Coronavirus: The End of the Crisis?

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Executive Summary

Hydroxychloroquine (HCQ) and Azithromycin (AZ) for the treatment of the Coronavirus (COVID-19) has received substantial attention in recent days. As described in more detail below, HCQ and AZ have very well-established safety profiles. A study from the South of France, showing the effectiveness of these drugs in the treatment of COVID-19, and the University of Washington protocols have specified the following:

- Perform baseline EKG, address any cardiology risks and monitor EKG throughout entire treatment period\footnote{2}
- Determine patient allergies or potential for adverse reactions and contraindications to both drugs
- Administer 200 milligrams of Hydroxychloroquine sulfate, three (3) times per day (a total of 600 milligrams per day) for ten (10) days\footnote{3}
- Administer Azithromycin at 500 milligrams on day 1, followed by 250 milligrams per day for four (4) days\footnote{4}

It must be emphasized that this article is written by attorneys who are reporting these treatment protocols from medical authorities.

HCQ and AZ are approved by the United States Food and Drug Administration (FDA) for diseases other than the Coronavirus. Medical practitioners might be reluctant to prescribe these drugs as an off-label use given possible liability. However, medical practitioners may protect themselves through informed consent, a well-established concept under New York State law, described in detail below.

Introduction

“Hydroxychloroquine and Azithromycin, taken together, have a real chance to be one of the biggest game changers in the history of medicine.” President Donald Trump, Twitter, March 21, 2020. New York State’s Governor Andrew Cuomo announced in a televised news conference on March 22, 2020 that these drugs will be the subject of clinical trials in New York State starting March 24, 2020.\footnote{6}

Treatment Summary

The utilization of Hydroxychloroquine (HCQ) and Azithromycin (AZ) as a treatment for the coronavirus (COVID-19) is the subject of a study from the south of France issued March 18, 2020.\footnote{7} We understand that this study will be published in the International Journal of Antimicrobial Agents.\footnote{8} A copy of the study is attached. The
study was performed under the direction of Didier Raoult, MD, PhD and Philippe Gautret, MD, PhD, both widely recognized infectious disease specialists.

In this study, HCQ and AZ were utilized to treat COVID-19 patients. The study involved 36 patients, which included 16 patients in a control group. The results showed patients prescribed both drugs were 100% virologically cured of COVID-19 within six (6) days. Patients that were not treated (control group) did not show significant improvement. As the authors of this study explained, “our study has some limitations including a small sample size...”. There were 20 patients that were treated: six (6) patients treated with HCQ and AZ, that resulted in the 100% virological cure and 12 patients treated with only HCQ, that showed substantial improvement but not as significant as when both drugs were used. Obviously, this is a small group, but the results appear promising. The authors ultimately “recommend that COVID-19 patients use [HCQ and AZ] to cure their infection and to limit the transmission of the virus...”.

Interestingly, the authors state these compounds could be useful “to prevent the transmission of the virus, especially for healthcare workers.” This raises the prospect for a preventative therapy. Didier Raoult MD, PhD and his team stated that, “[w]e think that it is not moral that this ... is not systematically included in the therapeutic trials concerning the treatment of Covid-19 infection ...”. Additionally, Didier Raoult, MD, PhD and Philippe Gautret, MD, PhD have suggested that:

(1) individuals without symptoms who test positive for COVID-19 should be treated promptly with HCQ and AZ to limit or avoid symptoms and reduce the spread of infection,

(2) if the symptoms have already resulted in significant respiratory issues, such as permanent lung damage, it is unlikely HCQ and AZ would be able to reverse this damage, and

(3) it is important to test everyone as soon as possible, especially high-risk healthcare workers, and treat immediately before symptoms arise.

Such a strategy would require increased tracking and testing for COVID-19. We understand that in China, and perhaps in South Korea, cell phones were used to trace people who were in recent contact with COVID-19 patients as a means to ensure thorough tracking and containment of the virus.

There is anecdotal information suggesting HCQ is currently part of the protocol for treating COVID-19 patients in South Korea and China and that hospitals in the United States are using HCQ for the treatment of COVID-19 patients. Daniel Dae Kim, a well-known actor from South Korea, recently shared his COVID-19 experience on social media, including his use of HCQ and AZ as treatment.

