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How to write a clinical case about pharmacotherapy

Cum se scrie un caz clinic despre farmacoterapie

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Abstract

Case reports are basic elements of medical knowledge; even if their role was minimized by the scientific accuracy and the methodology of clinical randomized trials, they are still the most valuable source of information, inexhaustible inspiration source for future research and a continuous reservoir of scientific novelty, which supports the permanent progress of medical science. This article tries to resume the main characteristics of a case report regarding pharmacotherapy, outlining the instructions for the inexperimented author, in order to ensure the publication's success.

Keywords: ***case report, adverse effects, pharmacology***

Rezumat

Prezentările de cazuri sunt elementele de bază ale cunoașterii medicale; chiar dacă rolul lor a fost umbrit de acuratețea științifică și metodologia trialurilor clinice randomizate, acestea încă mai reprezintă cea mai valoroasă sursă de informare, izvor de inspirație pentru cercetări viitoare și un rezervor permanent de noutate științifică, aflate în sprijinul progresului științific. Acest articol încearcă să sumarizeze principalele caracteristici ale unei prezentări de caz privind farmacoterapia, conturând instrucțiuni pentru autorul neexperimentat, pentru asigurarea succesului publicării.

Cuvinte-cheie: ***raport de caz, efecte adverse, farmacologie***

Introduction

Case reports are the oldest type of medical literature: since antiquity, the clinicians learned to use the experience of their colleagues, and their personal experience too[12]. In ancient Egypt, the practitioners wrote medical case reports in order to organize their medical thinking[8]. For a long time, case reports were the main concern of medical publishing, because medical progress is built on the reliable description of clinical experience. Innovations like penicillin, insulin, were initially case reported, then introduced in clinical practice[6]. The Kaposi sarcoma of the young homosexuals[11], the causal relationship between thalidomide and phocomielia, or between oral contraceptives and the venous thromboembolic disease[16], were all first case reported. Reporting cases of pulmonary hypertension secondary of using anorexigenic agents (as fenfluramine and dexfenfluramine) lead to the initiation of clinical trials to evaluate the possible causal relationship, culminating in their withdrawal from the market.

Case reports remain an important part of medical knowledge. Traditionally, the medical knowledge is built case-by-case, leading to medical science progress[13]. Case reports do not demonstrate the causality, but they can discover new disorders, describe new adverse effects, highlight new beneficial effects of the treatment, generate the scientific hypothesis for future research, all of these lead to medical progress[17]. Reporting a new suspected, previously unknown, serious adverse reaction to a medicine provides a valuable early alarm. Adverse reactions are frequently reported in medical literature; for example, more than 1,000 cases were reported in 2000 in Side Effects of Drugs Annual[2]. Medline reports over 40,000 cases yearly[7]. The information regarding drug safety is undeniably important the predictive positive value of a case report being estimated of more than fifty percent of the suspected adverse effects, being confirmed by future research[5]. Any suspected adverse effect needs to be validated by further research before using the information in clinical practice.

The format of a case report

Case reports are individual accounts that are useful for transmitting medical information[4]. There are well-set guidelines for the other types of medical writing (systematic review, meta-analysis), but there aren't any for case reports. Yet, the epidemiological and clinical journals displays author's instructions, with useful tips for writing a case. The case report contains enough information for the clinician reading the paper to understand the nature, the stage and the severity of the presented disease, the treatments administered and the measured parameters[14]. It is the author's charge to outline the limitations of the case report, and the lack of generalization. The author highlights the experimental inference, and reviews the competing hypotheses (natural resolution of the disease, the spontaneous variability of the symptoms). A case report will include the next five sections: abstract, introduction, case description, discussion and conclusion. Commonly, a case report is accepted when it has a length of 1,500-2,500 words and 20-30 references. An excess of references does not reflect the erudition of the author, but rather displays a lack of critical sense in choosing the bibliography.

