Recurrent pain in adolescents with cerebral palsy: a longitudinal population-based study

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This original article is commented by Huang on page 282 of this issue.

AIM To investigate the pain characteristics, pain interference with activities of daily living, and use of analgesics in adolescents with cerebral palsy (CP) and compare the results with previous findings.

METHOD Sixty-seven adolescents (median age 14y 4mo, range 12y 2mo–17y, 28 females, 39 males) classified in Gross Motor Function Classification System (GMFCS) levels III to V, who participated in a CP surveillance programme, were assessed on pain measures twice, 5 years apart. Primary caregivers marked recurrent pain sites and graded pain interference with activities of daily living and sleep. Information on pain severity was obtained through two questions from the Child Health Questionnaire (CHQ) and were transformed into a pain score scaled from 0 to 100, where 100 represented no pain. The use of short-acting analgesics was recorded.

RESULTS Over 5 years, the prevalence of recurrent pain, number of pain sites, pain intensity, and pain frequency all increased significantly. The most frequent pain sites were the hip/thigh in GMFCS level V and knee in GMFCS level III. The median CHQ pain score decreased from 60 to 40 (<0.001). Pain interference with activities of daily living increased (p=0.011) but not for sleep. Twenty-eight of 54 participants with moderate or severe pain (CHQ pain score ≤60) received no short-acting analgesics.

INTERPRETATION In adolescents with CP, pain increased over 5 years despite follow-up in a surveillance programme. For enhanced management of pain, we propose that an algorithm on pain should be included in surveillance programmes.

Parents and medical professionals consider pain a highly important target for interventions in adolescents with cerebral palsy (CP).1 A systematic review reported pain prevalence up to 75%.2 Prevalence was higher in children and individuals with greater motor impairment.3,4 Furthermore, individuals with more severe CP tended to have more intense and more frequent pain.3 A recent cross-sectional, register-based study revealed that pain prevalence at different sites varied for different levels of motor impairment, with more hip/thigh pain in individuals with greater motor impairment, more knee pain in individuals needing walking aids, and more lower leg/foot pain in those with less motor impairment.4 Importantly, pain influenced societal participation and quality of life negatively.3–7 According to the National Institute for Health and Care Excellence (NICE) guidelines on CP, pain should be addressed at each clinical encounter.8

Longitudinal studies on pain characteristics and interference with activities of daily living in the paediatric population with CP would be useful for patient education, pain management, and improvement of surveillance programmes; however, such studies are scarce.

With regard to pain management, the use of short-acting analgesics varies from one in three to one in four patients.7,6 In both studies, the proportion of the population with pain was greater than the proportion receiving analgesics, indicating that the full potential of analgesics might not be fully exploited. In line with this, a retrospective study confirmed that pain reported repeatedly in a CP surveillance programme was largely neglected in corresponding medical records.10 This indicates that we need to reconsider both how we assess pain in CP surveillance programmes and bridge the assessments into pain management.

The aims of the present study were to investigate pain characteristics, pain interference with activities of daily living, and the use of short-acting analgesics in a cohort of adolescents participating in a CP surveillance programme and compare the results with findings reported 5 years earlier.
METHOD

The study had both a cross-sectional and longitudinal design. All 136 eligible adolescents, born between 2002 and 2006, living in south-eastern Norway, and enrolled in the Norwegian Quality and Surveillance Registry for Cerebral Palsy, with bilateral CP and in Gross Motor Function Classification System (GMFCS) levels III to V were invited to participate. Data on CP type according to the Surveillance of Cerebral Palsy in Europe, communication function according to the Communication Function Classification System, and gross motor function according to the GMFCS were retrieved from the Norwegian Quality and Surveillance Registry for Cerebral Palsy.

The study was approved by the Regional Ethics Committee, REC South-East (no. 2012/2258 REK). Written informed consent was obtained for 77 adolescents (57%) in 2013 to 2014. Six participants were lost to follow-up 5 years later. Thus, 71 participants received a postal invitation to the second data collection; of these, 67 (94%) participated.

Pain assessment

Data were collected through a questionnaire sent by surface mail to primary caregivers and a telephone interview. The questionnaire consisted of selected questions from the Brief Pain Inventory (BPI), Norwegian version and Child Health Questionnaire (CHQ), Norwegian version. The CHQ has been validated for CP, the reliability of proxy reporting on pain interference in severe CP according to the BPI has been found to be satisfactory.

Pain occurring for at least 4 weeks or more was defined as ‘recurrent pain’ and further noted as ‘pain’. Pain sites with recurrent pain were marked on the BPI body outline.

