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DOI: 10.23804/ejpd.2018.19.02.07

Oral management of children with Henoch–Schönlein Purpura and associated Glomerulonephritis: a scoping review

ABSTRACT

Aim *To perform a scoping review of the existing literature in order to gather the most relevant information in the paediatric dentistry field related to the oral management of children affected by Henoch-Schönlein Purpura and associated Glomerulonephritis (HSPG).*
Methods *Using scoping review methodology for the screening and selection of valid articles, the steps of this review were the following: first, to pose a research question; second, to identify relevant studies; third, to select and retrieve the studies; fourth, to chart the critical data, and finally, to collate, summarise, and report the results from the included articles. Relevant articles published over a 25-year period, up to July 31, 2017, were identified and retrieved from four Internet databases: PubMed; EMBASE/Ovid; Ebsco/Dentistry & Oral Science Source, and the Cochrane Collaboration Library.*
Results *By title and abstract screening and after removing duplicates, four articles were finally included in the scoping review. According to the extracted data, the following are the most important clinical issues to be considered: (1) the disease can appear as a consequence of a dental treatment, such as those indicated for oral infectious processes; (2) children with HSPG are highly susceptible to dental caries and apical periodontitis, and (3) in affected children, oral infectious foci must be exhaustively eradicated in order to avoid the dissemination of the infection.*
Conclusions *Paediatric Dentists should be aware of HSPG, because the disease can be triggered or worsen subsequent to dental treatment. Adequate treatment of oral active infectious processes, together with an exhaustive oral preventive programme and long-term patient screening, are the best management approaches for children with HSPG.*

Keywords *Glomerulonephritis, Henoch-Schönlein purpura, Paediatric dentistry, Scoping review.*

Introduction

According to the American Academy of Paediatric Dentistry (AAPD), children and adolescents affected by complex medical conditions and with special needs may be at an increased risk for oral diseases throughout their lifetime. Therefore, in these individuals, oral health requires distinctive knowledge, as well as better awareness levels, and adaptation measures beyond those routinely considered [AAPD, 2016]. In particular, vascular and renal disorders are among childhood diseases that give rise to a spectrum of specific clinical and functional manifestations in oral hard and soft tissues [Gupta et al., 2015].

Henoch-Schönlein Purpura (HSP) is the most frequent purpuric self-limiting vasculitis occurring during childhood. It was described more than 200 years ago by Heberdon, and it is associated with group A streptococcal pharyngitis, and upper respiratory tract or Mycoplasma infections [Tahmassebi et al., 2007; Chen et al., 2015]. It is characterised by non-thrombocytopenic purpura and is accompanied by renal involvement or glomerulonephritis in approximately 40% of paediatric patients, diffuse colicky abdominal pain, arthralgia, rhinosinusitis, tonsillitis, and gastrointestinal bleeding [Tahmassebi et al., 2007; Inoue et al., 2008; Puspa-Petiwi, 2012; Hetland et al., 2017]. Red/purple spots are 5-10 mm in diameter, and unblanching haemorrhages are observed and frequently palpable, mainly on the skin of the legs and feet [Chen et al., 2015]; these are the result of small blood vessel leakage due to IgA-dominant immune complex depositions in their walls [Tahmassebi et al., 2007; Puspa-Pertiwi, 2012; Hetland et al., 2017]. This condition has a reported incidence of 14 cases per 100,000 children aged between 3 to 10

years, and occurs in twice as many males as females, mainly in Caucasians [Kawasaki, 2011; Hetland et al., 2017]. Some authors have reported that the disorder is more common in the spring and autumn seasons [Yang et al., 2005; Hetland, 2017]. In approximately 30% of affected patients, glomerulonephritis is slowly progressive and represents end-stage renal failure [Tahmassebi et al., 2007]. Diagnosis of Henoch-Schönlein Purpura associated with Glomerulonefritis (HSPG) is based on the medical history and clinical findings. The presence of elevated serum IgA, haematuria, and/or proteinuria are characteristic in many patients [Tahmassebi et al., 2007; Puspa-Pertiwi, 2012]. Disease severity and organ involvement dictate general treatment of the disease: if there is no renal involvement, management is only symptomatic, while in cases of glomerulonephritis, corticosteroids or other immunosuppressive and modulating drugs are prescribed [Hetland, 2017].

Because renal impairment is the principal cause of morbidity and mortality in children, prognosis of the disease greatly depends on the severity of the glomerulonephritis; also critical is appropriate management of the local and systemic infectious processes, when present [Chen et al., 2015]. In this regard, children affected by HSPG are highly susceptible to suffer dental caries, pulp infection/inflammation, periapical infections, and periodontopathies [Inoue et al., 2008]. In other words, the oral cavity of these patients constitutes major infectious foci for other organs of the body. Therefore, adequate management of oral infections is one of the most important clinical tasks carried out by paediatric dentists in their approach to children affected by HSPG, thus contributing to a better general prognosis of the disease.