The title

The title is precise, short and descriptive, in order to attract the interest of the reader. For a better indexing in the electronic database, the title must contain key words. Before we start writing, we will perform a research of the key-words in the available electronic databases (PubMed, Cochrane, Scholar Google, Medline) for an overview of the literature, related with the subject we want to report. The title must not be sequenced in subtitles, not too long nor too short, otherwise it is not able to reflect the specific content of the article.

The authors

Usually, the first author is the one who wrote the manuscript; anyone can be the first author, no matter his field, speciality and level of training (technician, specialist, resident – most of the times, the training doctor is the first one who comes in contact with the pacient); the last author is the one who validates and supports the published facts, objectively analyses the presentation of the results and the writing quality, and ensures credibility in the scientific community. The average number of authors is three, but often varies from two to eight. The order of the authors varyies with the contribution importance. The first author receives the correspondence.

The language

The information is easier to understand in the mother tongue, hereby it is legitimate to use it; however, for ethical reasons, the case reports describing new diseases, new adverse effects and new associations must be published in an international language (preferably English), allowing the entire scientific community to access the information.

The abstract

The abstract is a summary of the case report, which facilitates the reader's access to the electronic databases, and helps to establish the level of interest about the case report. It has 100-250 words, and the same format as the initial text (introduction and purpose, case description, discussion and conclusion). The abstract summarizes the information provided by the original article, directing the reader over the content of the paper.

The introduction

The introduction is the section attracting the reader's interest: short, concise, it provides the subject, the importance and the purpose of the presentation. It is a veritable review of the presented subject, exposing all the information available regarding the subject (background). All affirmations are accompanied with references, presented in chronological order, choosing the most important and relevant ones. Do not approach comparisons or contrasts, which are better illustrated in the Discussion section. No longer that three paragraphs, it must not be labeled with "Introduction".

Case presentation

The most important section, which describes chronologically the case, providing enough information so the reader can build hisor her own opinion, before being confronted with the author's opinion. We will avoid to mentiona the vague elements, not related with the case (normal vital signs, interdisciplinary consults). The author will establish a temporal and causal relationship, will indicate the effects of the treatment, the undesirable effects, the evolution, the treatment and the present state of the patient[18].

The case presentation usually begins with the demographic data of the patient: age, height, sex, race and occupation. Although the race and occupation could seem insignificant, this information may reveal pharmacodynamic differences. Do not use the patient's initials, date of birth, the admission date or other identifying markings, because patient's anonymity is mandatory. The author will present the main complaints, with their characteristics (length, intensity, aggravating factors), concomitant diseases, the medical and social history, the habits, recreational drug use and the clinical pathological findings.

Biological data: the author will choose the biological data for sustaining the main diagnosis, and excluding the differential diagnosis. Biological pertinent data, either negative or positive, will be presented, both with the reference range. The author will describe the diagnostic procedures, reporting the final results. Histologic images, radiologic, anatomopathology aspects, skin manifestations can be used, all preserving the anonymity of the patient. In the United States, Health Insurance Portability and Accountability Act (HIPAA) requires ensuring confidentiality of the patient before publishing a case[9].

The pharmacological history will include the name of the medication, the dosage, the administration form, the frequency and duration of administration. Both generic and producer's name will be mentioned, because there are differences of bioavailability, the drugs may have different compositions, adjuvants, preservatives, additives and dyes, all modifying the pharmacokinetics, the efficiency and the adverse reactions. We forget sometimes the over-the-counter medication, the herbal treatments, the vaccines, but it is important to document these elements because of the long lasting effects; the patient's compliance to treatment is important to notice, too.

Laboratory data regarding the hepatic and renal functions are important to understand the pharmacokinetics of the drug. The allergic status of the patient is very important to describe, including the type of the allergy, the allergy history, the date and name of the incriminated drug. The name of the drug will be specified as generic or as producer's name, and the combinations will be listed; we will not declare allergy to Biseptol, but to trimethoprim-sulfametoxazol, as we don't know exactly which component is responsible for the allergy.

