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EDITORIAL

Navigating the ethical terrain: Off-label and experimental treatments in medical case reports

Madhan Jeyaraman, Naveen Jeyaraman, Swaminathan Ramasubramanian, Sangeetha Balaji

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Madhan Jeyaraman, Naveen Jeyaraman, Department of Orthopaedics, ACS Medical College and Hospital, Dr MGR Educational and Research Institute, Chennai 600077, India

Swaminathan Ramasubramanian, Sangeetha Balaji, Department of Orthopaedics, Government Medical College, Omandurar Government Estate, Chennai 600002, India

Corresponding author: Madhan Jeyaraman, MS, PhD, Assistant Professor, Research Associate, Department of Orthopaedics, ACS Medical College and Hospital, Dr MGR Educational and Research Institute, Velappanchavadi, Chennai 600077, India. madhanjeyaraman@gmail.com

Abstract

This article explores the ethical considerations surrounding the reporting of off-label and experimental treatments in medical case reports, with a focus on fields such as oncology, psychiatry, and pediatrics. It emphasizes the balance between innovation and evidence-based medicine, highlighting the critical role of case reports in disseminating clinical experiences and advancing medical knowledge. The discussion delves into the ethical framework guiding case reporting, including principles of patient autonomy, informed consent, non-maleficence, beneficence, justice, and transparency. Challenges such as negative outcome reporting, commercial interests, and the balance between innovation and caution are examined. Recommendations for ethical vigilance, the development of comprehensive guidelines, and the role of regulatory bodies are proposed to ensure patient safety and uphold scientific integrity. The article concludes by underscoring the importance of a collaborative effort among clinicians, researchers, ethicists, and regulatory bodies to foster the responsible advancement of medical science while adhering to the highest ethical standards.

Key Words: Ethical considerations; Patient autonomy; Informed consent; Non-maleficence; Beneficence; Transparency; Evidence-based medicine

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Core Tip: This article underscores the imperative of ethical integrity in reporting off-label and experimental treatments within medical case reports, advocating for a balanced fusion of innovation and evidence-based medicine. It calls for collective action in developing comprehensive ethical guidelines and enhancing regulatory oversight to prioritize patient safety and uphold scientific rigor.

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INTRODUCTION

In the dynamic field of healthcare, the use of off-label and experimental treatments offers a blend of opportunity and challenges, particularly relevant in oncology, psychiatry, and pediatrics. These practices, essential for conditions lacking standard therapies, underscore the importance of balancing innovation with evidence-based medicine, especially in contexts like the off-label pediatric use of coronavirus disease 2019 (COVID-19) vaccines[1]. The role of case reports is critical in this scenario, acting as a crucial channel for sharing clinical experiences and enriching medical knowledge, thereby facilitating the exploration of new therapeutic avenues. This is evident in the progress and hurdles associated with stem cell therapy[2].

Case reports are fundamental in illustrating the practical applications and outcomes of these therapies, yet they raise ethical concerns, primarily patient safety and the risk of endorsing unproven treatments. Ethical scrutiny and informed consent are paramount, emphasizing the necessity of a cautious approach to prevent misuse and ensure ethical integrity. The legal aspects surrounding off-label treatments further demand a framework that harmonizes innovation with ethical responsibility[1].

This editorial aims to examine the ethical dimensions of reporting off-label and experimental treatments, proposing guidelines for responsible reporting. These guidelines are designed to protect patient safety while promoting medical science advancement in an ethically sound manner. The overarching goal is to encourage the sharing of clinical experiences in a way that positively influences the medical community, ensuring the quest for novel treatments aligns with medical ethics and patient safety principles.

ETHICAL FRAMEWORK FOR CASE REPORTS

In the realm of case reporting, the ethical framework ensures the protection of patient rights, well-being, and dignity, particularly when standard care is deviated from, such as in off-label or experimental interventions. This framework is built on the principles of patient autonomy and informed consent, non-maleficence and beneficence, justice, and integrity and transparency in reporting, guiding clinicians and researchers through the ethical complexities of treatment.