Pain severity according to the CHQ was recorded for the most severe pain site (selected by the respondent). The two CHQ questions were (1) ‘During the past 4 weeks, how much bodily pain or discomfort has your child had?’ with the response alternatives ‘none, very mild, mild, moderate, severe, and very severe’, and (2) ‘During the past 4 weeks, how often has your child had bodily pain or discomfort?’ with the response alternatives ‘none of the time, once or twice, a few times, fairly often, very often, and every day or almost every day’, and were given scores from 1 to 6 respectively. These scores were transformed by an algorithm into a CHQ pain score scaled from 0 to 100, where 100 represented no pain. After careful consideration and with the aim of defining a pain scoring system feasible for recommendations in a CP surveillance protocol, we categorized CHQ pain scores as 0 to 30 (severe pain), 40 to 60 (moderate pain), and 70 to 90 (mild pain). A change in CHQ pain score of 20 and less was considered as no change in pain, while a change of 30 or more was regarded as less or more pain.

The BPI questions on pain interference with activities of daily living and sleep were: ‘On a scale from 0 to 10 (10=total influence), which value best describes how much pain influenced your child’s ‘activities of daily living’ and ‘sleep’ respectively?’ The time span was modified from 2 to 4 weeks to correspond with the CHQ.

The telephone interview started with the definition of recurrent pain and consisted of the following questions with an open response: Did your child have recurrent pain in the last 4 weeks? What are the pain sites? What relieves the pain? What increases the pain? Has your child received any medication to relieve pain (such as paracetamol, ibuprofen, or naproxen) over the past 4 weeks? Use of intrathecal baclofen (ITB) was also recorded.

Statistical analysis

SPSS v27 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. Data were presented either as frequency, percentage, proportion, or median with range. Correlation between variables was explored by calculating Spearman’s correlation coefficient, $r_s$ (significant when $p<0.05$ and $r_s>0.30$). Non-parametric statistics (Mann–Whitney U test) were applied for ordinal variables and skewed continuous variables. In linear regression, variables were included in the multivariate linear regression analyses if $p<0.1$ in the univariate analyses. Normality of residuals was satisfied. In the longitudinal analyses, proportions were analysed with McNemar’s test, continuous variables with a paired samples $t$-test, and ordinal variables with a Wilcoxon signed-rank test. All tests were two-sided. Differences were significant if $p<0.05$.

Three participants (4.4%) had missing values on pain interference at the first data collection point. Imputation was not performed since this would most likely not influence the statistical analyses.

RESULTS

The characteristics of the participants are shown in Table 1. The number of participants with pain increased from 45 to 62 over the 5-year period ($p<0.001$) and the median number of pain sites in each participant increased from one (range 0–6) to three (range 0–13; $p<0.001$).

Pain prevalence increased at all sites and the increase was statistically significant in the neck and knee (Table 2). Pain prevalence increased across all GMFCS levels and the increase was statistically significant in GMFCS level III. The hip/thigh was the most common pain site in GMFCS level V, while the hip/thigh and lower leg/foot were the most common sites in GMFCS level IV and the knee in GMFCS level III. The prevalence of abdominal pain was highest in GMFCS level V.

There was a significant correlation between pain intensity and pain frequency ($r_s=0.494$, $p<0.001$). Both pain intensity and frequency increased during the 5-year period (both $p<0.001$). The median CHQ pain score decreased from 60 to 40 ($p<0.001$). Decrease across GMFCS levels...
was: GMFCS level III, 100 to 40 \( (p=0.002) \); GMFCS level IV, 60 to 50 \( (p=0.050) \); and GMFCS level V, 50 to 30 \( (p=0.007) \). There were 34 (51\%) participants with more pain (lower CHQ score) than 5 years before, 27 (40\%) with no change, and six (9\%) with less pain. In the univariate analyses, lower age and GMFCS level V were possible predictors of low CHQ score \( (B=7.8, 95\% \text{ confidence interval} [CI]=3.6–12.1, p<0.001) \) and negative correlations between CHQ pain score and both interference with activities of daily living and sleep \( (r_s=−0.521, p<0.001) \) and \( r_s=−0.370, p=0.002 \) respectively). Participants classified in GMFCS level III had significantly lower interference with activities of daily living (GMFCS level III vs GMFCS level IV \( r_s=0.043 \) and GMFCS III vs GMFCS level V \( p=0.001) \) and sleep (GMFCS level III vs GMFCS level IV \( r_s=0.009 \) and GMFCS level III vs GMFCS level V \( p=0.001) \) than participants in GMFCS levels IV and V. There were no significant differences between GMFCS levels IV and V regarding pain interference with activities of daily living and sleep \( (p=0.235) \) and \( p=0.050 \) respectively). Median pain interference with activities of daily living increased over the 5-year period from 1.5 (range 0–10) to 3.0 (range 0–10) \( (p=0.011) \), while median pain interference with sleep was 1.0 (range 0–10) at both data collection time points \( (p=0.767) \) in 64 participants.

