Review Protocol

1  **Review title**
Deformational Plagiocephaly: A systematic Review on Causes and Hypotheses

2  **Original language title**
see above

3  **Anticipated or actual start date**
November 2014, Search updated in February 2016

4  **Anticipated completion date**
April 2016

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1 Funding sources/sponsors

Internal Institutional Funding from the Mannheim Institute of Public Health

1 Conflicts of interest

None
Collaborators

In addition to the abovementioned working group, our student assistant Janina Beckmann (JB) has worked on the first screening of articles and should be acknowledged. Furthermore, we used the expertise of Jennifer Hilger and other staff researchers from the Mannheim Institute of Public Health to synthesize the data.

Review question(s)

To review systematically the existing evidence (original data articles) on determinants of positional deformational posterior plagiocephaly (pDPP) in otherwise health infants (key question 1. (KQ1))
- to systematically summarize new hypotheses that have been proposed to explain the development (KQ2)).

Searches

A systematic keyword search limited to infants and humans containing the keywords “plagiocephaly, non-synostostotic”, different terms for “head or cranial deformation”, “head shape” and excluding synostotic forms and operative treatment (see search strategy for more details) will be performed in all major biomedical databases, including Pubmed, Embase, Web of Science, Cochrane, Lilacs, medpilot, CINAHL as well as two study registries (http://apps.who.int/trialsearch/Trial.aspx?TrialID=ACTRN12605000023651 http://clinicaltrials.gov/show/NCT01902563). Articles in english, spanish and dutch published between 1985 and 2013 will be eligible for inclusion. We will use the PRISMA statement for systematic reviews for preparing our systematic review methods and this protocol.

URL to search strategy

not existing

Condition or domain being studied

Positional deformational posterior plagiocephaly (pDPP) as the outcome studied in our review is a condition in which the malleable infant skull is molded by external forces, leading to a flattened, asymmetrical cranium, and, depending on severity,
Facial asymmetry, frontal bossing, ear misalignment and asymmetrical orbits. Cranial sutures remain open and intact (deformational Plagiocephaly (P) is therefore also termed non-synostotic P). The molding can occur in utero due to a restrictive intrauterine environment (prenatal P), during birth (perinatal P) or can develop postnatally as a consequence of gravitational forces usually associated with infant position. The latter form, also known as positional P, is the most common form of deformational P and is the outcome looked at in our study. It usually affects the posterior part of the skull (posterior P).

1 Participants/population

Regarding the study populations, inclusion criteria entail on the outcome, sample and exposure level: 1) outcome: deformational positional plagiocephaly, 2) sample: healthy children, 3) Exposure: lifestyle or environmental risk factors for positional plagiocephaly. To increase generalization and validity of the studies, healthy children would be ideally recruited in primary care settings. In addition, the following exclusion criteria regarding sample and recruitment will be applied: 1) exclusion of articles with samples with only newborns, children with cerebral palsy, very preterm children, very low birth weight, traumatic birth, NICU-population, 2) exclusion by more formal criteria (articles written in a foreign language and all non-scientific articles).

2 Intervention(s), exposure(s)

The exposures of interest in this systematic review are lifestyle and environmental risk factors for the development of posterior deformational positional plagiocephaly (pDPP) in children without other health problems (see exclusion criteria). After a first pilot search, the exposures included in the review will be categorized into the following categories: 1) Biological factors 2) Obstetric factors 3) Infant care practice 4) Lifestyle of mothers/parents 5) Sociodemographic factors.

2 Comparator(s)/control

A precondition for articles to be included into the systematic review is that they compare children not exposed to the above-mentioned lifestyle and environmental risk factors with those exposed regarding the outcome of pDPP.

2 Types of study to be included
Due to the two-pronged design of this systematic review (see KQ 1 and 2), we could include publications reporting either original research on etiological factors of pDPP or discussing hypotheses related to the etiology of pDPP in term infants without developmental problems. As initial probatory searches did not many yield high-quality study designs, we restricted the study designs to at least case series, with single case studies excluded for key question (KQ) 1. Regarding KQ 2, we did not restrict study designs at all.