Patient autonomy and informed consent

Central to ethical case reporting is patient autonomy, which upholds individuals' rights to make informed health care decisions. This principle gains additional significance in reports involving off-label or experimental treatments. Clear, open communication about the treatment's nature, benefits, and risks is imperative for informed consent, especially for treatments diverging from standard care. Such a process respects the patient's informed choice[1].

Non-maleficence and beneficence

These principles compel health care providers to avoid harm and act in the patient's best interest. When contemplating off-label or experimental treatments, evaluating potential risks against benefits is crucial due to their uncertain outcomes. This ethical balance, demanding a cautious approach to prioritize patient well-being, is reflected in the pediatric off-label use of COVID-19 vaccines[1].

Justice

Case reporting's ethical dimension includes justice, emphasizing equitable treatment access. It prompts reflection on how reporting off-label or experimental treatments might influence their accessibility and potential disparities. The discussion on crowdfunding's ethical implications in pediatric neurology illustrates the challenges of ensuring equitable access to advanced treatments[3].

Transparency and integrity in reporting

Ethical reporting mandates transparency and integrity, requiring disclosures about the experimental status of treatments and honest outcome reporting. This commitment to openness supports the scientific integrity of case reports, enabling informed decision-making by the medical community based on accurate and comprehensive information. The need for

clear communication regarding the experimental nature of treatments and their outcomes reinforces the ethical responsibilities of authors in case reporting[1].

These ethical principles—patient autonomy and informed consent, non-maleficence and beneficence, justice, and transparency and integrity (Table 1)—form the cornerstone of ethical case reporting, guiding the responsible disclosure and communication of off-label or experimental treatments.

Ethical considerations in clinical decision-making

In clinical decision-making, the ethical deployment of off-label or experimental treatments is critical, requiring meticulous evaluation of evidence and consideration of alternatives to uphold patient welfare. This process involves a detailed examination of the treatment's scientific basis, effectiveness, and safety for the patient's needs[1]. Such assessments ensure interventions are grounded in robust scientific rationale, emphasizing the necessity for evidence-backed decisions in clinical practices that extend beyond standard care.

The ethical framework for clinical decisions also mandates conducting comprehensive risk-benefit analyses. These analyses, which are crucial for ethical decision-making, compare the intervention's potential advantages against possible risks, including both immediate and long-term effects. The precision medicine approach illustrates the criticality of understanding individual risks *vs* therapeutic benefits in creating personalized treatment plans[4]. This process ensures that decisions about off-label or experimental treatments are informed, prioritizing patient safety and adherence to the principle of non-maleficence.

Peer consultation and review by institutional ethics committees further solidify the ethical foundation of clinical decisions. Through peer consultation, clinicians can share knowledge and perspectives, addressing ethical challenges collaboratively. This practice is essential when navigating the complexities of off-label treatments. Meanwhile, ethics committees provide a formal review process, ensuring decisions meet ethical standards and guidelines. The collective input from peers and ethics oversight reinforces the medical community's commitment to ethical integrity in clinical practice, as exemplified by discussions on the ethical considerations for off-label pediatric use of COVID-19 vaccines by Lanphier and Fyfe[1].

This holistic approach to clinical decision-making underscores the importance of evidence-based practice, thorough risk assessment, and collaborative review in maintaining ethical standards in medicine. It highlights the collective duty of healthcare professionals to ensure patient-centric decisions that are scientifically justified and ethically sound, particularly when exploring treatments beyond established norms.

Role of case reports in advancing medical knowledge

Case reports have long been regarded as a cornerstone in the edifice of medical knowledge, providing insights into rare conditions, unusual presentations of common diseases, and the outcomes of novel or off-label treatments. Their value extends beyond mere academic curiosity, bridging significant gaps in the existing body of evidence, particularly in areas where randomized controlled trials are impractical or unethical. The utility of case reports in enriching the evidence base is multifaceted, offering a unique lens through which rare diseases and innovative treatment applications can be examined. This is especially pertinent in conditions with low incidence rates, where case reports may constitute the primary source of evidence, guiding clinical decision-making and research directions[1].

