Neonatal brachial plexus palsy : impact throughout the lifespan

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CHAPTER NINE

Summary and General discussion

SUMMARY

This thesis describes various aspects of the impact of neonatal brachial plexus palsy (NBPP) throughout the patients' lifespan, with a special focus on activities of daily life and participation, Quality of Life (QoL), healthcare usage and information needs. Furthermore, it is concerned with the development and evaluation of measurement instruments for the outcomes of NBPP.

Chapter 1, the general introduction, describes the characteristic features of NBPP with regard to the extent and severity of the lesion and its natural course. Conservative treatment, including pediatric physical therapy, as well as primary and secondary surgical treatment options are described. Important aspects and consequences of NBPP are listed in relation to the International Classification of Functioning, Disability and Health, the ICF.[1] Using this model, common assessment instruments to measure the outcome of NBPP are introduced.

The outcome of secondary shoulder surgery in children with NBPP has been described in several studies, but mainly at the level of the ICF Body Functions and Structure component. An exploration of the outcomes concerning the ICF Body Functions and Structure, Activity and Participation components, including parental expectations and satisfaction was lacking so far. **Chapter 2** describes the comprehensive evaluation of the short-term effects of a combined internal contracture release and a muscle tendon transfer (mm. Latissimus Dorsi and Teres Major) in children with NBPP with respect to arm and hand function, QoL and parental satisfaction. The aim of this procedure is to improve active shoulder external rotation range of motion (ROM) and thus the ability to bring the hand to the head and to the mouth, the use of the affected arm in bimanual activities, and to prevent progression of shoulder deformity. A prospective study on the effect of an external rotationplasty, including 10 children, aged 3-10 years old has been conducted. Children were assessed preoperatively and 3, 6 and 12 months post-operatively. This study showed that all aforementioned functions and activities improved significantly in the year following the intervention. However, a negative effect on shoulder backward flexion ROM and bringing the hand to the back was seen. Parent-reported QoL regarding upper extremity functioning and global functioning improved significantly over a period of 12 months. The majority of parents were satisfied with the results of the surgery and their expectations regarding the improvement of daily activities and sports were mostly met.

Studies describing the long-term outcomes of secondary shoulder surgery for children with NBPP usually combine the data of those children with and without primary (nerve) surgery history. **Chapter 3** describes separately the functional sequelae over time of children with and without primary (nerve) surgery. A retrospective study was conducted using data gathered according to a standardized clinical protocol. This study included 115 children with NBPP, both with (n=82) and without prior primary (nerve) surgery (n=33). Average follow-up time was 6 years (standard deviation 3.3 years). Data on active and passive ROM as well as

Mallet scores gathered before surgery and at 1, 3, 5 and 10 years after surgery, were compared. Overall, shoulder passive and active external rotation, (glenohumeral) abduction and forward flexion ROM as well as almost all Mallet score items improved significantly over time. Over the course of time the positive effects of surgery decreased to some extent, but the differences with the preoperative situation remained statistically significant. Just as in the study described in Chapter 2, backward shoulder flexion and the ability to bring the hand to the back, as measured with the Mallet score, decreased significantly.
Children without prior primary (nerve) surgery had better preoperative shoulder function than children who had undergone primary (nerve) surgery. These conservatively treated children had an overall better shoulder function after secondary shoulder surgery at all follow-up time-points. Only active and passive external rotation, both in 0° and 90° abduction, were slightly better at all follow-up time-points for children who had undergone primary (nerve) surgery.
These outcomes indicate that these subgroups comprise patients with a different phenotype (i.e. severity of brachial plexus lesion) and outcomes for these different cohorts should be reported separately. Thereby, an overestimation or underestimation of the results of the secondary intervention will be prevented. Thus, more tailored and personalized information on the expected treatment outcome can be provided to children and their parents, ensuring the quality of the shared decision-making process.