When available, it is important to note the serum level of the drug, the time of measurement and the relation with the dosage (seric peak). If possible, the seric level must differentiate between total and circulant value (as for valproic acid, or fenitoine). Sometimes, it is useful to specify the method of measurement. The patient's diet is also important because food interacts with medication, causing a lower or higher serum level, or modifying the pharmacological effect of the drug. Before suspecting a drug allergy, it is preferable to eliminate the possible dietary causes.

The Discussion

The Discussion is the most important section of the paper, in which the author exploits the reasoning, highlights the originality of the case, compares with literature, derives new knowledge and formulates practical applicability. This section illustrates the scientific culture of the author, providing explanations of the reported facts. Avoid repeating information presented in the section Introduction. Personal comments are allowed, unlike the other sections, which which must remain impersonal.

Table 1 Shows the way Naranjo score is calculated

Calculating the score:	Yes	No	Don't know
1) Are there previous conclusive reports on this reaction?	+1	0	0
2) Did the adverse event appear after the suspected drug was administered?	+2	-1	0
3) Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0
4) Did the adverse reaction reappear when the drug was readministered?	+2	-1	0
5) Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0
6) Did the reaction appear when a placebo was given?	-1	+1	0
7) Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0
8) Was the reaction more severe when the dose was increased or less severe when dose decreased?	+1	0	0
9) Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0
10) Was the adverse event confirmed by any objective evidence?	+1	0	0

Table 1: Naranjo nomograme; Definite: score > 9; Probable: 5-8; Possible: 1-4; Doubtful: < 0

The probability that a medicine causes adverse reactions is estimated on the clinical judgement; we can use the notions of adverse effect as: definite, probable, possible and doubtful, in order to quantify the causal relationship. The Naranjo nomogram is a validated nomogram, a 10 item questionnaire, with a score which fits the adverse effect as: definite, probable, possible and doubtful[15].

A definite adverse effect is any adverse effect, undesirable and unintended, after using a medicine, in the recommended dosage, for prophylactic, diagnostic and therapeutic purposes. The definition excludes the treatment failure, the intentional overdose and drug abuse[9]. A definite reaction implies: toxic level of drug in tissues after administration; previous known reaction to the suspected drug; confirmation by interruption of the drug and recurrence with a new administration. A probable reaction includes: effects appeared after drug administration; previous known effect to the incriminated drug; confirmation by interruption of the drug; there is no other clinical explanation for the suspected effect. A possible reaction includes: appearance after administration of the drug; previous known effect to the incriminated drug; the effect is not explained by the patient's pathology. A doubtful reaction is a reaction which implies other factors than the incriminated drug.

The section Discussion is represented by a personal text, accompanied with few references. The literature data may be illustrated in a chart, which are easier to interpret. The author justifies why the case is important, and formulates recommendations and conclusions.

The Conclusion:

The Conclusion is the section based on the evidence listed in the Discussion section; the author justifies the conclusion, and formulates recommendations, paying close attention to the clinical applicability of the presented fact; he or she may recommend pharmacovigilance and may outline future possibilities of research[10]. This section must be concise, not more than a paragraph.

The tables, figures and illustrations are additional elements with informational autonomy, having a title, legend and footnotes. It expresses clearly what is difficult to read; the information will not be duplicated in the text.

The references

The references are listed at the end of the presentation, using specialized informatical programs (EndNote, RefWork, Papirus). The standard number of references is 15 to 30; we can use more, but not fewer references. They allow the access to the databases, publications and articles. Some journals may limit the number of references.

Conclusion

Case reports have their role in the progress of medical science. They permit discovery of new unexpected effects (adverse or beneficial), having a high sensitivity for detecting novelty and therefore remain one of the cornerstones of medical progress, providing many new ideas in medicine. ■

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