

The importance of case reports

Dr. Barun Kumar Nayak

Head of Ophthalmology Department
P.D.Hinduja National Hospital and Medical
Research Centre
Editor- Indian Journal of Ophthalmology

- Peer-reviewed medical journals are the means for disseminating new knowledge and Science
- Do case reports justify its publication?

- Some journals publish no case reports whereas there are some journals which publish case reports only

Why two extremes?

A case report described and discusses an instance of disease in a patient

The essential characteristic of a publishable case report is educational value

Writing case reports is one of the best ways to get started in medical writing. They are little mysteries that hold readers' interest and take less time to prepare

Value of case reports

➤ It describes important scientific observations that are missed or undetectable in clinical trials

- Case report linked the **FDA** approved anorexic agents (fenfluramine and dexfenfluramine) with primary pulmonary hypertension

↓
Trials evaluating incidence, mechanism, risk factor

↓
Withdrawal of drug from market

- Case report of kaposi's sarcoma in a young homosexual man

↓
Development of AIDS

First line of evidence for new therapies

- Physostigmine in myasthenia gravis
- Potassium iodine in erythema nodosum
- TNF – α antibody treatment in psoriasis
- Dapsone in Behcet disease
- Insulin for type 1 Diabetes mellitus

Value of case reports

- Rare indications
- Difficult to conduct trial with adequate sample and power
- Difficult to get funded by pharmaceutical companies
- 1995 Mycophenolate mofetil was approved in the United States and UK for immunosuppression after renal transplants and 1997 off label use was reported in pyoderma gangraenosum, autoimmune anemia, pemphigus vulgaris, bullous pemphigoid, systemic vasculitis and IgA nephropathy.

Thalidomide off label uses

➤ Observational evidence

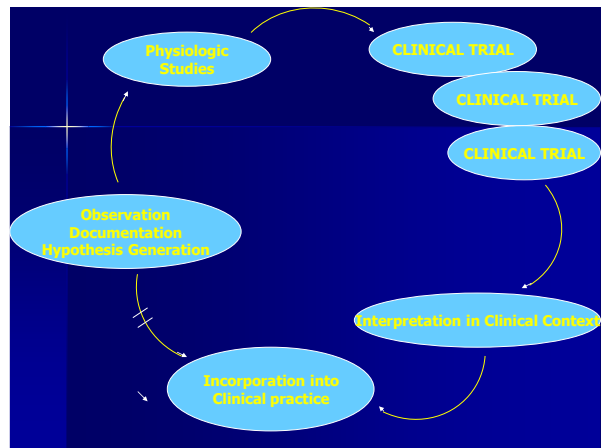
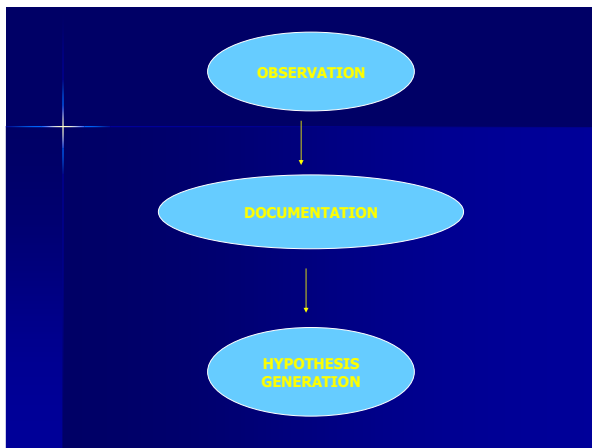
- Brain neoplasm
- Crohn disease (lenalidomide failed trial)
- Discoid lupus erythematosus
- Erosive lichen planus
- Erythema multiforme
- Prevention of graft – versus- host disease
- Subacute cutaneous lupus erythematosus

➤ Randomized controlled clinical trials

- Behcet syndrome
- Cachexia caused by HIV
- Graft-versus-host disease
- Mycobacteriosis
- Prevention of recurrent aphthous stomatitis (negative)
- Recurrent aphthous stomatitis

Side effects of drugs described in case reports

- Anti TNF antibody - Vitiligo/ Vasculitis
- Interferon α - Psoriasis exacerbation
- IV immunoglobulin - stroke



Value of case reports (contd)