Patient or parent-reported outcome measures (PROMs) become increasingly more important in the evaluation of treatment outcome. Most validated instruments for outcomes in NBPP are only available in English, which makes them unsuitable for use in Dutch studies. It is therefore necessary to officially translate, cross-culturally adapt and validate instruments for the Dutch language. The Pediatric Outcome Data Collecting Instrument (PODCI) is a PROM for musculoskeletal conditions, validated for use in NBPP, which was previously not available in Dutch. The PODCI is available in a 2-10 and a 10-18 year old parent-reported version, and a 10-18 year old self-reported version. It includes 83-86 questions (depending on the version), yielding 5 subscale scores and a total score. **Chapter 4** concerns the translation and cross-cultural adaptation, according to international guidelines for cross cultural adaptation[2-4], of the aforementioned PODCI versions into the Dutch language. Furthermore, the validation of the 2-10 year parent-reported version for use in children with NBPP was described. The final Dutch PODCI 2-10 year old parent-reported version was first field-tested in 10 children with NBPP, aged 3-10 years old. For validation, the questionnaire was used in 10 children undergoing secondary shoulder surgery and was administered preoperatively and 12 months post-operatively. For test-retest reliability the PODCI was administered twice again with an interval of 2 weeks after the 12 months post-operative follow-up. It was concluded that the Dutch PODCI is a useful and reliable tool to evaluate QoL and functioning in children with NBPP. Overall, it’s internal consistency, responsiveness to change, construct validity and test-retest reliability was found to be good.

Because of a lack of available outcome measures concerning hand use in children with unilateral paresis, the Hand Use at Home questionnaire (HUH) was recently developed and tested in children with NBPP and unilateral Cerebral Palsy (UCP). This instrument measures the spontaneous hand use during daily life activities in the home environment, in children with unilateral upper limb paresis. Using Rasch analysis, the HUH was found to be a valid measure which showed good psychometric properties in terms of construct validity, internal consistency and discriminative capacity.[5] **Chapter 5** describes further evidence for the construct validity and test-retest reliability of the HUH questionnaire in the same patient groups. To measure the construct validity, 191 children with NBPP and 79 children with UCP were included. Parents of these children filled out the HUH once and additionally filled out the PODCI (NBPP only) or the Children's Hand use Experience Questionnaire (CHEQ; UCP only). For test-retest reliability 56 parents (16 children with NBPP and 40 with UCP) filled out a second HUH within 2-4 weeks after the first.

Results of this study showed that the HUH is a valid and reliable measure to be used in children with NBPP or UCP aged 3 to 10 years old. A significant correlation was found between the HUH and NBPP lesion-extent, indicating that greater lesion-extent is related to a lower amount of spontaneous hand-use. A relatively weak correlation was found between the HUH and treatment history in children with NBPP. In children with UCP a weak correlation with the Manual Ability Classification System (MACS) levels was found, indicating that a good ability to handle objects is not directly associated with a high amount of spontaneous use of the affected arm/hand. Test-retest reliability of the HUH was found to be excellent, based on a good Intra Class Correlation coefficient (ICC) and good agreement between the first and second HUH scores (Bland-Altman[6]). Based on these results it was concluded that the HUH can be used by parents of children with unilateral upper-limb paresis, aged 3-10 years, to report spontaneous hand-use of their child during daily activities. It provides clinicians and researchers with more insight into daily-life upper-limb performance. Future research into the ability of the HUH to detect changes over time should be conducted to provide the remaining psychometric properties of the HUH.

Most research on the consequences of NBPP has so far been mainly aimed at outcomes on the level of the Body Functions and Structure component of the ICF, in particular in very young children. To investigate activities and participation, QoL, family impact and healthcare use and information needs of patients with NBPP, the so-called ZAP Plexus study (Zorg (Care), Activities and Participation in patients with NBPP) was initiated in 2014. All patients who had ever visited the Leiden Nerve Center, a tertiary referral NBPP expert center within the Leiden University Medical Center (LUMC), were invited to participate in this cross-sectional study using electronic questionnaires. Invitations were sent to 1142 patients and/or parents of whom 508 (45%) participated. Of the participating patients 59 (12%) were between 0 and 1 years old, 226 (45%) between 2-9 years old, 180 (35%) between 10-18 years old and 43 (8%) were between the age of 19 and 61 years. The next three chapters describe the first analyses of the obtained data.