The relationship between CHQ pain score and the use of analgesics is shown in Table 3. Twenty-six participants received analgesics and 41 did not. Their median CHQ pain score was 20 (range 0–60) and 50 (range 10–100) respectively \( (p<0.001) \). Regarding changes in pain, 18 of 34 participants with more pain did not receive analgesics and neither did 8 of the 12 participants with a pronounced pain increase (CHQ score decrease \( ≥60) \). There was a positive correlation between the use of analgesics and pain interference with activities of daily living and sleep \( (r_s=0.682, p<0.001) \) and \( r_s=0.415, p<0.001 \) respectively).

The median CHQ pain score was 30 (range 10–100) in the 15 participants receiving ITB. Ten of 15 participants receiving ITB received analgesics and five did not. Their median CHQ pain score was 20 (range 10–60) and 70 (range 30–100) respectively.

Longitudinal data on pain characteristics and interference are available in Figure S1 and Table S1 (online)
Table 3: Caregiver-administered short-acting analgesics during the last 4 weeks in relation to pain severity at the two data collection points

| Pain score | Present | Previous |
|------------|---------|----------|
| CHQ 100    | Medication \(n=26\) | Medicine \(n=12\) |
|            | No medication \(n=41\) | No medication \(n=55\) |
| CHQ 70–90  | 0       | 5        |
| CHQ 40–60  | 11      | 16       |
| CHQ 0–30   | 15      | 12       |

Medication consisted of short-acting analgesics (paracetamol/ibuprofen/naproxen). CHQ, Child Health Questionnaire.

DISCUSSION

The main findings of this study were that the prevalence of recurrent pain was high in adolescents with CP and that pain prevalence, the number of pain sites, pain severity, and pain interference with activities of daily living all increased over a period of 5 years despite follow-up in a CP surveillance programme.

Pain prevalence was higher (93%) than in previous studies (37–77%).5,6 One reason could be that we recorded pain regardless of pain severity or level of pain interference. Also, our population was restricted to ages 12 to 17 years and GMFCS levels III to V, a group with expected high pain prevalence.4 The increase in pain prevalence was statistically significant only in GMFCS level III, which could be attributed to weight gain, extensive physical strain, and increasing contractures.5,11

Pain prevalence at each site was higher than reported by Eriksson et al.,4 possibly due to a narrower age range in our study population. In line with previous studies, the most frequent pain site was the lower limbs.4,12 A trend of most frequent pain in the abdomen and hip/thigh in GMFCS level V and most frequent knee pain in GMFCS level III was supported.4 Furthermore, increasing frequency of neck pain in GMFCS level V and knee pain in GMFCS level III was reported. Our data on neck pain must be taken with caution since this group consisted of only 11 participants. Nonetheless, positional factors such as lack of adjustment of the wheelchair and prolonged sitting or lying without support are potential causes. An increase in knee pain could be caused by increased crouch gait and lack of correct adjustment or omitted use of orthoses, which is common in adolescents in GMFCS level III.22

Our participants had moderate-to-severe pain (60%) and daily pain (40%) more often than previously reported by Parkinson et al.1 (37% and 11% respectively), which is probably explained by the inclusion of only GMFCS levels III to V in the present study. The finding of younger age as a predictor of more severe pain within the 12 to 17 year age group is not in agreement with the study by Eriksson et al.4 One reason could be the narrow age range. We found no significant difference in pain severity between participants with spastic and dyskinetic bilateral CP.

Pain interfered with activities of daily living, thus adding to the knowledge base that pain in CP has a negative impact on daily life.4,7,21 The finding of higher pain interference with activities of daily living in GMFCS levels IV and V was in line with the study by Christensen et al.24 Longitudinal studies are useful to evaluate the natural history of pain and the effects of treatments and interventions. Our study had an observation time of 5 years, which ensured a comparison between childhood and adolescence in the same individuals. Two longitudinal studies previously reported changes in pain in a paediatric population with CP.24,25 These studies reported no significant change in mean pain scores. In contrast, we found a more adverse pain development, with an increase in pain and pain interference with activities of daily living over 5 years. Comparing the results is difficult because of differences in study population (population- vs hospital-based), age (mean=14y 7mo vs 8y 8mo vs 8y 6mo), age range (12y 2mo–17y vs 3–16y vs 3–18y), time span between data collection points (mean=5y 1mo vs 2y 4mo vs 1y), and inclusion of GMFCS levels III to V only versus including all GMFCS levels.24,25