2 Context

Postnatally acquired deformational posterior plagiocephaly (pDPP) is now one of the most prevalent abnormal findings in otherwise healthy infants and represents a frequent reason for seeking pediatric advice. Contributing factors however remain a matter of debate. While there is ample knowledge about pDPP development in children with developmental problems or preterm children in intensive care environments, less is known about what factors (presumably lifestyle and environmental factors) lead to pDPP in the normally developed children without inborn developmental risk factors. Such lifestyle and environmental factors principally might be malleable, which is a precondition for potential improvement via public health interventions. This context explains why we excluded children with special complications (e.g. premature, NICU population, cerebral palsy) from our search.

2 Primary outcome(s)

A diagnosis of pDPP is the primary outcome to be compared between exposed and non-exposed groups of healthy infants. Regarding the definition of pDPP, we did not introduce exclusion criteria because of the anyway limited number of eligible studies. This means that pDPP will be operationalized differently across different studies. The three main operationalization strategies are based upon the degree of deviation/difference in transcranial diameter using either 1) neuroimaging (mostly skull radiographs), 2) photography or 3) clinical observation and diagnosis. Anthropometric indices that help in categorizing a child’s head form are the cranial length ratio as well as the cephalic index, which sets into relation length and width of the cranium. The primary outcome pDPP should ideally be measured at different time points within the first year of life in children over 3 months of age. An age below 3 months will lead to overestimation of plagiocephaly because directly postpartum nearly every child shows some signs of plagiocephaly due to constraint intrauterine environments.

2 Secondary outcomes

None.
**Data extraction, (selection and coding)**

**Study selection:**
All articles will be introduced into Endnote (Endnote X7.3.1; Thomson Reuters, New York) and checked for duplicates. One person (planned: JB) will screen all articles by title regarding the following inclusion criteria: 1) outcome: deformational positional plagiocephaly, 2) sample: healthy children, 3) Exposure: lifestyle or environmental risk factors for positional plagiocephaly. In addition, the following exclusion criteria regarding sample and recruitment will be applied: 1) exclusion of articles with samples with only newborns, children with cerebral palsy, very preterm children, very low birth weight, traumatic birth, NICU-population, 2) exclusion by more formal criteria (articles written in a foreign language and all non-scientific articles). Then, two duplicate reviewers (planned: HRP, JB) will further screen abstracts and, if needed, full texts according to the above-mentioned criteria. All references of the relevant articles will then be screened to identify still missing relevant reports (post hoc inclusion). In a last step, all relevant articles fulfilling the sketched inclusion criteria will be categorized as containing original data or hypotheses/debate.

**Data collection process**
All articles fulfilling the abovementioned inclusion and exclusion criteria and containing original data (analysis data set) will be extracted and their quality rated by duplicate reviewers (planned: HRP, JK). In case of non-agreement, a third rater (planned: FDB) will be asked and discussion among the three raters will lead to a common rating.