In **Chapter 6** parent-perceived family impact, QoL and upper extremity functioning in 59 children with NBPP in the very young age group (6-30 months old) are described. The parents of these 59 children were asked to fill out the PedsQL™ Family Impact Measure (FIM), the TNO-AZL (Dutch Organisation of Applied Natural Science and Academic Hospital Leiden) Preschool children's QoL (TAPQOL) questionnaire and a set of questions regarding upper extremity functioning of their child.

This study showed that lower FIM scores were associated with younger age, greater lesion-extent, affected side (right), primary (nerve) surgery treatment history and currently being in follow-up. The parents' perception of the children's' QoL was comparable to a healthy reference group for 66% of the TAPQOL scales. Having more upper extremity functioning problems was associated with greater lesion-extent and nerve surgery treatment history. Parents who reported more of these problems tended to worry more than parents who reported less problems.

The findings from this study confirm that parents to some extent find that having a child with NBPP has an impact on their family. No study in very young children has previously reported that right-sided lesions and more upper extremity functioning problems were associated with a greater impact on the family. It is essential for healthcare professionals to take these findings into account at an early stage when counselling parents and their family in order to reduce the impact on the family.

The ZAP plexus study results regarding healthcare use since birth and in the past 12 months, and information needs are reported in **Chapter 7.** Data from 465 patients between the age of 0 and 18 years old who completed questions on contacts with the plexus team and/or 11 other healthcare professionals and current information needs regarding 12 NBPP related topics were analysed. Furthermore, patient and NBPP characteristics and follow-up status at the Leiden Nerve Center (early/late/no discharge) were recorded.

Fifty-nine patients were 0-2 year of age, 226 were 2-9 years old and 180 were 10-18 years of age. There were 193 patients (42%) who had been discharged from follow-up, 83 of whom were categorized as 'early discharged' (defined as <1 year of age, due to spontaneous lesion recovery).

This study showed that healthcare use of children with NBPP in The Netherlands is considerable from the moment of the initial diagnosis. All parents reported to have had contact with at least 1 and up to 11 healthcare professionals (range depending on lesion severity) shortly after birth in addition to the involvement of the plexus team. Healthcare use decreased over time with 288 parents reporting to have had contact with at least 1 and up to 7 healthcare professionals (range depending on lesion severity, treatment history and follow-up status) over the past 12 months besides the possible involvement of the plexus team. Healthcare use in the past 12 months was statistically significantly associated with ongoing treatment in the Leiden Nerve Center, with greater lesion-extent, surgical treatment, lower QoL and diminished physical functioning. A relatively large proportion of discharged patients (81/193, 42%) still had contact with healthcare professionals due to their NBPP. Amongst them were 34 patients who were considered to be (almost) completely recovered (discharged <1 year of age). Their healthcare use indicates that, contrary to expectations, these patients may experience functional limitations. Furthermore, a relatively large proportion (228/465, 49%) of parents/patients, including 65 discharged children (either early discharged: 23/83, 28% or late discharged: 42/110, 40%), reported information needs regarding a variety of NBPP related topics (treatment, sports and physical functioning, assistive devices etc.). These findings make it clear that after discharge from specialist care, a considerable proportion of patients experience limitations and have information needs, warranting a stricter follow-up protocol and information provision.

In **Chapter 8** restrictions in participation from the patients' perspective in adolescents and adults with NBPP are described. Seventy-five adolescent and adult patients (16-61 years of age) participated of whom 33 were between 16 and 18 years, 22 between 19 and 25, 11 between 26 and 35 and 9 were between 36 and 61 years of age. Patients completed questions on the influence of NBPP on their choices regarding education and work and on their work-performance. Furthermore, the Impact on Participation/Autonomy questionnaire (IPA; 5 domains) and the Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-P; 3 domains) were administered. Additionally, health-related quality of life was assessed using the Short Form 36 (SF-36) and the Disability of the Arm, Shoulder and Hand (DASH) questionnaires and patient and NBPP characteristics were recorded.