The aim of the present article was to perform a scoping research of the literature in order to gather the most relevant studies in the paediatric dentistry field related to the oral management of children affected by HSPG. Thus, we attempted to collect this important clinical information from published articles, with the aim of better understanding the oral cavity role during the disease course, therefore to recommend the most suitable management options in the paediatric dental setting.

Methods

A scoping review of the literature was carried out according to some issues from the PRISMA (Preferred Reporting Items for Systematic Reviews and Met-Analyses) statement checklist [Moher et al., 2010]. We also implemented the Arksey and O'Malley [2005] methodological framework and recommendations for this type of review.

Initially, we developed a protocol including all aspects pertinent to scoping review methodology: (1) problem formulation through the design of a well-structured research question; (2) definition of inclusion and exclusion criteria in order to identify relevant studies; (3) literature search and reference list screening; (4) selection and retrieval of studies relevant to the research question; (5) charting of data from selected studies, and finally (6) collating, summarising and reporting the results from the most important articles on HSPG in children. The process finished with the discussion and interpretation of the collected clinical findings of the included studies.

Justification

The significance of the present review was the need among paediatric dentistry practitioners to identify the current state of knowledge regarding the general fundamentals of the HSP condition with renal impairment in paediatric population, and the considerations to bear in mind when managing children affected by the disease within the clinical setting. This aim may be achieved by providing a succinct synthesis of evidence from available and relevant published studies. We understand the eventual contribution of this scoping review to the existing literature regarding the topic, despite its inherent methodological limitations.

Research question

The following focused research question was structured prior to conducting the literature search, according to the PICO (Patient, Intervention, Comparison, and Outcome) format: For children with Henoch-Schönlein purpura and glomerulonephritis undergoing dental treatment, what are the best management approaches in the clinical setting?

Article selection criteria

Article selection considered only studies published in the English or Spanish languages, focusing on children with HSPG, aged under 12 years, whose purpose was to describe or discuss the clinical condition, and with clinical results or findings related to the paediatric pentistry field (e.g., oral health status/care, dental treatment considerations or safety/precaution measures, side effects, quality of life, etc.). The methodological designs included randomised clinical trials, observational or descriptive studies (cohort, case-control, and cross-sectional designs), narrative literature reviews, clinical case series, and case reports. Genetic, biochemical or *in vitro* studies, editorials, conference abstracts, comments, personal opinions, and letters were excluded.

Literature search strategy

Comprehensive electronic and manual searches were performed by two independent authors (ACE-G and FJT-N) for relevant available articles focused on

