Nollet, resulting in 29 peer reviewed scientific papers up till now. PhD theses were written by Barbara Ivanyi in 1999, Frans Nollet in 2002, Herwin Horemans in 2005, Merel Brehm in 2007, and Janneke Stolwijk-Swüste in 2009.

At present 4 PhD students in the Dept of Rehabilitation are doing research in the field of polio.

Research focuses on clinical studies. Some results are summarized and can be categorized as:

- I Epidemiological and longitudinal studies
- II Diagnostic studies
- III Physiological studies
- IV Intervention studies
- V Methodological studies

Epidemiological and longitudinal studies

Polio victims from the last large epidemic in The Netherlands in 1956 with almost 1800 cases were studied 39 years later. In this population-based study among 260 respondents almost 60% experienced signs of new weakness, increased disabilities and handicaps and diminished health-related quality of life. The use of devices and adaptations had increased.(8,12)

A cohort of 103 polio patients was followed for six years. 27 of them had stable polio and 76 post-polio syndrome.(7,14) It appeared that health-related quality of life of the patients with PPS was lower compared to the stable functioning polio individuals. Over the years physical functioning did not change much. However, it appeared that the severity of paresis at baseline was a prognostic factor for decline in physical functioning in six years. These results supported the concept of overuse, that a (slow) decline in muscle mass, as a late effect of polio, may lead to a decline in physical functioning as the reduced muscle capacity becomes less able to meet the demands of daily physical activities.

In a systematic review of the literature we concluded that so far no conclusions can be drawn from the literature with regard to the functional course or prognostic factors in late-onset polio sequelae.(23) The rate of decline in muscle strength is slow, and prognostic factors have not yet been identified. Long-term follow-up studies with unselected study populations and age-matched controls are needed, with specific focus on prognostic factors.

Therefore we are presently conducting the CARPA-Polio study (Comorbidity and Aging Effects in Rehabilitation Populations on Activities). The longitudinal CARPA study focuses on the effects of aging and co-morbidity on functioning over time in 3 patients groups: Polio, M Parkinson, hip and knee osteoarthritis. The CARPA-Polio cohort includes 168 polio individuals.(26) Individuals range in age between 45 and 85 years and in contrast with many other studies, co-morbidities are not excluded but its influence on the time course is studied to reflect what happens in reality with aging. At the moment the participants in the study have been followed for 5 years. Some results have been published and included in the thesis by Janneke Stolwijk-Swüste. Age and co-morbidities were found to be negatively associated with physical functioning and physical independence. The influence of these factors on the changes over time is limited.(31) More

publications from this cohort-study will follow in the next years. At this moment the 8-years measurements are underway.

Diagnostic studies

The value of muscle computed tomography (CT) was studied. It was shown that muscles of post-polio patients experiencing new muscle weakness showed significantly more CT scan abnormalities compared with stable post-polio patients.(5) Muscle CT scan evaluation was considered a useful adjunct to muscle strength assessment and is now routine procedure in clinical practice. Furthermore, sleep complaints were inventoried. It appeared that up to half of post-polio patients reported complaints of disordered sleep, which was likely to influence daytime functioning. This was not further analyzed.(4) In the CARPA-study we have investigated respiration further in collaboration with pulmonologists from the Center for Home Ventilation in Utrecht. A paper is in preparation.

Physiological studies

Aspects of muscle function and exercise capacity were studied. It appeared that exercise capacity of polio individuals was mainly determined by the available muscle mass. No convincing evidence was found for a poor cardio respiratory condition. Results were comparable to normally active healthy controls.(11) We confirmed reports from others that polio individuals, especially those with post-polio syndrome may have difficulty with activating their muscles and are thus not fully able to recruit the available capacity.(13, 19) A clinical relevant finding is that the energy cost of walking is directly related to the severity of polio residuals.(24) This implicates that in case of two severely affected legs walking may cost twice (or even more) energy as compared to healthy people. Together with a reduced muscle mass this implies that 'one has to do more with less' substantiating the concept of overuse as a major cause of post-polio complaints. However, it appeared that only those individuals with severely reduced walking ability, reduced their walking activity in daily life.(22)

Intervention studies

In 2003 we reported a study on the effects of pyridostigmine (a drug that improves neuromuscular transmission) on fatigue, muscle strength and functioning in post-polio syndrome.(15) Unfortunately, we found no effect, which was in line with the results published earlier by Trojan et al. Our hope was that an effect could be found with different outcomes in selected polio individuals, those with proven neuromuscular transmission disturbances.(10) However, this was not the case. Since, some limited effects were found on 2 minutes walking distance, a potential benefit of pyridostigmine can not entirely be ruled out. However, that would require another study, accounting for individual differences in drug uptake. At present no such study is undertaken.