Of the 75 participating patients, 20 (27%) were full-time students, 28 (37%) were students who also had a job, 21 (28%) were employed, 2 (3%) were unemployed and 4 (5%) were work-disabled due to their NBPP. The patients' overall HRQoL was comparable to the general population. 27/75 patients reported that neonatal brachial plexus palsy had affected their choices regarding education and 26/75 those regarding work. 33 of the 66 patients who have or had work reported impact on their work performance. On the Impact on Participation/Autonomy questionnaire, 80% (49/61) reported restrictions in the work-and-education domain, 74% in social-relations and 67% in autonomy-outdoors. 37 of the 61 patients who filled out the USER-P reported participation restrictions and they reported to be somewhat less satisfied with the participation possibilities that they had.

More restrictions in participation were associated with worse upper extremity functioning (DASH), lower QoL and more pain (SF-36) but not with lesion extent, treatment history or affected side. This may indicate that all NBPP patients, regardless of the initial severity of their lesion, may perceive restrictions in participation in later life.

The above findings are relatively new and warrant the need for optimization of care. Guiding patients in making choices on education and work at an early stage and providing tailored physical as well as psychosocial care may prevent or address restrictions, which may improve participation.

GENERAL DISCUSSION

Neonatal brachial plexus palsy (NBPP) is a birth injury to the brachial plexus with a large heterogeneity in lesion extent and severity resulting in a wide variety of functional limitations. The prognosis for spontaneous recovery has been reported as good, but a considerable proportion of patients (about 35%) is left with remaining impairments, resulting in problems in daily life activities, participation and overall quality of life (QoL).[7,8] Multiple treatment options are available, including surgery and conservative strategies, all aiming to improve the patient's functioning. As most research has so far mainly been focused on impairments of arm and hand function, more insight into the consequences of NBPP and its treatment including a broader range of aspects of health status is needed. This thesis aimed to comprehensively describe functional outcome of secondary shoulder surgery as well as the overall impact of NBPP throughout the lifespan. The latter was done within the Zorg (Care), Activities and Participation in patients with NBPP study (ZAP Plexus) conducted in the Leiden University Medical Center (LUMC).

FUNCTIONAL OUTCOME OF SECONDARY SHOULDER SURGERY

This thesis showed that, in line with previous research, secondary shoulder surgery improves function at the level of the ICF component Body Functions and Structure.[9-21] By the use of a comprehensive instrument to measure functional outcomes at the level of the ICF component Activities and Participation (i.e. the Pediatric Outcome Data Collecting Instrument; PODCI), and measuring parental satisfaction, it was shown that improvements on these aspects after surgery were also considerable. These latter findings underpin the need to define the outcomes of surgery at the level of activities and participation in future research, further supporting the important role of surgery in creating value for patients. Furthermore, this thesis also showed that both patient characteristics and outcomes of secondary shoulder surgery are different for children who have had primary (nerve) surgery as compared to outcomes for those who have only been treated conservatively. Outcomes should therefore be described separately for these subgroups.

OUTCOME MEASUREMENT IN NBPP

The abovementioned PODCI, covering different components of the ICF, was translated and cross-culturally adapted into a Dutch version according to international guidelines.[2-4] It was validated in a small series of children with NBPP who underwent shoulder surgery. Moreover, its application in a large cohort, including patients with and without nerve and/or secondary surgery, supported its usefulness in the Dutch NBPP population.

