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Important considerations for designing and reporting epidemiologic and clinical studies in dental traumatology

REVIEW ARTICLE

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Abstract – The purpose of this article is to suggest important considerations for *epidemiologic and clinical studies* in the field of dental traumatology. The article is based on the authors' experiences from research in this field and editorial board work for the scientific journal *Dental Traumatology*. Examples are given of issues where development is important. The importance of planning ahead of the study and consulting with experts in other fields is emphasized.

Many manuscripts submitted to *Dental Traumatology* have significant flaws in design, methodology and reporting, which result in several time-consuming revisions and sometime rejections. Knowing the amount of work put into a project, it is always very unfortunate to delay or deny a publication, which for obvious reasons create a lot of frustration for the authors. During the past 20 years of the journal's existence, a vast amount of experience has been collected in the editorial board in reviewing studies for the journal, which is the background for this article.

The scientific field of dental traumatology has, like other specialist areas over the years, developed a series of standards in various types of studies that make it possible to compare the results of different studies. Comparison of results is a basic prerequisite for the development of any scientific field. To give an example, if classification of types of injuries in an epidemiologic study or a clinical study is not precise or healing complications (e.g., pulp necrosis, root resorption, and loss of periodontal support) are not clearly defined, comparisons of studies become meaningless. Other examples of flaws are incorrect sampling, insufficient number of patients, absence of important clinical registrations, insufficient description of the patients and controversial statistical methods used. Very little of what we do today is evidence-based. Hence, there is a need for strong high-quality studies to lay a base for evidence-based traumatology.

The purpose of this article is to share experience and to come up with recommendations for common issues in various types of studies and articles planned to be submitted to this journal. In this article, suggestions for *epidemiologic* and *clinical* studies in dental traumatology will be presented. In a second article, suggestions for *experimental studies* (*in vivo* and *in vitro* studies) in dental traumatology will be elucidated (1), and a third article will address the *principles of writing a manuscript* for publication in *Dental Traumatology* (2).

Epidemiologic studies

Epidemiology is the 'study of disease occurring in human populations' (3). Traumatic dental injuries occur very frequently in the society, with high prevalence and affecting individuals and have also impact in costs for the society (4–11). Results from epidemiological studies can help to identify groups and individuals at risk and serve as a base for interventions, public health recommendations and distribution of health resources. Moreover, trends over time in a society can be detected and cost effectiveness can be analyzed. Prior to starting a new study, it is important that the investigator performs a careful literature study of similar published studies in terms of design, methodology and reporting of results so as to compare the results with such studies later.

Classification

A uniform classification of injuries is necessary to enable comparison to previous and future studies. Epidemiologic

studies usually deal with the frequency and/or etiology of different types of dental injuries in given populations. Many studies published in the past suffer from serious flaws in methodology, mainly due to classification problems. For obvious reasons, the classification of injuries must be clearly defined. The WHO classifications, which are related to the clinical diagnosis and prognosis, should today be the first option used in clinical studies (12). In field screening where radiographic examination is not possible, a derivate of this classification can be used (12). In clinical studies, it should also be considered that most traumas affecting a single tooth can be more than a single injury type. Thus, most severe injuries show a *fracture component* (crown, crown root, root, or alveolar fracture) plus a *luxation component* (concussion, subluxation, extrusion, intrusion, lateral luxation, or avulsion). Data from emergency service institutions should report all these events. Finally, the surrounding tissue, e.g., the *gingiva* may have suffered contusion, abrasion, laceration, and loss of tissue, and the registration of such injuries should also be considered (12).

Prevalence, incidence, and trends

Prevalence studies are important for planning trauma health services in a society. For obvious reasons, trauma is like caries a cumulative event in relation to age (7, 8, 12). It is therefore important to account for trauma *prevalence* by well-designed cross-sectional studies. The ages 6 and 12 years are very representative for the trauma problem in a given population. The age 6 is important because it includes most of trauma problems encountered in the primary dentition, and the age 12 is important because it represents the end of the most trauma-active period of a person's life. Using fixed ages for trauma prevalence makes it easier to compare trauma profiles in different populations and countries (7, 8, 12). To assess the prevalence, both treated and untreated traumatic injuries must be taken into consideration.