Another area of interventions is innovation and biomechanical optimization of custom-made leg braces. We demonstrated that the energy cost of walking can be reduced substantially by improving braces.(27) A chapter on state-of-the-art carbon composite orthoses for post-polio syndrome was written for the latest edition of the Atlas of Orthoses and Assistive Devices by the American Association of Orthopedic Surgery issued in 2008.(28) At the moment, a grant from the national health council has been obtained to write a clinical prescription guideline. Research on the innovation of braces is ongoing in collaboration with orthopedic technicians and industry.

Methodological studies

In scientific research it is important to investigate the measurement properties of the instruments that are applied: questionnaires, time scored tests, strength tests, (electro)physiological measurements and so on. A number of papers have been published in this area. It appears that strength measurements with a hand-dynamometer, but also in a fixed chair-dynamometer show large variations and are not very sensitive to detect small changes over time in individuals.(9,19) This implies that it is not easily possible to conclude that strength has really declined in evaluating a person with post-polio syndrome over time. It appears that walking

tests and measurements of energy consumption are better able to detect individual changes, although the sensitivity to detect change is less in polio individuals than in healthy controls. (21,24) In a recent paper, we recommended the Medical Outcomes Study Short Form 36 scale Physical Functioning and a 2-min walk test at self-selected speed to be used as core qualifiers for physical functioning, the major increasing disability in late-onset sequelae of poliomyelitis, to assess perceived physical performance and walking capacity in research and clinical practice. (29)

Research in progress

CARPA-continued

At present we are following up the CARPA cohort that is focusing on aging and co-morbidity. The 8-years measurements are presently being conducted. Within these data several aspects are being studied among others fatigue.

PhD student: Irene Tersteeg, MD

Funding: The Netherlands Organisation for Health Research and Development (ZonMW)

FACTS2PPS

A multi-center intervention study to reduce fatigue and improve functioning. Two different strategies are being investigated physical exercise and a cognitive behavioral approach. The FACTS2PPS study (30) is part of a larger project FACTS2NMD coordinated by AMC and involving also other neuromuscular disorders (FACTS2MND, FACTS2FSD). The Total FACTS2NMD consortium involves 5 PhD students, one of them fully dedicated to patients perspectives.

PhD Students: Fieke Koopman, MD and Eric Voorn, MSc

Funding: the Prinses Beatrix Fonds (PBF); The Dutch Public Fund for Neuromuscular Disorders and The Netherlands Organisation for Health Research and Development (ZonMW).

Trial Register: <http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=1371>

MUPPET

Muscle and motor Unit changes in Post-Polio syndrome Evaluated after Ten years.

In this study the patient group that was involved in the pyridostigmine trial (15) is reinvestigated after 10 years in comparison with healthy controls focusing on changes in muscle strength and motor-unit characteristics.

PhD Student: Alice Bickerstaffe, MD

Funding: the Prinses Beatrix Fonds (PBF); The Dutch Public Fund for Neuromuscular Disorders.

ORTHOTIC PRESCRIPTION GUIDELINE PPS

In this project a guideline is developed for polio based on evidence and expert opinions including clinicians from different disciplines (rehabilitation medicine, orthopedics, neurology, physical therapy), orthotists, biomechanical engineers, insurance representatives and patients. Based on the 'Process Description for Devices' all steps in the prescription process are being described. The guideline will be formatted as a handbook.

Project leader: Merel Brehm, PhD

Funding: The Netherlands Organisation for Health Research and Development (ZonMW), The National Health Council.

Senior-researchers involved: Anita Beelen, PhD, Merel Brehm, PhD, Carine van Schie, PhD.

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