**Data extraction:**
Data extraction will be performed in duplicate by two independent extractors (planned: HRP, JK). Extracted data items in the analysis sample (articles with original data on risk factors) will entail authors, year of publication, country of origin, study design, method of outcome measurement, study/sample size, exposures and exposure category included as well as variables indicating potential bias. Exposure categories will be (based upon our pilot searches): Lifestyle, obstetric factors, style of care, biological infant factors, social factors.
Quality Rating scheme to assess potential biases:
The quality rating scheme used in this systematic review will be developed based upon existing literature and will contain study-level (e.g. study design, recruitment, follow-up) and outcome-level assessment of risk of bias. The latter will include the documentation and assessment of the method measuring the summary outcome, namely pDPP. Based upon first pilot searches, we expect a sample of relatively low-grade-evidence studies. This means that many well known quality assessment instruments (e.g. Cochrane GRADE system\(^9\), CASP (critical appraisal skills programme) for case-control and cohort studies\(^10\) might not be suitable to use. Therefore, we decide to use the Effective Public Health Practice Project (EPHPP) Quality Assessment (http://www.ephpp.ca/tools.html), which is recommended in the Cochrane handbook for non-randomized studies, has been shown to have high reliability and inter-rater agreement\(^11\), and was deemed to be appropriate in systematic reviews by Deeks et al.\(^12\). The EPHPP uses 17 questions in six areas, including A) selection bias, B) study designs, C) confounders, D) blinding, E) data collection method and F) withdrawals and drop-outs. In our systematic review, we expect enough information to rate four out of the six EPHPP component areas, which however might not allow to calculate a global EPHPP rating. Priority will be given to the following EPHPP areas:

- **Selection bias (A),** measured by the question Q1: “Are the individuals selected to participate in the study likely to be representative of the target population?” (with responses: 1=very likely, 2=somewhat likely, 3=not likely, 4=can’t tell.) and Q2 “What percentage of selected individuals agreed to participate?” (with responses: 1=80-100%, 2=60-79%, 3=<60% agreement, 4=not applicable, 5=can’t tell).

- **Study designs (B),** although we only expect weaker study designs (ratings 4-5 in EHP list).

- **Bias through confounding (C) will be assessed with the help of a predefined list based on theory and literature (probably containing: race, sex, marital status, age, socioeconomic status (income, class, education), health status). The number of variables adjusted for in the analyses of associations between exposure and plagiocephaly outcome in the single studies will be expressed as percentages of the predefined list: (rating: strong=>80% of the potential confounder list, moderate =60-79%, weak=<60%).

- **Withdrawals and drop-outs (F) in longitudinal studies, assessed by two questions: Q1) Were withdrawals and drop-outs reported in terms of numbers and/or reasons per group? (1=yes, 2=no, 3=can’t tell, 4=not applicable) and Q2) Indicate the percentage of participants completing the study. (If the percentage differs by groups, record the lowest). The following component ratings will be assigned: strong if 80-100% of participants completed the study, moderate=60-79% or n/a, weak=<60% or can’t tell (no description of withdrawals or drop-outs).

In addition to the EHP questions, we will add a global assessment for selection bias ( ”Was the sample highly selective?”) and limited generalizability (”Was the sample representative for the “normal child” without pre-, peri- or early postnatal developmental problems?”) (both with responses: Yes, no, can’t tell).

If during the quality rating process, substantial inter-rater differences occur, discussions between the two planned original raters (HRP, JK) and a third experienced researcher (planned: FDB) will be undertaken until agreement or consensus is reached.
By this quality rating, we will be able to assess risk of selection, detection and assertion bias. We will however not be able to exclude publication bias across all studies as our search primarily relies on data bases with completed studies.
Strategy for data synthesis

Given the limited study design quality and missing comparability (e.g. in outcome measurement) across studies that we expect based upon pilot searches, we decide against a quantitative synthesis and will use a narrative descriptive synthesis. We will not focus on individual data but on the risk factors/exposures extracted from the single articles. Evidence on potential risk factors as well as putative hypothetical causes will be interpreted with consideration to hierarchy of evidence, methodological and outcome measurement quality as well as sample representativeness. Exposures will be identified as potential “evidence-based” risk factors based on 1) supportive evidence from at least cohort and case-control studies and 2) at least one more significant result from one cross-sectional or case series study.

Analysis of subgroups or subsets

None planned.

Type of review

- epidemiologic

Language

English

Country

Germany

none

Reference and/or URL for published protocol

None

Keywords

deformational plagiocephaly, positional plagiocephaly, molding, etiology, “back to sleep”, supine sleep
factors, systematic review

3 Details of any existing review of the same topic by the same authors
7 Not applicable.