Incidence studies, where the population is examined at given time intervals (usually during 1 year), are very useful. These, rather rare, cross-sectional studies give very valuable information about the trauma activity in a given population during a year (4, 7, 8, 12, 13). Seasonal variations caused by trauma can be assessed by this design. It is important to report on the number of participants entering the study and the number that were not possible to examine. For obvious reasons, also the calibration and examination methods used should be reported. There is a need for studies of trends in prevalence and incidence in dental traumatology over longer periods.

Sampling

It is not possible to study all people in a society who have been subjected to a certain type of trauma. For this reason, sampling is necessary. Random sampling or sampling by probability are the two methods used (14). If done properly, a representative sample of the population can be drawn. In dental traumatology, we often see grab samples, which means that all patients treated at specific institution are used in the sample. Nothing is wrong with this practice for, say, clinical studies as long as we understand that drawing conclusions with regard to the generalization to the whole population in a society will be limited with grab sampling (14). Hence, for epidemiological studies this is not a suitable method. Many manuscripts submitted to *Dental Traumatology* of already-completed studies are unfortunately rejected for insufficiencies in the sampling methodology or too small a sample. It is therefore important to consult with a statistician at the planning stage of the study to make sure that the sampling method is correct and the sampling size is sufficient for the study.

Clinical studies

There are limitations to prevalence and incidence studies because they provide only weak evidence of causes and effects; furthermore, the contribution of individual effects cannot be determined. Hence, we need studies with cases to further test risk and effects of prevention and treatment.

Clinical studies are most important and strongly needed as the whole clinical fundament of dental traumatology rest on approximately 50 studies of satisfactory quality, a fact in grave contrast to the severity of the problem and the number of clinical questions that are still not documented. This is not a problem specifically for the field of dental traumatology but also for dentistry and many fields of medicine. There is today a paucity of clinical studies in traumatology published where documentation of sufficient quality is given so that definite conclusions can be made. Prior to starting a new study, it is important to perform a careful literature study of similar already-published studies in terms of design, methodology, and reporting of results to enable comparison of results. As described earlier, a good sampling method must be applied and as well as consultation with a statistician regarding sample size. When registering complication rates, these must be related to *preinjury factors* (e.g., age of patient, tooth development stage, type of tooth, caries, and previous injuries), *injury factors*, i.e., trauma type, severity of trauma type (e.g., mm of displacement), trauma location (e.g., location of root fracture position), *treatment factors* such as reposition (partial, total), splinting (including time and method), *antimicrobial treatment* (e.g., chlorhexidin, antibiotics), and subsequent endodontic treatment (when and how). All these *pre-injury*, *injury*, and *treatment factors* have been shown to have a relation to healing events and should always be documented (15–18).

Ethical approval

Experiments involving human subjects should be subjected to approval by ethical committees before the experiments can start. Today, manuscripts to a journal will only be published if such research has been conducted in full accordance with ethical principles of the World Medical Association in the Helsinki declaration (version 2008 http://www.wma.net/en/30publications/10policies/b3/index.html) and the additional requirements,

if any, of the country where the research has been carried out. Manuscripts to scientific journals must today be accompanied by a statement that the experiments were undertaken with the understanding and written consent of each subject and according to the above-mentioned principles. A statement indicating that the study has been independently reviewed and approved by an ethical board should also be included. In the online submission, there is a requirement that all authors submitting manuscripts to *Dental Traumatology* online must answer in the affirmative to a statement 'confirming that all research has been carried out in accordance with legal requirements of the study country such as approval of ethical committees for human and/or animal research or other legislation where applicable'. Editors reserve the right to reject articles if there are doubts as to whether appropriate procedures were followed.

Prospective or retrospective studies

For obvious reasons, it is extremely difficult to perform prospective clinical studies related to the acute phase of the injury where the trauma situation for the patient will normally preclude an informed consent from the patient or the parents. It cannot be regarded ethical to have such discussions with patients or parents in the emergency situation. In the later non-emergency phase, however, such a possibility exists (e.g., choice of endodontic procedure), and such studies should be encouraged. It is an extra strength of evidence if such prospective studies can also be randomized according to the Cochrane Institute (www.cochrane.org).

The prospective study is optimal because examination forms can be used and procedures are existent from the start of the study, which may ensure a better quality of the data (19–23). Retrospective studies are often the compromise, and in these cases all efforts should be made to secure all existing data (laboratory data, radiographs, and emergency service charts) necessary for the study (4–6, 8). Every clinic should have careful recording routines to facilitate follow up. Special recording sheets for trauma have been recommended (20–24).