The PODCI measures upper extremity functioning in terms of difficulty in performing activities, either or not using the affected arm/hand. However, it does not measure spontaneous use of the affected arm/hand in daily life. Although there are various instruments available measuring arm/hand use, such as the ABILHAND kids[22] and the Children's Hand Experience Questionnaire (CHEQ)[23,24], these instruments are either not developed for NBPP, they have not been used in NBPP outcome studies or they do not measure parent-rated spontaneous hand use in the home environment. As a result of a national cooperation with the Sint Maartenskliniek rehabilitation centre Nijmegen, a new outcome measure, the Hand Use at Home (HUH) questionnaire was developed and tested to fill this gap.[5] The psychometric properties of this newly developed instrument were proven to be good.[5]

To further study the value of both the PODCI and the HUH in patients with NBPP, including their sensitivity to change, large prospective follow-up studies, irrespective of the treatment provided, are necessary. These studies should include well-chosen follow-up time-points (i.e. six-monthly, as six months is a time period in which rehabilitation goals are usually met or revised) and previous as well as inter current therapy, lesion extent and potential aspects other than age possibly interfering with motor development in children in general (e.g. dyspraxia, learned non-use, concurrent medical diagnoses), should be well documented and accounted for during analyses.

Generic Quality of Life questionnaires

In NBPP research the need for outcome measures, either disease-specific or generic, not only taking into account clinical impact but also the patient's perspective is underlined in a recent systematic review, performed by researchers in the LUMC.[25] This review suggested that generic QoL instruments like the TNO-AZL (Dutch Organisation of Applied Natural Science and Academic Hospital Leiden) preschool children's QoL (TAPQOL), children's QoL (TACQOL), and Adult QoL (TAAQOL) questionnaires might be of added value for this purpose.[25,26] These instruments have been used in the ZAP Plexus study, however the results of the TAPQOL only have yet been analysed in very young children (up to 2 years old). When TAPQOL scores were compared to those of healthy age-matched peers, few differences were found. Therefore, the question remains whether generic standardized questionnaires (in contrast to disease specific or individualized measures) are sensitive enough to detect problems in the NBPP population. Moreover, to date it has not yet been investigated whether the TAPQOL, TACQOL and TAAQOL can be used consecutively over time to provide comparable QoL outcomes throughout the lifespan in individual patients. Future studies should be conducted to investigate whether these instruments can be used in long-term follow-up studies.

Besides the aforementioned generic QoL instruments there are other options available such as the PedsQL™ QoL family of questionnaire.[27,28] These questionnaires have been used in several rehabilitation studies, which makes it possible to compare outcomes in children with NBPP to other patient groups.[29-31] Furthermore, there are different optional modules available for use, such as the PedsQL™ Family Impact Module (FIM) which has indeed been used in one of our studies. Using the PedsQL™ QoL questionnaires could facilitate the monitoring of different kinds of aspects of impact of NBPP throughout the pediatric lifespan using the same family of instruments.[32]

Family impact

This thesis showed that according to the perception of parents, having a 6 to 30-month-old child with NBPP had impact on their family. Younger age, greater lesion-extent, affected side (right), primary (nerve) surgery and currently being in follow-up were found to be associated with a greater family burden. The impact of having a child with NBPP on the family in the early postpartum period was not evaluated. Particularly in that phase the burden to the family may be substantial as the NBPP occurs during birth and can thus not be anticipated by parents. Adding family impact measures, such as the PedsQL™ FIM, to routine assessments and monitoring from birth on might detect family impact in an early stage, so that possible parental counselling can be started if needed.

Long term consequences of NBPP

Another part of this thesis showed that adolescents and adults perceive restrictions in participation, mainly related to work and choice of education due to their NBPP. The extent of restrictions in participation were found to be related to lower QoL and more pain. The presence of pain and functional limitations in adolescent and adult patients have been previously reported[33-35], however, NBPP participation restrictions and impact on study and career choices have only been described in a relatively old study.[36] Even though adolescent and adult patients with NBPP seem to perceive functional limitations, pain and participation restrictions, they are not frequently seen in NBPP expert centers, nor in rehabilitation settings.[34,37] As research in adult NBPP patients is scarce, and most adult patients are lost to clinical follow-up, it is not fully known what the consequences of NBPP are on the long term. In contrast, knowledge on this issue is very important as interventions in childhood are in principle performed to increase the level of functioning at adolescence and beyond.

