Lessons for teaching from the pandemic

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Abstract

In the context of the current COVID-19 pandemic, what are the lessons clinical pharmacology could learn to improve our teaching practice and involvement in research and ethics committees to make sure we are better prepared for the next emergency. Is there something in the light of the hydroxychloroquine hype that we as clinical pharmacologists or our professional societies could have done better? We propose updating the way we teach about drug development, rules and ethics of off-label prescribing and critical appraisal of primary sources when guidelines and top-level evidence are not available. Clinical pharmacology should play a leading role in the future re-definition of processes and guidelines for emergencies such as the one we faced in 2020.

Teaching (clinical) pharmacology

While the focus of our curriculum is currently on the development of novel drugs, it may be worthwhile to include more examples of drug repurposing and the resulting research and ethical questions concerning off-label use of old drugs in a different new settings and populations. Thalidomide and rituximab are just some of the examples that can be used to demonstrate the processes that lead to use in different indications from those originally developed for a drug. (1). Students should understand that even "old" drugs need to go through approval if their indications are to be expanded.

With our colleagues in medical ethics, we should make sure students understand the proper use of off-label prescription and experimental treatment. Just because a drug has been used for a long time does not make it inherently safe and "free to use". Informed consent of the patient is still required (2).

In the age of guidelines and EBM, we need to make sure our students and future colleagues are prepared to deal with uncertainty when the comforting blanket of randomised controlled studies and meta analyses is suddenly jerked away from them. Balancing risk and benefit is one of the most challenging parts of drug prescription, especially so at a time like this.

Skills in critical appraisal of evidence are an essential tool of any prescriber, even for those who are "just consumers" of science. The recent torrent of COVID studies was a prime opportunity to practice critical reading. When there is no time for proper peer review, each of us must be their own reviewer. While the main burden may lie with our colleagues teaching epidemiology and scientific methodology, we should make sure our students leave their pharmacology course prepared to read and appraise papers on drugs.

As is so often the case, those who are full of doubt and checking twice were initially silent while the (over)confident were heard around the world, with politicians gladly repeating their unsubstantiated claims just to be seen by the public as the ones in charge, with a plan. Preparing our students to deal with primary sources of uncertain quality can help them make decision when guidance "from the top" disappears. Studies of poor quality with surrogate outcomes and no control should not be considered evidence justifying off-label use of drugs without ethical approval and patient consent.

Role of professional societies

While pharmacological societies, including the EACPT, were quick to warn about the risks of unfounded and potentially dangerous over-reaction to the initial fear of using ibuprofen or angiotensin blocking drugs in COVID (and in both cases, we were shown to be right), our voice regarding hydroxychloroquine was maybe drowned by the many louder calls for action. It is understandable that microbiologists and intensivists initially included HCQ in their guidelines. Our western society suffers from action bias; it is considered a lesser error to act and fail than to fail to act. Furthermore, we clinical pharmacologists were perceived as "commenting from the side lines", we were not the ones bed side with critically ill patients to take care of with everyone watching. Still, our expertise and certain well-founded "skepticism", had we managed to have ourselves heard, could have brought valuable insight into the initial chaos.

Clinical pharmacologists in research

It is now clear that the systems we have in place, both in academic research and in the industry, are not well suited for emergencies when immediate answers are required by our colleagues standing bed side and by those in charge of making policy decisions. The academic world is used to grant applications, reviews, publications and more reviews. The system emphasises quality over speed, proper methodology over quick answers. Can clinical pharmacology contribute to development of procedures for future emergencies? Can we perhaps make do with non-blinded studies? What randomisation is good enough? Are we happy with surrogate outcomes? Clinicaltrials.gov returns 262 studies on the role of hydroxychloroquine and/or chloroquine in COVID-19 (3). Most of them are single centre, of questionable methodological quality. At a time when there were already millions of confirmed cases with tens of thousands recovered, many of whom were treated, we were still struggling to find answers. It wasn't until the results of the RECOVERY trial that we got high quality data (4). Clinical pharmacologists could play a key role in coming up with a framework for rapid "real world" trials that could provide us with answers in future emergencies.

Hospitals and ethics committees

In many hospitals, the processes that are normally in place for experimental treatments were disrupted by the pandemic. Ethics committees did not meet, there was no one to prepare and file proposals anyway. As a result, patients got treated with an experimental (albeit "old and known") drug without proper informed consent, without ethics approval.

Clinical pharmacologists serving on these committees should take lead in preparing proper procedures for emergency authorisation with an informed consent that can be updated as more information becomes available. The framework needs to be prepared in advance with clear roles and responsibilities, since at a time of crisis it is perhaps not reasonable to expect intensive care physicians to deal with the paperwork required. Clinical pharmacologists seem to be the logical choice for leading this process and assisting clinicians in this context.

Summary

Clinical pharmacology as a medical specialty plays a key role in clinical situations that deviate from the routine, where guidelines and summaries of product characteristics fail. It is therefore not surprising that at times such as the current pandemic, our colleagues expect us to provide insight and guidance. We should take a critical look at the past six months to learn what we could improve in our teaching and clinical practice so that both our students and ourselves are better prepared next time a crisis of similar magnitude arises.

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