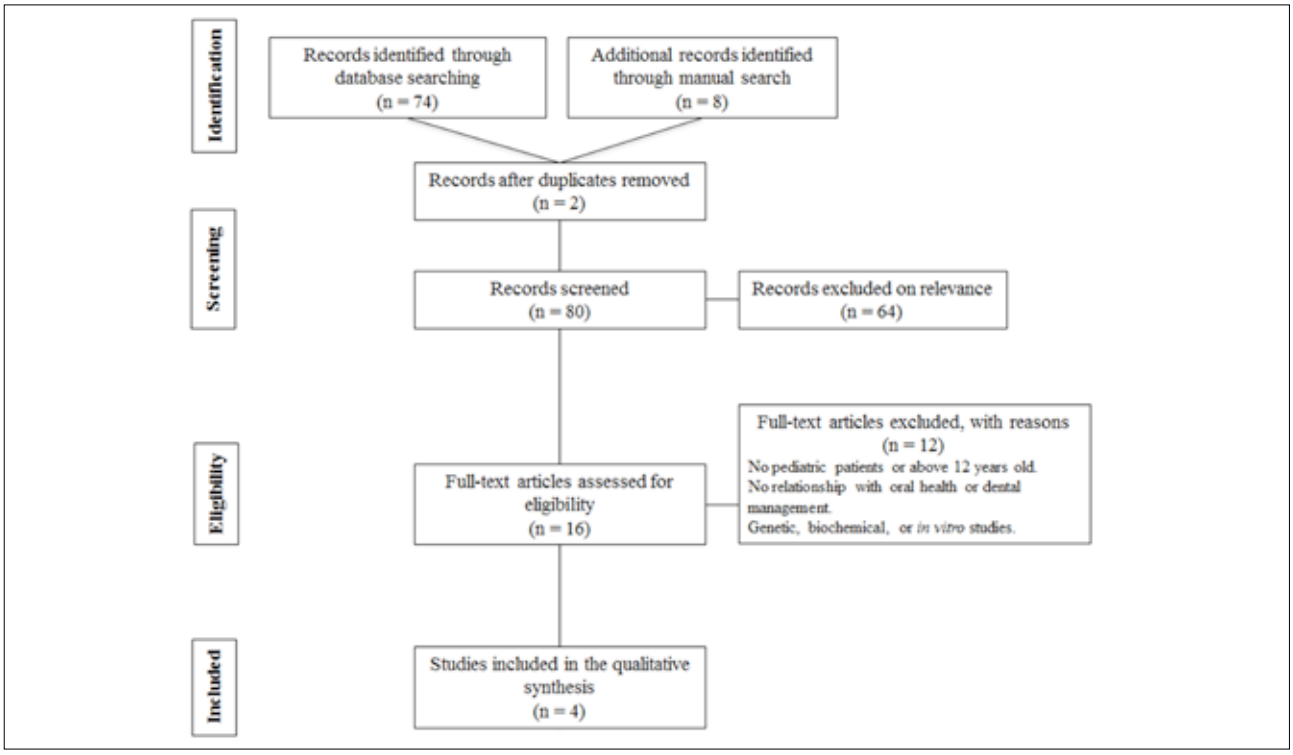


FIG. 1 Main characteristics of the articles finally selected for the scoping review.

the topic, published in the last 25 years (between January 1993 and September 2017) accessible on the most important Internet databases (Medline/PubMed, Embase/Ovid, Ebsco/Dentistry & Oral Science Source, and the Cochrane Collaboration Library). This process was carried out during the months of May through July, 2017. The search strategy was carefully adapted for each database to identify the appropriate studies. The search terms chosen, MeSH or free-text terms, keywords, and Boolean operators, alone or in combination, were as follows: "Henoch-Schönlein purpura"; "renal impairment"; "glomerulonephritis"; "children"; "paediatric dentistry": and "dentistry for children". The final search algorithm was: ("Henoch-Schonlein purpura"[All Fields] AND ["renal impairment" OR "glomerulonephritis"[All Fields] AND "children"[All Fields] AND "paediatric dentistry" OR "dentistry for children"[All Fields]).

From each database, retrieved article-title lists and abstracts were fully screened. The full-text version of potentially relevant articles was obtained if the inclusion criteria were fulfilled and if the article contained relevant clinical information. A complementary hand search was also performed on the reference list of each selected article.

Article data extraction and assessment

From each pre-included publication, the following data were collected, using a predesigned, standardised, and piloted spreadsheet: authors/country/year; study design, and clinically significant findings. Full-text articles were assessed by another three independent and experienced reviewers (JCF-A, AJP-G, and JAG-R) in order to judge whether findings from the included articles were clinician-centered and relevant to the paediatric dentistry practice. Both reviewers were previously calibrated, with a Cohen's kappa inter-rater agreement score of 0.87. Any discrepancy was resolved by discussion between reviewers for mutual agreement, and if necessary with the intervention of a third reviewer (FJT-N). Finally, descriptive tabulating for included studies was performed.

Charting of data

For all included studies, specific relevant clinical information concerning the paediatric dental management of children with HSPG was collected, including diagnosis methods, oral hygiene/prevention approaches, dental consequences of the disease, special medical considerations (including potential side effects), restorative/pulpal/surgical interventions in primary and young permanent teeth, and oral health maintenance (control and follow-up).

Results

Search outcomes

Figure 1 displays the flowchart of articles screened through the article evaluation and selection processes.

First author (year), and country	Methodological design	Relevant clinical findings/outcomes
Herrström et al. [1996], Sweden	Case-control study	Henoch-Schönlein purpura and glomerulonephritis are examples of diseases that have a well-established immunologic-mediated aetiology
		Aim: To investigate the possible relation between amalgam as a risk factor for inducing HSP and/or G in children
		64 participants, median age: 9-10 years
		Odds Ratios (OR) 95% Confidence Intervals (95% CI):
		HSP = 1.42 (0.49, 4.11)
		G = 0.59 (0.25, 1.38)
		Both = 0.84 (0.40, 1.75)
		These results are statistically non-significant and do not indicate increased disease risk regarding amalgam
Tahmassebi et al. [2007], UK	Case report	Differential diagnosis of HSPG is with: acute abdomen, meningococcal meningitis or septicemia, rheumatoid arthritis, systemic lupus erythematosus, rheumatic fever, idiopathic thrombocytopenic purpura, drug reactions, and child abuse
		In most cases, the disease usually lasts from 4-6 weeks
		There may be familial susceptibility to HSPG
		Aim: To report an unusual case of an anxious 14-year-old female, who developed acute HSPG following endodontic treatment on the upper left central incisor initially exhibiting periapical periodontitis
		First HSPG signs and symptoms appeared 2 weeks after treatment
		Microbiological analysis report stated streptococcal organisms were present in +++ amounts
		The patient was discharged 12 weeks after the disease was diagnosed
Inoue et al. [2008], Japan	Cross-sectional study	Chronic tonsillitis related to oral disease (dental caries/pulp infections, apical periodontitis, and periodontal disease), rhinosinusitis, and otitis media in children have been proposed as risk factors in the development of HSPG
		40 participants with HSPG with a mean age of 6.7 years
		In 53% of cases (21 patients), there was a significant association between oral disease and HSPG
		The authors recommend the extensive eradication of oral infectious foci, including periodontal therapy, root canal treatment, and antimicrobial drugs
Puspa-Petiwi [2012], Indonesia	Narrative literature review	No form of therapy has ever been shown, to our knowledge, to decrease duration of the disease or prevent recurrences
		HSP has a high probability of being spontaneously cured if supportive treatment is the primary intervention
		Nephritis is the most serious long-term complication. This condition occurs in 50% of older children, and only in 25% of those younger than 2 years
		HSP is considered to be associated with odontogenic infectious diseases
		Once discharged, patients and parents should be warned that the condition might reoccur