ICF core set

To be able to determine the impact of NBPP throughout the lifespan it is important to create a common core set , such as an ICF core set, as a universally accepted overall framework to assess the outcome.[38] This framework for NBPP is not yet available. A proposition to create an ICF core set for NBPP has been made by researchers from the LUMC, encompassing 4 steps.[38] The first step concerns the conduct of a systematic review to identify outcome measures, which has already been finished.[25] The second step, a qualitative study using focus groups to identify important concepts of functioning and health in children with NBPP, has been completed as well.[39] The last 2 remaining steps, namely an expert survey and a cross-sectional study, are planned. The cross-sectional study step has been partly described in this thesis (the ZAP Plexus study) but the conduct of a cross-sectional, multicenter study remains for future research.

To be able to evaluate aspects within this future core set it is important to use a solid set of internationally accepted outcome measures. Currently, no consensus exists on which instruments are best and should be used, so that in NBPP studies multiple outcome measures are currently employed.[25,40-42] Most of these instruments concern the Body

Functions and Structure component of the ICF whereas very few address the ICF components Activity and Participation.[25] A new initiative by the Leiden Nerve Center called iPLUTO (international PLexus oUtcome sTudy group) has been launched to create consensus on which outcome measures, covering all components of the ICF, should be used.[43] According to this initiative, a worldwide expert survey was circulated among leading clinicians and researchers aiming to create an international standard on how to evaluate and express results of NBPP treatment and outcome. The preliminary results of this survey showed that about 50% of the 70 respondents agree that Patient/Parent Reported Outcome Measures (PROMs) on the level of the ICF component Activities and Participation should be included in the minimal dataset of outcome measures.[43] However, less than 20% of the respondents reported that they (or their center) have sufficient experience with PROMs to judge which PROMs should be included.[43] Therefore, ongoing efforts to disseminate and discuss the results of our study with practitioners treating the sequelae of NBPP worldwide are needed.

HEALTHCARE IN NEONATAL BRACHIAL PLEXUS PALSY

Early referral

Early referral to a specialized NBPP expert center when a more severe lesion is suspected, is very important.[44] However, also in case of doubtful severity, referral to such a tertiary center is warranted, as this thesis showed that seemingly spontaneously recovered children do report problems in later life. With an incidence rate of 1-2 per 1000 live born children[45] and about 170000-180000 births a year (CBS: statline.cbs.nl 2012-2015), approximately 200-350 children with NBPP are born every year in The Netherlands. However, the exact incidence in the Netherlands is not known. Better registration of all new NBPP patients has been tried through the Dutch Signaling Centre for Child Healthcare (Nederlands Signalerings Centrum Kindergeneeskunde, NSCK; www.nvk.nl/onderzoek/NSCK.aspx) but to date this registration system only showed few new cases each year, not by far reaching the expected number of new infants with NBPP. As data from the 3 NBPP expert centers in The Netherlands are not collectively gathered, it is unfortunately not known how many new born patients with NBPP are seen each year in these centers together. A national, as well as an international collaboration and joint data analysis – both of treated and untreated children – is of utmost importance. With the iPLUTO initiative a uniform gathering of data at fixed time points is aimed for, enabling pooling and comparison of outcome data for different treatment strategies and their outcomes.

Early and later discharge from NBPP expert centers

As stated before, this thesis provides evidence that some children who were discharged from follow-up from the Leiden Nerve Center, either because of good spontaneous recovery soon after birth or through effective surgical treatment, received active treatment for their NBPP later on. Moreover, a number of them reported problems regarding physical, mental or social functioning. Therefore, the question remains whether the current criteria for discharge are adequate. A long-term natural history clinical follow-up study may provide further answers to this question.

