



Commentary

Exit Conservative Peer Review and Welcome to Predator Journals!

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Prestigious Journals such as the 'New England Journal of Medicine' are criticized by scientists for lack of objectivity in its peer review process [1]. Comparative Journals, such as 'Science', published fake data, without anyone noticing it [2]. Research misconduct cases, related to individual scientists falsifying data or manipulations within the science publishing community is a hot topic. In 2017 China's Ministry of Science and Technology found hundreds of scientists guilty of supporting in a peer-review fraud scam related to the nomination of fictitious peer reviewers. An Expert Group on Scientific Misconduct in Sweden, on request from the Karolinska Institute, analysed a case where the well-known and respected Journal 'The Scientist' was covering for years of fraudulent data produced by the surgeon Paolo Macchiarini. Evidence of scientific misconduct leading to the death of 3 patients was found by the expert group in all six of Macchiarini's publications it reviewed.

Meanwhile, to counteract these critical aspects in science, at one of the universities of Amsterdam (The Netherlands), a special chair is created to address scientific integrity, leading to a number of important papers and congresses in this new emerging field [3,4]. In 2017, the holder of the chair, Professor Lex Bouter, organized the 5th World Conference on Research Integrity in Amsterdam and subsequently became chair of the World Conferences on Research Integrity Foundation.

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Clearly the old system is rambling and needs to be revised, redesigned and optimized. This is quite important, as in our postmodern society the general public tends more and more to disbelieve scientific facts, and use the above cases to support their point that science is useless and one should follow one's intuition only. The major problem of an increasing number of people being reluctant to use vaccinations, is a clear indicator of an increasing public distrust of science.

We live in an interesting time, and with the emergence of many new and innovative medical journals on the net, a new form of peer review is emerging. It is about time! Most of these new Journals, not PubMed indexed, are strangely enough classified as 'predator journals'. This we feel, is caused by an old reflex of the medical establishment, not understanding the importance of 'predators' in the ecosystem of scientific literature. It is to be expected that these 'predators' will change the scientific landscape, and most probably revolutionize the old and imperfect system. I will argue that given the world-wide access to the internet and the assistance of powerful search engines such as Google, a new approach to medical data-reporting is needed. One that is not conservative as the current peer review system is, which dominates all PubMed indexed journals.

My position is provoked by a recent experience I gained based on a peer review process of a paper we submitted to a journal in the field of neurology, a real PubMed indexed Journal of some reputation. In the first round of review two reviewers brought up certain points for improvement and we adapted the paper accordingly. However, after submitting the revision, in the second round of review, surprisingly new points emerged and our paper was declined based on an absurd reason, brought up by both reviewers: an ethics committee should have been involved. The paper however did not describe results from a clinical trial. We gave a description of our experiences related to the first neuropathic pain patients treated with a compounded topical formulation containing the co-analgesic phenytoin. It was a non-interventional, non-randomized, non-controlled case series. In the Netherlands, it is accepted by all relevant authorities, that physicians can and are allowed prescribe to patients compounded medication for 'off-label' use based on scientific rationale and/or data. The only restriction is, that the prescribing physician has to explain to the patient the drug prescribed has not been officially approved for the indication it is now used. Patients in our center are always informed and give their verbal consent for such off-label use. An ethics committee is not needed for such treatment.

What did both reviewers say about our reversed new version? They expressed a new concern related to why the authors have not sought to inform and get permission from the local/regional ethics board for treating patients with the cream containing phenytoin. The paper subsequently was declined.

Missed Opportunities

Both reviewers explicitly pointed out that in the report of our case-study no ethics committee was involved and that this was apparently a crucial omission. This is odd, because repositioning of old drugs in new indications is happening all the time, and falls under 'off-label

use'. To collect a database of patients being treated by such repositioning is not a clinical study, and no ethics committee thus is needed. If we would need such committee, all progress in the field of repositioning would become difficult, as review by ethics committee's costs time and money. And who pay for this? It would be a missed opportunity! Moreover, the balance between safety and efficacy of old drugs, which are registered for years, is quite well known.

Now it seems to us that bringing forth this issue of an ethics committee should be regarded as an old reflex based on the invasiveness of evidenced based medicine in our thinking. Such reflex is perhaps useful if it concerns studies with new chemical entities, not yet registered, but in our case, it was not constructive.

This conservative way of thinking also leads to 'tic the box' behavior when physicians treat patients according to guidelines. In the case of therapy refractory patients there are no guidelines. Our patients tell us frequently, after having visited academic centres, that the doctors told them: "you have to learn to live with 'it' ('it' stands for the pain)". Our conditioning therefore not only obstructs the reporting of clinical observations; it also seems to induce a therapeutic paralysis: nothing can be done once the guidelines have been followed. It is of great importance to highlight the lack of action of clinicians outside the well-established guidelines, and sadly enough it seems a general attitude when facing an innovative approach, such as the repositioning of a drug in a new indication. We need more papers covering items related to the repositioning of old drugs, to show the medical community that one can proceed helping patients, also when guidelines are not there to guide us. Which is the case in treatment-refractory patients.

One very clear example from literature is the absence of interest in a compound as alpha lipoic acid as a treatment for painful diabetic neuropathy. Although a number of placebo-controlled studies have supported the safety and efficacy of this supplement, it is not part of treatment guidelines, and apart from Germany, physicians have never heard of the compound [5]. The same hold true for the analgesic and anti-inflammatory natural compound palmitoylethanolamide, which clearly reduces pain in compression neuropathy [6].

In modern times communication from medical researchers to the medical field should not be hampered by conservatism, as we have seen above in the reaction of both reviewers to our presentation of a non-randomized, non-controlled case series. We demonstrated by sharing our first observations the safety of topical phenytoin cream, our case collection was the first in the world of patients treated with topical phenytoin cream [7].

We feel science is obstructed by such peer review, and moreover it seems quite paternalistic to let two reviewers decide whether a paper will contribute to science or not. I am now urged to say: "let the reader decide". Publish as soon as possible, so that others may benefit from results and let the value of a paper be judged by the readers. Do we have any hard evidence, that peer review improved our science? No, we do not!

Old Peer Review System Ripe for Revamping

The old peer review system is now ripe for redesigning. And it is redesigned by many of the so called 'predatory' journals. Peer review in those journals exist, but it functions more as a first sieve, not as a

canon. It is as with the taxi-uber controversy: the ancient taxi system is now replaced by a much more flexible uber system, and the replacement goes fast. Just as fast as the introduction of many 'predatory' journals, hundreds have been introduced lately, and they present a forum for many scientists to quickly publish their data. One could suggest to those journals to evolve into a platform for a more dynamic way of presenting scientific data, perhaps following a blog-format. The first step for authors to publish a paper would be to publish it in a Journal designed blog-environment, comparable to scientific groups in linked-in. The second step would be an open discussion within members of the peer group, and subsequently the paper is published in the final version in the journal.

Let us stop the ineffective and inefficient peer review system, and find new more open ways to communicate, ways which are not paternalistic. 'Predator journals' may play a key role here!

The case and argumentation presented here, serves also to support the fact that publishing case studies/clinical data in the medical field is of daily interest for interns, Practitioners and clinicians to keep updated and find new inspiration via out-of-the-box treatment concepts. To be valuable for a worldwide audience however, there should nevertheless be a peer reviewing and like in conservative journals, it is crucial that it always remains constructive.

Conflict of Interest

The author is a patent holder of two patents related to the topical formulations of phenytoin in the treatment of neuropathic pain.

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