Based on the treatment procedure in the study described above and guidance compiled from hospitals like the University of Washington in Seattle, the following is a summary of treatment procedures (please consider that we are attorneys, not medical professionals, and are reporting from medical authorities):
- Perform baseline EKG and address any cardiology risks and monitor EKG throughout entire treatment period\textsuperscript{[12]}
- Determine patient allergies or potential for adverse reactions and contraindications to both drugs
- Administer 200 milligrams of Hydroxychloroquine sulfate, three (3) times per day (a total of 600 milligrams per day) for ten (10) days\textsuperscript{[13]}
- Administer Azithromycin at 500 milligrams on day 1, followed by 250 milligrams per day for four (4) days\textsuperscript{[14]}

Treatment Safety

HCQ has been widely available and used in medicine since 1955.\textsuperscript{[15]} The primary approved uses of HCQ are for treatment of malaria, lupus and rheumatoid arthritis.\textsuperscript{[16]} The safety profile of HCQ has become established over decades of learning and understanding the risks and side effects associated with its use alone and in combination with other drugs.

Similarly, AZ has a safety profile that has been established since its use beginning in 1991.\textsuperscript{[17]} The most commonly known use of AZ is Zithromax or Z-Pak, which is approved for use to treat acute bacterial exacerbations of chronic obstructive pulmonary disease, acute bacterial sinusitis, community-acquired pneumonia, pharyngitis/tonsillitis, uncomplicated skin and skin structure infections, urethritis and cervicitis and genital ulcer disease.\textsuperscript{[18]}

Having a thorough understanding of the safety profiles of both of these drugs is crucial to the acceptance of their use as a potential treatment of COVID-19. Fortunately, we have decades of studies demonstrating the safety of these drugs, including one such study which states “[b]oth azithromycin and chloroquine have been safely administered individually in all trimesters of pregnancy.” The report concludes that “[t]he combination may be safely administered any time during pregnancy…”\textsuperscript{[19]} While these studies use chloroquine, rather than HCQ, it is understood that HCQ has a better safety profile than chloroquine.\textsuperscript{[20]}

Legal Implications for Use of HCQ and AZ as Off-Label Drugs

In addition to the approval and marketing of prescription drugs in the United States, the Food and Drug Administration (FDA) also oversees labeling. All prescription drugs available in the United States today have their own FDA-approved label which contains important information including, among many others, the approved uses of the drug. When a medical practitioner prescribes the drug for a use that is not specified on the FDA-approved label it is considered an "off-label" use.

Currently, there is no authority limiting medical practitioners from prescribing off-label prescription drugs. The Agency for Healthcare and Research Quality, the lead Federal agency charged with improving the safety and quality of America's health care system, states that as many as one in five prescriptions written today are for an off-label use and that the practice is “legal and common.”\textsuperscript{[21]} Indeed, the FDA website currently states, "[f]rom the FDA perspective, once the FDA approves a drug, healthcare providers generally may prescribe the drug for an unapproved use when they judge that it is medically appropriate for their patient."\textsuperscript{[22]}
A doctor’s need to prescribe drugs off-label stems from science and medicine moving faster than the FDA’s bureaucracy and regulation. The pace of medical discovery invariably runs far ahead of FDA’s regulatory machinery, and off-label use is frequently state-of-the-art treatment.[23] The editor of the Journal of the American Medical Association testified before Congress that for a product to have the most effective potential benefits, law and regulation should and must follow, not precede, science. There are too many variations in clinical circumstances and too much time delay in regulations to allow the government to impede the physician’s ability to practice in these regards when it is medically appropriate.[24]

While drug manufacturers are aware of the prevalence of off-label uses, many may lack an incentive to get approval for the off-label uses due to the expensive and lengthy FDA-approval process. With drugs that have been approved for as long as HCQ and AZ, there is little economic benefit for manufacturers to obtain FDA approval. This concept may also explain the wide use and acceptance of prescribing off-label drugs.

Despite a seemingly wide-spread use of off-label prescription drugs, medical practitioners should be confident they can be protected from potential malpractice claims. The law prescribes a number of ways a medical practitioner may seek to substantially reduce potential liability associated with prescribing off-label use prescription drugs.

Informed Consent in New York State

It is essential that a medical practitioner disclose to a patient the alternatives, risks and benefits associated with a particular treatment prior to administering such treatment. When a patient agrees to treatment, it is considered “informed consent.” The lack of informed consent can cause serious issues for a medical practitioner. New York Public Health Law § 2805-D addresses informed consent.[25] Below is a summary of New York Public Health Law § 2805-D in relevant part. A complete version of the statute is attached.

A medical practitioner must obtain informed consent in those cases involving either (a) non-emergency treatment, procedure or surgery, and (b) a diagnostic procedure which involved invasion or disruption of the integrity of the body.[26] A medical practitioner’s failure to obtain informed consent from a patient in these situations can lead to malpractice liability.