Description of the patient population

It is very important that adequate information about the patients is given, such as age groups, as a strong relation between age and root development has been found in most healing complications (25). Inclusion and reasons for exclusion should be listed. How was follow up carried out, by whom, for how long, and how many patients were missed in the follow-up period. This is a matter of concern in clinical studies because in certain types of studies (e.g., follow-up studies of implants) if more than one-third of patients are missed at follow up, then the study is not considered reliable.

Use and content of examination form

In previous studies, it has been demonstrated that the use of trauma examination forms can increase the amount of important information from 53% to 75–100% (19–23). The content of the examination form must be described so other researchers can use a similar registration and later compare results.

Sensibility testing of injured and control teeth

It is very important to report the type of test used (e.g., thermic, electrometric, laser Doppler) and the results of the test (24), as this information has a significant relation to subsequent pulp healing and at follow-up visits to the sensibility of diagnosing pulp necrosis (24).

Radiographic examination

The radiographic procedure used is strongly related to likelihood of diagnosing luxation and root fractures (19, 26). It is therefore important to describe the exact procedure (intraoral conventional or digital, panoramic and/or digital cone technique) (24). In case of intraoral radiographs, the *number* of radiographs taken is of interest as more than one radiograph may increase the chance of correctly diagnosing the type of luxation (27) and the presence of root fractures (26).

The use of standardized techniques and predetermined intervals for radiographic examinations may also augment the chances of diagnosing healing complication and is strongly recommended (19). Finally, the use of digital radiography, especially subtraction radiography, is recommended (27–30). In recent years, cone beam CT has been more and more in use. Radiographic examination in the follow-up studies solely for research must always take into account ethical consideration of radiation dose and subjected to ethical committee approval before starting a study.

Treatment protocols

The use of a treatment protocol is recommended. The International Association of Dental Traumatology (IADT) published updated protocols for injuries in the primary and permanent dentition in 2007 (31–33). Where treatment is performed, it is mandatory to describe precisely the *reposition procedures* (manual or by surgical or orthodontic means), *splinting procedures* (i.e., rigid, non-rigid), and the material used and for how long.

Drugs used

It is important to report the administration of medication used (Brand name, company, city country), dose of administration, and application method (local or systemic) and for how long (34).

Follow-up period and evaluation of final outcome

Scheduling of the follow-up period (recall times) and the examination procedures performed at these occasions should be recorded. Suggested follow-up periods have been reported by the IADT where suitable observation periods have been selected for the maximum chance of diagnosing healing complications (31–33, 35). In studies where evaluation of final outcome of a treatment method

is carried out, it is important whether another professional than the one(s) involved in the treatment will be doing the final evaluation, e.g., in the form of an audit (36, 37). If applicable, it is also of value to let the patients evaluate the final outcome of a treatment method (37).

Diagnosing healing complications

This is a very critical phase in all clinical studies, and new authors should use methods that have been proven to be reasonable and reliable in relation to *sensibility* (diagnosing pathologic conditions) and *specificity* (diagnosing healing conditions) (38). Furthermore, the criteria used for diagnosing *pulp necrosis* must be described. Guidelines for this have been reported (38).

Root resorption

Root resorption is a very important healing complication and should be classified into *repair*, *infection-related resorption*, and *ankylosis* (38). Furthermore, the location of the attack on the root: *external*, i.e., root surface, or *internal*, i.e., root canal, should be mentioned (39). For clinical studies on progression of root resorption, a radiographic index should preferably be used (40–43). Finally, *cervical-invasive resorption* should be reported as it has been shown to have a possible trauma etiology (38, 44). Finally, *periodontal ligament support* complications should be mentioned, including *loss of marginal bone support* (based on radiographs), *abnormal gingival pocketing*, and *gingival retraction* (38).

Tooth loss

Tooth loss as a direct cause at the time of accident or because of later complications should be registered and the time when the loss occurred.