TABLE 1 Main characteristics of the articles selected for the scoping review.

The initial search strategy generated in total 82 potential relevant titles/abstracts. After careful screening, only 16 studies were considered eligible and were thoroughly reviewed. Finally, four publications fulfilled the selection criteria and were included in the scoping review; the principal characteristics and findings of these studies are described in Table 1.

Discussion

HSPG is a rare inflammatory condition of childhood. Despite its being a benign and self-limited disorder, it involves relevant clinical significance for paediatric dentists. However, there is a scarcity of publications related to oral health or dental management in

children. In the present study, only four relevant related publications [Herrström et al., 1996; Tahmassebi et al., 2007; Inoue et al., 2008; Puspa-Pertiwi, 2012] were finally included in the scoping review. Thus, some pertinent and useful clinical information could be condensed.

Three clinical issues should be seriously considered by paediatric dentistry practitioners when treating this type of patient: (1) the disease can appear as a consequence of a dental treatment, for example, treatments indicated for managing severe or long-standing oral infectious processes, such as exodontia procedures, root canal treatments, or periodontal therapies; (2) children with HSPG are highly susceptible to oral diseases, particularly to dental caries (70%) and apical periodontitis (5%) [Inoue et al., 2008], and (3) in already affected children, particularly those with severe renal impairment, oral active infectious foci must be exhaustively eradicated in order to avoid dissemination of the infection to other internal organs in the human body, such as to the kidney or the skin, which may cause systemic serious sequelae, and thus worsening the prognosis of the disease [Inoue et al., 2008]. In summary, clinicians need to consider dental disease and dental treatment as potential triggers for HSPG in their paediatric patients [Tahmassebi et al., 2007].

It is also necessary, as part of oral infection control in the child during the disease course, to reduce to the minimum the risk of causing a streptococcal bacteremia after an invasive dental treatment [Puspa-Pertiwi, 2012]. In this respect, Puspa-Pertiwi [2012] mention that single, oral active infectious lesions may contain up to 300 species of aerobic and anaerobic bacteria. These pathogens produce diverse inflammatory cytokines and cell-degradation derivatives, which may enter the bloodstream during transient bacteremia, resulting in damage to the inner lining of the blood-vessel walls and the persistence of active immune reactions. Therefore, and like other patients (e.g., cardiovascular diseases), children with HSPG should be carefully considered as candidates to receive prophylactic antimicrobial therapy before any dental procedures. This decision should be made together with the child's paediatrician or nephrologist after a comprehensive evaluation of her/his health status. Different antibiotic prophylaxis regimens for dental procedures in at-risk children have been issued by the AAPD [AAPD, 2016 (2)].

Maintaining oral health in children with HSPG is also extremely important, because the oral cavity is the chief entryway for bacteria that may increase the risk of additional systemic impairment during disease development. Thus, an aggressive preventive programme must be implemented in these patients, focused primarily on exhaustive oral hygiene, fluoride varnish applications, dietary counseling, and the placement of pit-and-fissure sealants. Finally, and according to Tahmassebi et al. [2007], even when the patient with HSPG has been discharged, close follow-up and screening with repeated urinary analysis are strongly recommended, due to the potential progress of renal impairment.

Conclusions

Paediatric dentistry practitioners should have knowledge and be aware of the course of HSPG and the oral health status of their patients, in order to avoid additional systemic complications. This task is carried out with other health professionals, such as the paediatrician and the nephrologist. The main purpose will be always to enhance oral health-related quality of life in this vulnerable population.

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