Moreover, case reports play a pivotal role in influencing clinical practice. They serve as early sentinels of novel disease entities, unexpected complications of treatments, or adverse drug reactions, thus alerting the medical community to emerging trends in patient care. However, this influence is not without its challenges. The anecdotal nature of case reports can lead to premature adoption of unproven therapies, potentially resulting in adverse patient outcomes. This underscores the ethical responsibility of authors to meticulously report the outcomes of such treatments, emphasizing not only the therapeutic successes but also the limitations and potential risks associated with their findings[5].

To navigate these ethical quandaries, it is imperative to establish and adhere to rigorous guidelines for the ethical reporting of case reports, especially those involving off-label or experimental treatments. Firstly, transparency in reporting should be paramount. Authors must disclose the rationale behind the use of off-label or experimental therapies, supported by a thorough review of the existing literature. Additionally, ensuring patient confidentiality is crucial. Identifiable patient information must be scrupulously protected to uphold the principles of privacy and respect for patient autonomy. Lastly, a balanced presentation of results is essential. Authors should provide an unbiased account of both positive and negative outcomes, facilitating a comprehensive understanding of the treatment's efficacy and safety profile. By adhering to these guidelines, case reports can continue to contribute to collective medical knowledge while maintaining ethical integrity and patient safety[1].

Challenges and controversies

In the landscape of medical research and treatment, a series of challenges and controversies persist, particularly in the realm of reporting outcomes and the interplay between commercial interests and medical innovation (Table 2). One of the foremost dilemmas lies in the reporting of negative outcomes. The ethical conundrum surrounding the disclosure of adverse outcomes or treatment failures is profound, with the shadow of publication bias looming large. This bias, a preference for publishing positive over negative results, can skew the medical literature, potentially misleading healthcare professionals and patients alike about the efficacy and safety of treatments[1]. The ethical imperative for transparency and honesty in reporting, balanced against fears of reputational damage or financial loss, creates a complex scenario for researchers and publishers.

Further complicating the landscape is the impact of commercial interests, particularly the influence exerted by pharmaceutical companies and other stakeholders in the healthcare sector. These entities play a crucial role in the development

Table 1 Ethical principles and considerations in reporting off-label and experimental treatments

Ethical principle	Description	Application in case reporting
Patient autonomy and informed consent	Ensures patients are fully informed about the nature, benefits, and risks of off-label or experimental treatments and consent to their use	Detailed process for obtaining and documenting informed consent in case reports
Non-maleficence and beneficence	Obligation to do no harm and to act in the best interest of the patient, assessing potential risks against benefits	Criteria for evaluating the risk-benefit ratio of off-label or experimental treatments for reporting
Justice	Focus on equitable treatment access and the implications of reporting on treatment availability and disparities	Analysis of how case reports address or could exacerbate health care access disparities
Transparency and integrity	Requirement for honest reporting of the experimental status of treatments and outcomes, including adverse effects	Guidelines for transparent and unbiased reporting, including disclosures of conflicts of interest

Table 2 Challenges and ethical dilemmas in reporting

Challenge	Ethical dilemma	Proposed solution
Reporting of negative outcomes	Balancing the ethical need for transparency with potential reputational or financial consequences for authors and sponsors	Implement policies for mandatory reporting of all outcomes, positive and negative
Commercial interests	Managing conflicts of interest that may influence the reporting and perception of off-label and experimental treatments	Strict disclosure requirements and independent review to mitigate the impact of commercial interests
Balancing innovation with caution	Navigating between the advancement of medical science and ensuring patient safety in the face of uncertain treatment outcomes	Development of comprehensive guidelines that prioritize rigorous scientific evaluation and patient safety

and dissemination of medical treatments, including off-label and experimental therapies. However, their vested interest in the success of these treatments can lead to conflicts of interest, impacting the impartiality of research findings and the integrity of treatment recommendations[1]. The influence of commercial entities raises questions about the balance between advancing medical innovation and ensuring that such advancements are genuinely in the best interest of patient health and safety.