Healthcare use and the role of physical therapy

Healthcare use in children with NBPP, as shown in this thesis, is considerable but decreases over time depending on lesion extent, functional recovery and treatment history. In our research the pediatric physical therapist was the most frequently mentioned healthcare professional with whom patients had had, or still had, contact. The data on healthcare use in adults with NBPP have not yet been fully analysed. However, from the ZAP Plexus study it is known that about 20% of the adult patients reported having contact with a physical therapist. This makes this healthcare professional one of the most contacted healthcare providers for NBPP throughout the lifespan.

Unfortunately, literature on the effectiveness of physical therapy in the treatment of NBPP is scarce. Book chapters on pediatric physical therapy and rehabilitation usually provide general recommendations on the content of the therapy program, e.g. monitoring motor performance, joint mobility and muscle strength over time. Furthermore, they include instructions for parents on how to handle (e.g. pick up, carry, bathe and clothe) their baby and how to perform exercises to maintain passive range of motion (ROM). Multiple sources report to start therapy within 1-3 weeks after birth, but in-hospital treatment may start as soon as the day after birth.[37,46,47] Within the LUMC, pediatric physical therapy for new-born children with NBPP starts directly after birth, according to a protocol of passive ROM exercises to be carried out 7-8 times a day by pediatric physical therapists, in close cooperation with parents and nurses (personal communication S.M. Buitenhuis / J.C. van Egmond-van Dam).

The importance of continuous passive ROM exercises to maintain freedom of movement throughout time in all upper extremity joints has been underlined.[37,47-52] These exercises are performed to prevent possible contractures and joint deformities from occurring, and to keep active movement unrestrained. Combining these exercises with glenohumeral joint movement may further prevent joint and muscle contractures, and may normalise shoulder movements in growing infants.[46,49,50] There is, however, no conclusive evidence base for the effectiveness of passive ROM exercises in general. One recent study suggested that the performance of passive ROM exercises was not associated with the prevalence of shoulder joint deformities in NBPP, but that these deformities were linked to active ROM possibilities of the child.[53] In addition to passive ROM exercises the use of serial casting, orthoses, dynamic splints or botulinum toxin for contracture prevention have been described.[54-57] These studies, however, did not report on the precise content of the additional physical therapy program.

Another role of the physical therapist is monitoring and improving motor development and motor function over time, including stimulation of weight bearing activities (e.g. crawling etc.), postural alignment and muscle strength (with special attention to the rotator cuff muscles). [46,47,50] In children with NBPP, the use of the affected arm might be less than that of the unaffected arm and children with right-sided lesions have been reported to develop left-handedness.[58,59] By using compensatory strategies during activities, children may learn how to perform activities mostly using their unaffected arm, probably ignoring their affected arm leading to a 'learned non-use', developmental disregard or dyspraxia.[46,60] This phenomenon should be recognised by pediatric physical therapists and/or occupational therapists and addressed during therapy.

Constraint induced movement therapy, and possibly bimanual intensive training, have been suggested and described to possibly improve function (counteracting learned non-use)[46,49,50,61,62] However, in our clinical practice overuse as a possible result of these interventions leading to physical complaints have been frequently reported. Moreover, these interventions have not been systematically studied in NBPP and their added value to rehabilitation programs remains to be proven.

Adherence to complementary home based exercises applied and/or supervised by parents also plays an important role in the physical therapy treatment of NBPP.[47,49-51,53,63] The general notion is that children of whom parents perform or supervise these exercises consistently have better function, however, this is difficult to prove. The use of multimedia for dynamic exercise modelling was found to increase compliance, by improving both the frequency and duration of exercise.[51] The use of virtual reality (gaming) in pediatric rehabilitation is currently being tested in SMART labs in pediatric rehabilitation centers (Rijnlands and Sophia rehabilitation centers) and could possibly add to the child's exercise motivation. However, motivation and effectiveness of the exercises may decrease over time, necessitating periodical evaluation, and if needed alteration of the program.[51,63]

INFORMATION NEEDS AND INFORMATION PROVISION

Half of the patients and their parents/caregivers (49%) in the ZAP Plexus study reported that they needed far more information than given at the outpatient clinic, whereas 18% found that they had received contradicting information from different healthcare professionals. These findings underline the need to provide parents and/or patients with NBPP with adequate and uniform information. In addition, it is also important to optimize communication and the dissemination of knowledge and expertise among care providers. It is strongly recommended to develop and distribute modular information tailored to the individual patients'/parents' information needs, for example through short movies and/or electronic information brochures, provided through an interactive website. The information should be personalized according to aspects such as the lesion extent, treatment and different stages of development (e.g. when going to school, when choosing sports, study or a profession etc.).