Statistics

It is of interest to know that several studies have shown that trauma materials contain a multiplicity of *confounding factors*, e.g., *age* per se is strongly related to *root development*. Certain trauma types occur preferably at certain root developmental stages (N.V. Hermann, J.O. Andreasen, F.M. Andreasen, S.S.A. Christensen, 2011a–d, in preparation). In one large clinical study, a univariate analysis found 18 factors were related to pulp necrosis, whereas a subsequent analysis (regression analysis) showed that 14 factors were *confounding factors* and only four factors were actual in operation (27). If such a univariate analysis was the only tool, then 14 factors would have been wrongly linked in the future to the etiology of pulp healing (27). For each independent variable analyzed, it is important to give the actual numbers in the group represented and the number of teeth showing complications, and the percentage may be supplemented with the odds ratio (OR) (35). Also, the confidence interval (CI) as a measure of precision (or uncertainty) is a valuable figure to give (45). It cannot be overemphasized that it is important to consult with a statistician in the planning stage of a study. It is very disappointing to have a manuscript rejected because a confounding factor has not been controlled or the sample is too small.

Life table analysis

Especially in trauma situations, it is very important to gain information about the time line for complications, and this reporting method is strongly recommended (35). The number of patients at risk and the number of patients suffered an event at each control time should be indicated on the time line (35). If various treatment approaches are examined in a life table, the appropriate test to check out whether the two time lines differ is a log rank test (35).

Randomized clinical studies

A randomized controlled study is ranked the best study design for showing high evidence. As mentioned before, in the emergency trauma situation it is difficult to apply such design but in the later treatment it is possible, e.g., comparing different treatment procedures, materials, etc. Homogeneity of patients is important so rigorous inclusion and exclusion criteria must be applied. Furthermore, patients must agree to take part in such a study. The randomization and evaluation should be blind. For more information on the strict criteria for such studies, guidelines from the Cochrane Institute (36) are recommended (http://www.cochran.org). Clinical trials should be reported using the CONSORT guidelines available at http://www.consort-statement.org prior to starting the study. All manuscripts to scientific journals reporting results from a clinical trial must indicate that the trial was fully registered at a readily accessible website, e.g., http://www.clinicaltrials.gov.

Review articles

Traditional review articles performed by a senior expert in the field are valuable because such a person knows the literature and how to apply this in clinical practice. However, there is a risk that the lack of structure in such review articles will result in a selection of certain articles to support a personal point of view. The experts' personal experience is often included in such articles, and objective writing is not possible without a more defined structure. For this reason, a systematic review is better at giving objective overviews.

Systematic reviews

Systematic reviews summarize original research following a set of rigorous rules made in advance which the reviewer has to follow step by step. This will result in an article where the strength of evidence can be more clearly visible to the reader. A systematic review starts with defining the clinical question and finding all relevant studies in the literature. Searching several databases such as Medline and Cochrane can be supplemented by reading of recent reviews and textbooks to include articles that may have been missed in one database. Hereafter, the studies

that meet high scientific standards are selected and the scientific quality is studied and combined and compared. Rules have been developed by the Cochrane Institute http://www.cochrane.org, and authors of systematic reviews are strongly recommended to follow these strict rules (36).

Meta analysis

This approach, which involves the pooling of similar studies, has lately become increasingly popular. First of all, this type of analysis was primarily designed to allow the compilation of series of randomized studies where a treatment variable was under investigation. There are some 'inborn' risks of meaningless or false results (46–50). Even under these strict conditions, serious false conclusions have been made when studies have been compiled with different predictors for treatment failures (46, 49, 50). Lately, meta analysis has also been used for non-randomized studies, a situation which significantly augments the risk of false conclusions. The risks being related to first of all whether the *treatment factor* under investigation is not the 'treatment variable factor' but just one of a number of treatment factors, secondly when strong healing predicators are not similar in the different studies and finally when healing classification differs. All of these considerations indicate that meta analysis is not always suitable for ordinary cohort dental trauma studies. Furthermore, systematic reviews must include studies with a high scientific strength. There is also a risk that combined studies are not always comparable because of differences in design or material. Always consult with your nearest Cochran Center (www.cochran.org) when designing your evidence-based review. Gone are the days when researchers worked alone. Team work with experts in other fields is a prerequisite for good research today.

Summary

It goes without saying that this article has no intentions to be a complete manual of how to plan studies in epidemiology and how to design clinical studies. There are excellent textbooks on these topics. Instead, based on years of experience from research in dental traumatology and as editors in this field, our aim is to address the most common and important issues that should be considered when planning for epidemiologic and clinical studies in dental traumatology. Careful preparation and cooperation with others before embarking on new research endeavors will enable us to come up with good articles generating new knowledge and proceed further on the road to evidence-based traumatology.

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