Balancing innovation with caution presents perhaps the most intricate challenge. The medical field's intrinsic push toward innovation and the discovery of new treatments and therapies is a fundamental driver of progress. However, this quest for advancement must be carefully weighed against the imperative to protect patients from undue harm. The rapid development and off-label use of treatments, spurred on by urgent health crises or unmet medical needs, underscore the need for a delicate equilibrium. The drive to introduce novel therapies must be tempered by rigorous scientific scrutiny and ethical consideration, ensuring that patient welfare remains at the forefront of medical advancement[2,5].

Recommendations

The dynamic nature of medical science, with its constant evolution and introduction of novel therapies, mandates a continuous commitment to ethical vigilance. Clinicians, researchers, and publishers alike must remain steadfast in their dedication to ethical principles, particularly when dealing with off-label and experimental treatments. This entails a meticulous assessment of the risks and benefits of such interventions, the safeguarding of patient rights through informed consent, and the unbiased reporting of treatment outcomes. Ethical vigilance is essential to fostering a medical community that prioritizes patient welfare and the integrity of scientific inquiry. Looking forward, there is a clear necessity for the development of more comprehensive ethical guidelines that specifically address the challenges posed by off-label and experimental treatments. Such guidelines would benefit from the inclusion of diverse perspectives, encompassing clinicians, patients, ethicists, and legal experts, to ensure a well-rounded approach to ethical decision-making. Additionally, the role of regulatory bodies in overseeing the dissemination of information on experimental treatments warrants further exploration. These entities play a crucial role in ensuring that the information reaching both the medical community and the public is accurate, reliable, and ethically sound (Tables 3 and 4).

CONCLUSION

The ethical landscape of reporting off-label and experimental treatments in medical case reports is fraught with challenges, but offers significant opportunities for advancing medical knowledge and patient care. Upholding ethical principles such as patient autonomy, informed consent, beneficence, non-maleficence, justice, and transparency is paramount to navigating this complex terrain. Case reports serve as invaluable resources in shedding light on novel therapeutic approaches, yet they demand rigorous ethical scrutiny to ensure patient safety and uphold the integrity of medical science. As the medical community continues to explore uncharted therapeutic avenues, a collaborative effort involving clinicians, researchers, ethicists, and regulatory bodies is essential to develop comprehensive ethical guidelines that balance innovation with caution. This collaborative approach will safeguard patient welfare while fostering the responsible advancement of medical science, ensuring that the pursuit of novel treatments remains aligned with the

Table 3 Recommendations for ethical vigilance and reporting

Area of focus	Recommendation
Ethical guidelines development	Formulate comprehensive, clear guidelines specifically addressing off-label and experimental treatments, with input from a multidisciplinary team
Regulatory oversight	Enhance the role of regulatory bodies in monitoring and guiding the reporting on experimental treatments to ensure accuracy and ethical compliance
Education and training	Provide ongoing education for clinicians and researchers on ethical reporting practices and the importance of maintaining integrity in medical research

Table 4 Key areas for collaborative effort

Stakeholder	Role in advancing ethical reporting
Clinicians	Share clinical experiences and adhere to ethical guidelines in reporting of off-label and experimental treatments
Researchers	Conduct and report research with integrity, following ethical guidelines and contributing to the body of evidence on new treatments
Ethicists	Provide guidance on ethical dilemmas and contribute to the development of comprehensive ethical guidelines
Regulatory bodies	Oversee the reporting practices and dissemination of information to ensure public access to reliable and ethically reported data on new treatments

highest ethical standards.

FOOTNOTES

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Country of origin: India

ORCID number: Madhan Jeyaraman 0000-0002-9045-9493; Naveen Jeyaraman 0000-0002-4362-3326; Swaminathan Ramasubramanian 0000-0001-8845-8427; Sangeetha Balaji 0000-0002-1566-1333.

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