IMPLICATIONS AND DIRECTIONS FOR FUTURE CARE AND RESEARCH

The most important findings of this thesis include the observed limitations in activities and participation, the associated healthcare use as well as the healthcare and information needs, even in patients with NBPP who are discharged from follow-up. Furthermore, a possible lack of attention was found for the impact NBPP has on family life as a whole.
Most experts agree upon the need for more and better assessments of all these aspects in NBPP patients and their family, yet there is little consensus on a core set of outcome measures to be used at long-term follow-up. Therefore, the following implications to improve patient care can be made:

- Family impact
    - From birth on more attention should be paid to the family impact of the NBPP and, if indicated by a simple screening test or parents themselves, early counselling of parents and their families should be initiated.
    - Healthcare professionals providing mental support (i.e. psychologists, social workers) should be part of NBPP expert teams and counselled if needed.
- Routine follow-up
    - A stricter monitoring protocol reaching into adulthood should be used taking into account all components of the ICF. Constructing an international database as a result of the iPLUTO initiative is recommend.
    - Implementation of the HUH questionnaire at the Leiden Nerve Center and other NBPP centers around the world.
    - NBPP expert teams should pro-actively reach out to patients and/or their parents, for example via e-mail or phone, to verify whether or not impairments on the level of body functions and structure and/or restrictions in activities or participation exist.
- Information needs
    - Information provision to meet the information needs of patients and/or parents should be optimized and tailored according to individual patients’ and parents’ needs and preferred modes of delivery.
- Physical therapy
    - A physical therapy consensus management protocol (including recommendations on forms, duration, frequencies, resistance, home exercises and parental involvement etc.) for different ages and development stages throughout the lifespan should be established and systematically evaluated.

All recommendations described above should be discussed, developed and implemented in close collaboration with patients and parents and the patient organisation.

The following directions for future research should be considered:

- New research
  - A follow-up study on family impact of NBPP at birth and at one, three, six and 12 months of age and yearly thereafter to gather additional information on the impact on the family over time.
  - A follow-up study on participation, in particular work-related problems and needs, reaching out to all adolescent and adult patients with NBPP.
  - Comparison of different physical therapy treatment protocols (types of exercises and their intensity, duration and frequency), to provide evidence for best practice in physical therapy.
  - Wearable accelerometers, or other forms of activity monitors, worn for at least a week, should be used to evaluate daily activities in a more objective way. Such instruments could also be used to perform predefined tests at home, prior to the visit at the clinic, or in case of functional deterioration.
- ZAP Plexus based future research
  - A cross-sectional study, and possibly afterwards a follow-up study, on physical activity and sports participation in children with NBPP to be able to provide more adequate information on these topics in clinical care.
  - An analysis of the remaining ZAP plexus data for gaining further insight into the impact of NBPP (i.e. sensibility and sensitisation, upper extremity function, healthcare use and information needs in adult NBPP patients, QoL and participation) and to provide evidence on what instruments are able to detect problems in the NBPP population.
  - Further investigate the value of both the PODCI and the HUH in patients with NBPP, including their sensitivity to change.
  - A follow-up ZAP plexus study, aiming to further describe the course of NBPP and its consequences over time in the now defined and well-described cohort.

All these efforts are necessary to increase insight into all NBPP patients' health status and healthcare needs which will lead to improved patient care in this lifelong condition. With improved care aiming for better participation within society, supporting the patient to adapt to each phase in life if needed, the impact of NBPP throughout the lifespan can be reduced resulting in better quality of life.

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