Factors that aggravated pain (Table S2) were in line with a previous report.7 The most prevalent factor was staying in the same position over time. This information should be discussed with primary caregivers to secure 24/7 positioning strategies. Passive muscular stretching both relieved and increased pain. Other actions that most often relieved pain were rest, change of position, and use of analgesics. In line with the study by Tedroff et al.,9 who reported a positive correlation between the frequency of use of analgesics and pain interference, we found positive correlations between the use of analgesics and both pain interference with activities of daily living and sleep. Although the number of participants receiving analgesics increased over 5 years, 28 out of 54 participants with moderate or severe pain did not receive analgesics. This suggests that the pain-relieving potential of analgesics was not fully exploited. Nonetheless, the use of analgesics should be based on individual preference and potential side effects as well as pain severity and interference. We have not been able to find studies on pain and the use of analgesics in children with CP receiving ITB. The finding that most had moderate or severe pain and received analgesics indicates the need for close follow-up of pain even if ITB is used.
Data from Sweden show that the prevalence of hip dislocation declined after the introduction of a surveillance programme that included an algorithm on hip management. In contrast, the high prevalence of recurrent pain suggests that our CP surveillance programme was not helpful in initiating adequate pain management. This is in line with the study by Westbom et al. After this study, the Nordic CP surveillance protocols were revised and questions on pain intensity, frequency, and interference with activities of daily living and sleep have since been included. Also, the Swedish CP surveillance protocol now includes questions on pain intensity for each pain site. We support these inclusions and suggest that information on laterality of pain in the limbs and pain duration should be included. We propose that an algorithm on pain assessment and management based on the CHQ pain score should be included in the surveillance protocol (Fig. 1). One could consider differentiation in GMFCS levels in the algorithm, such as more detailed assessment of hip pain in GMFCS level V, since hip pain might be an indicator for surgical treatment of hip subluxation if the migration percentage is equal to or greater than 40%. Physical assessment by a physician should be included in cases of moderate and severe pain. The local multidisciplinary team should consider all causes of pain and all available treatment alternatives and outline an action plan for each pain site. The proposed algorithm should be adjusted to the local health care system to be feasible.

This study has several limitations. First, data were based on proxy reports of pain; by definition, pain is subjective and should be self-reported whenever possible. Most of our population was in Communication Function Classification System levels IV and V; therefore, proxy reporting had to be applied to include the whole sample. Furthermore, a recent study found no significant differences in self- versus proxy-reported pain in a CP surveillance programme. Second, we did not ask about the duration of pain episodes. This information could have contributed to the understanding of why some participants with moderate and severe pain did not receive analgesics. Third, the questionnaires sent out in paper form were answered during a telephone interview by one-third of primary caregivers. However, there were no significant differences in the number of pain sites or CHQ pain scores with regard to the response form. Finally, interviews were performed by a different researcher than 5 years earlier, which could challenge the reliability of longitudinal comparison.

The study has several strengths. First, it is population-based and there were no significant differences between participants and non-responders. This ensured generalizability of the data. Second, the response rate at the second data collection point was high, probably because the

Figure 1: Algorithm on the grading, management, and follow-up of recurrent pain. The Child Health Questionnaire (CHQ) pain score was calculated according to the CHQ manual. The pain management suggested for mild pain is relevant for moderate and severe pain; the pain management suggested for moderate pain is relevant for severe pain.
method included a telephone interview. Furthermore, most responders were the same person at the two data collection points, which strengthens the reliability of the comparison between the two time points.

In conclusion, pain is a considerable problem in adolescents with CP. We propose extended pain assessment and an algorithm on pain management to be included in CP surveillance programmes with the aim to bridge the gap between programmes, guidelines, and pain management.

ACKNOWLEDGEMENTS
We thank all participants and their caregivers for their time and contribution to this study. We thank statistician C. Brunborg at the Oslo Center for Statistics and Epidemiology for valuable advice. The Norwegian Dam Foundation granted a PhD scholarship to S M Larsen (grant no. 2019/FO235195) supported by the Norwegian CP Association. The Norwegian South East Regional Hospital Trust partly funded K Ramstad’s work (grant no. 2013083).

CONFLICT OF INTEREST
The authors have stated that they had no interests which might be perceived as posing a conflict or bias.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

SUPPORTING INFORMATION
The following additional material may be found online:

Figure S1: Longitudinal data on the number of pain sites, CHQ pain score, pain interference with daily activities and sleep, pain intensity, and pain frequency in 67 participants with CP 5 years apart.

Table S1: Longitudinal data on pain characteristics in adolescents with CP collected 5 years apart
Table S2: Proxy-reported factors which relieved and increased pain (open response)

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