- 103 reports published in Lancet
- Followed after 5 yrs
- 24 reports were followed by Publication of RCT or in the registry of RCT

Case reports for authors

- Opportunity to Publish (Beginners)
- Easy to write
- Good learning practice

Drawbacks of case reports

- False alarms can be raised.
Eg. Debendox/ bendeclin (combination of pyridoxine and doxylamine succinate) marketed for morning sickness in pregnancy. Based on reports of malformations it was withdrawn from US but still available in Canada without evidence of human teratogenicity

Drawbacks

Readability is high and they are Influential

BUT

- Less citable (Max- meta analysis and min-case reports)
- Reduce Impact Factor, hence editors do not like case reports

Drawbacks

- Publication bias (90%) reporting successes versus 10% reporting failure
- Methodology is not robust
- Most of the once-popular discarded therapies are based on case reports

CONTD...

- Thalidomide – extreme example of primarily off-label use. Licensed in 1998 for treatment and prevention of erythema nodosum leprosum (extremely rare) and multiple myeloma was added in 2006, but > 90% of the physicians who prescribed it was for off-label use

HIV cachexia indication RCT was published 11yrs after approval by FDA

Drawbacks

- Off-label use drugs are not allowed to be advertised in U.S
- Companies promote educational supplements
- Promote publications of Case reports

Criteria for publishable case reports

- Advance medical science and spawn research;
- Describe rare, perplexing, or novel diagnostic features of a disease state;
- Report therapeutic challenges, controversies, or dilemmas;
- Describe a new surgical procedure;
- Report how a drug can enhance a surgical procedure
- Teach humanistic lessons to the health care professionals;
- Review a unique job description of a health care professional that improves patient care;
- Report new medical errors or medication errors;
- Discover a device malfunction that results in patient harm;
- Describe adverse effects and patient toxicity of a radiopaque agent;
- Describe life-threatening adverse events;

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- Describe dangerous and predictable adverse effects that are poorly appreciated and rarely recognized;
- Describe rare or novel adverse drug reactions;
- Describe a therapeutic failure or a lack of therapeutic efficacy;
- Describe rare or novel drug-drug, or drug-food or drug- nutrient interactions;
- Report unlabeled or unapproved uses of a medication
- Explore the use of pharmacogenomics to manage diseases;
- Use life-saving techniques not previously documented;
- Use pharmacoeconomics principles that improve patient care;
- Uncover barriers to patient adherence;
- Discover an interaction between a drug and a laboratory test that yields a false-positive or false-negative result;
- Describe the effect of drugs in pregnancy and lactation
- Detect novel pharmacokinetic or pharmacodynamic principles; and
- Use technology to improve patient outcomes.

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Guidelines for writing patient case report manuscripts

□ **Abstract**

- Introduction and objective
- Case report
- Discussion
- Conclusion

□ **Introduction**

- Describe the subject matter
- State the purpose of the case report
- Provide background information
- Provide pertinent definitions
- Describe the strategy of the literature review and provide search terms
- Justify the merit of the case report by using the literature review
- Introduce the patient case to the reader
- Make the introduction brief and less than three paragraphs

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□ **Patient case presentation**

- Describe the case in narrative form
- Provide patient demographics (age, sex,height, weight, race, occupation)
- Avoid patient identifiers (date of birth, initials)
- Describe the patient's complaint
- List the patient's present illness
- List the patient's medical history
- List the patient's family history
- List the patient's social history
- List the patient's medication history before admission and throughout the case report

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- Ensure that the medication history includes herbals, vaccines, depot injections, and non-prescription medications, and state that the patient was asked for this history.
- List each drug's name, strength, dosage form, route, and dates of administration
- Verify the patient's medication adherence
- Provide renal and hepatic organ function data in order to determine the appropriateness of medication dosing regimens
- List the patient's drug allergy status, including the name of the drug (brand or generic) and the date and type of reaction

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- List the patient's adverse drug reaction history and the dates of the reaction
- Provide pertinent serum drug levels and include the time of each level taken and its relationship to a dose
- Provide the patient's dietary history
- Provide pertinent findings on physical examination
- Provide pertinent laboratory values that support the case.
- Provide the reference range for laboratory values that are not widely known or established
- List the completed diagnostic procedures that are pertinent and support the case
- Paraphrase the salient results of the diagnostic procedures
- Provide photographs of histopathology, roentgenograms, electrocardiogram, skin manifestations, or anatomy as they relate to the case