For medical practitioners, it shall be a defense to any malpractice action based upon an alleged failure to obtain such an informed consent that: (i) the patient assured the medical practitioner he/she would undergo the treatment regardless of the risk involved, or the patient assured the medical practitioner that he/she did not want to be informed of the matters to which he would be entitled to be informed; or (ii) consent by or on behalf of the patient was not reasonably possible. [27] Notably, under New York law, a medical practitioner likely need not obtain informed consent in an emergency. [28]

Thus, prior to prescribing HCQ and AZ, or any off-label use medication, medical practitioners should be certain that their patients are fully informed of the risks associated with the proposed treatment. Medical practitioners can prove informed
consent was obtained prior to the administration of an off-label treatment in the following ways:

- Provide the patient with ample written literature on the drugs in a format that can be easily read and comprehended by the patient. Written literature should be available in a variety of languages.
- Have the patient provide an ink signature on a form wherein the patient acknowledges that the use of HCQ and AZ in the treatment of COVID-19 is an off-label use and states that the patient fully understands the procedure, as well as, the potential for risks, benefits, side effects and alternatives (including no treatment) associated with the treatment and authorizes the medical practitioner to proceed with such treatment. The form itself should state the treatment procedure, as well as, the potential for risks, benefits, side effects and alternatives specific to the individual patient.
- Have the treating medical practitioner engage in an oral conversation with the patient about the treatment wherein the potential risks, benefits, side effects and alternatives are thoroughly explained to the patient in a manner that is simple enough for the patient to understand. Also, allow the patient to: (1) ask questions to his/her satisfaction and (2) confer with family advisors, if desired. Medical practitioners should seek to have a witness present during this discussion, as well as, a translator if necessary.

Assumption of Risk Defense in New York State

New York law recognizes assumption of risk defense in negligence tort liability actions. This can also be applicable in a malpractice case. Assumption of risk can be expressed or implied. The New York Court of Appeals stated that, “[e]xpress assumption, which was held to preclude any recovery, resulted from agreement in advance that [medical practitioner] need not use reasonable care for the benefit of [patient] and would not be liable for the consequence of conduct that would otherwise be negligent.”[29] “Implied assumption was founded not on express contract, but on plaintiff's voluntarily encountering the risk of harm from defendant's conduct with full understanding of the possible harm to himself or herself.”[30]

The Court of Appeals for the Second Circuit has stated, “[e]xpress assumption of risk is a total bar to recovery.”[31] Quoting an earlier Second Circuit decision, the Court states, “[i]n Schneider, we stated that "[w]hile a patient should be encouraged to exercise care for his own safety, we believe that an informed decision to avoid surgery and conventional chemotherapy is within the patient's right `to determine what shall be done with his own body.'" 817 F.2d at 995 (citations omitted). This conclusion led us to hold that a patient may expressly assume the risk of malpractice and dissolve the physician's duty to treat a patient according to the medical community's accepted standards.”[32]

The bottom line is that “[t]he standard for proving negligence in a malpractice case is whether the treatment deviates from accepted medical standards.”[33] However, even when deviating from accepted medical standards, medical practitioners can substantially limit or potentially eliminate their liability. Thus, it is critical that medical practitioners use discretion in their decision to administer HCL and AZ and as to the sufficiency of their disclosure and informed consent practices with their patients. This practice should be applied to the prescription of all off-label uses of drugs.
Conclusion

As we continue into this unchartered territory that is COVID-19, we are hopeful that medical practitioners can rest assured of the legal protections in place that are associated with the prescription of an off-label drug use. Medical practitioners should use their discretion on a case by case basis, but the objective is that they should not feel inhibited by what might be considered an off-label use stigma. These unprecedented times call for unprecedented actions, but we must still be logical and rational in our actions. 

Please do not regard this paper as medical or legal advice. The authors of this article are not medical practitioners. Appropriate legal and medical professionals should be consulted for each specific situation.

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[2] https://twitter.com/ArunRSridhar/status/1239989367822639104/photo/1


[4] Id.


[7] Id.


[10] The authors received this information via communication with Didier Raoult, MD, PhD and Philippe Gautret, MD, PhD

[11] https://twitter.com/ArunRSridhar/status/1239989367822639104/photo/1

[12] https://twitter.com/ArunRSridhar/status/1239989367822639104/photo/1

[14] Id.


[18] https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/050710s039,050711s036,050784s023lbl.pdf


[20] https://www.nature.com/articles/s41421-020-0156-0


[22] https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/understanding-unapproved-use-approved-drugs-label

[23] https://www.nature.com/articles/3901619.pdf?origin=ppub

[24] Id.


[30] Id.

[31] Boyle v. Revici, 961 F.2d 1060, 1063 (2d Cir. 1992)

[32] Id.