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- Obtain permission from the patient to use the patient's photographs, or follow institutional guidelines
- Provide the patient's events in chronological order
- Ensure a temporal relationship
- Ensure a causal relationship
- Ensure that the patient case presentation provides enough detail for the reader to establish the case's validity

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□ Discussion

- Compare and contrast the nuances of the case report with the literature review
- Explain or justify the similarities and differences between the case report and the literature
- List the limitations of the case report and describe their relevance
- Confirm the accuracy of the descriptive patient case report
- Establish a temporal relationship
- Report the validity of the case report by applying a probability scale such as the Naranjo nomogram
- Summarize the salient features of the case report
- Justify the uniqueness of the case
- Draw recommendations and conclusions

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□ Discussion

- Provide a justified conclusion
- Provide evidence-based recommendations
- Describe how the information learned applies to one's own practice
- List opportunities for research
- Ensure that this section is brief and does not exceed one paragraph

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Guidelines for case report writing

- ▣ Abstract
- ▣ Introduction
- ▣ Case presentation
- ▣ Discussion
- ▣ Conclusion

Check list for Case Reports

- ❖ Abstract: should summarise the whole case
- ❖ Introduction: rationale adequately explained & substantiated by references
- ❖ Case Description : brief adequate & clear
- ❖ Investigations adequate & with normal values for uncommon ones
- ❖ Discussion : diagnosis and recommendations supported potential issues refuted/ addressed

Usual questions which the editors expect reviewer to answer

- ▣ Introduction
- ❖ Is the rationale for reporting the case adequately explained?
- ❖ Is the rationale for reporting the case adequately substantiated by references?

CONTD...

Description of the case

- ❖ Is the case described adequately?
- ❖ Is the case described briefly?
- ❖ Is the case described clearly?
- ❖ Are the results of investigations described adequately?
- ❖ Are the results of less common laboratory investigations accompanied by normal values?

CONTD..

Comments

- ❖ Is the evidence to support the author's diagnosis presented adequately?
- ❖ Is the evidence to support the author's recommendations presented adequately?
- ❖ Are other plausible explanations considered and refuted?
- ❖ Are the implications and relevance considered of the case discussed?
- ❖ Do the authors indicate directions for future investigations or management of similar cases?

- Confidentiality
- Informed consent
- IRB approval

Laws / Acts of interest

- Health Insurance Portability & Accountability Act.1996 (HIPAA)
US Dept of Health & human sciences
- Identifiable Personal Information (IPI)
- Personal Information Protection & Electronic Documents Act (PIPEDA)
Canada 2000

Protection of Patients' anonymity

- Name / Initials / Address
- Hospital No / Unique Identifiers
- Dates
- Race / Biometrics
- Pedigree / Photographs
- Disguise identifying information
 - Patients' characteristics
 - Personal history

When to take Informed Consent?

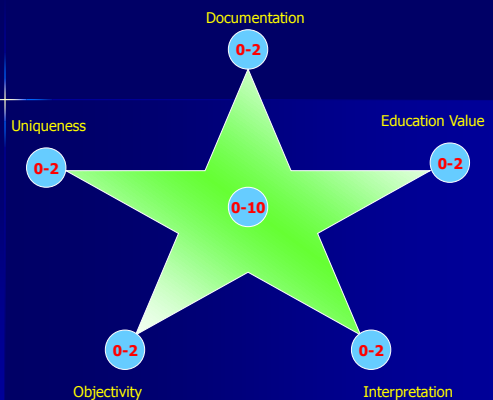
- ❖ Before writing manuscript
 - Pt. may be worried about final report
 - What if author does not complete report?
- ❖ After writing manuscript
 - If pt refuses
 - May resent refusal
 - Pt worried about saying "no"
- ❖ If manuscript rejected
 - Informed consent in vain
 - Unnecessary mental trauma for patient

Solution !!??

- Take IC after the case report is accepted for publication
- Limitation – puts author at risk of patient refusal

Written Informed Consent

- Eliminates risk of litigation
- Protects authors journal & publishers
- Fails to protect from future negative personal consequences



Thank you