Do No Harm or Harm Reduction: The Ethical Dilemma

Medical profession is a noble profession, which comes with lot of responsibilities. The relationship between the doctor and patient is a fiduciary relationship and doctors must adhere to the principles of medical ethics (autonomy, non-maleficence, beneficence and justice), rules (fidelity, confidentiality, privacy and veracity) and virtues (compassion, kindness, respect, etc.) in their interactions with the patients, which have been laid down by various professional bodies and associations as professional codes of conduct and standards for doctors. The Hippocratic Oath, the oldest of these codes of ethics, still holds true today.

Let's take a look at different codes of ethics and the principles therein.

In the **Hippocratic Oath,** the aspect that is instructive and serves as guide to physicians in respect of non-maleficence states that: "*I will follow that system of regimen, which, according to my ability and judgment, I consider for the benefit of my patients, and abstain from whatever is deleterious and mischievous. I will give no deadly medicine to anyone if asked, nor suggest any such counsel.*"

In the **Declaration of Geneva**, and as amended in Sydney 1968, physicians were expected and indeed mandated to: "*…maintain the utmost respect for human life from the time of conception; even under threat, ... not [to] use medical knowledge contrary to the laws of humanity.*"

The International Code of Medical Ethics states that: "*A doctor must always bear in mind the obligation of preserving life.*"

In India, at the time of registration with the Medical Council, the doctors are given a declaration as per the Appendix 1 of **Indian Medical Council (Professional Conduct, Etiquette and Ethics) Regulations, 2002** which is reproduced hereunder:

> ***"A. DECLARATION***
>
> *At the time of registration, each applicant shall be given a copy of the following declaration by the Registrar concerned and the applicant shall read and agree to abide by the same:*
>
> *1) I solemnly pledge myself to consecrate my life to service of humanity.*
>
> *2) Even under threat, I will not use my medical knowledge contrary to the laws of Humanity.*
>
> *3) I will maintain the utmost respect for human life from the time of conception.*
>
> *4) I will not permit considerations of religion, nationality, race, party politics or social standing to intervene between my duty and my patient.*
>
> *5) I will practice my profession with conscience and dignity.*
>
> *6) The health of my patient will be my first consideration.*
>
> *7) I will respect the secrets which are confined in me.*
>
> *8) I will give to my teachers the respect and gratitude which is their due.*
>
> *9) I will maintain by all means in my power, the honor and noble traditions of medical profession.*
>
> *10) I will treat my colleagues with all respect and dignity.*
>
> *11) I shall abide by the code of medical ethics as enunciated in the Indian Medical Council (Professional Conduct, Etiquette and Ethics) Regulations, 2002."*

The **World Medical Association in its Medical Ethics Manual** has stated that:

> *"Beneficence - literally, 'doing good'. Physicians are expected to act in the best interests of their patients.*
>
> *Non-maleficence - literally, not doing wrong. Physicians and medical researchers are to avoid inflicting harm on patients and research subjects."*

United Nations Educational, Scientific and Cultural Organization in Universal Declaration on Bioethics and Human Rights which addresses ethical issues related to medicine, life sciences and associated technologies as applied to human beings, taking into account their social, legal and environmental dimensions. The relevant articles of the said Declaration are reproduced hereunder:

> ***"Article 4 - Benefit and harm:***
>
> *In applying and advancing scientific knowledge, medical practice and associated technologies, direct and*

indirect benefits to patients, research participants and other affected individuals should be maximized ***and any possible harm to such individuals should be minimized.***

Article 5 - Autonomy and individual responsibility:

The autonomy of persons to make decisions, while taking responsibility for those decisions and respecting the autonomy of others, is to be respected. For persons who are not capable of exercising autonomy, special measures are to be taken to protect their rights and interests.

Article 8 - Respect for human vulnerability and personal integrity:

In applying and advancing scientific knowledge, medical practice and associated technologies, human vulnerability should be taken into account. Individuals and groups of special vulnerability should be protected and the personal integrity of such individuals respected.

Article 10 - Equality, justice and equity:

The fundamental equality of all human beings in dignity and rights is to be respected so that they are treated justly and equitably.

Article 11 - Non-discrimination and non-stigmatization:

No individual or group should be discriminated against or stigmatized on any grounds, in violation of human dignity, human rights and fundamental freedoms."

Indian Council of Medical Research in 2000 in its book titled as **"Ethical Guidelines for Biomedical Research on Human Participants"** has stated that:

"*All the research involving human participants should be conducted in accordance with the* ***four basic ethical principles, namely autonomy (respect for person/participant) beneficence, non-maleficence (do no harm) and justice****. The guidelines laid down are directed at application of these basic principles to research involving human participants."*

International Ethical Guidelines for Biomedical Research Involving Human Subjects prepared by the **Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO)** provides the general ethical principles as:

"GENERAL ETHICAL PRINCIPLES

All research involving human subjects should be conducted in accordance with three basic ethical principles, namely respect for persons, beneficence and justice. It is generally agreed that these principles, which in the abstract have equal moral force, guide the conscientious preparation of proposals for scientific studies. In varying circumstances they may be expressed differently and given different moral weight, and their application may lead to different decisions or courses of action. The present guidelines are directed at the application of these principles to research involving human subjects.

Respect for persons incorporates at least two fundamental ethical considerations, namely:

a) respect for autonomy, which requires that those who are capable of deliberation about their personal choices should be treated with respect for their capacity for self-determination; and

b) protection of persons with impaired or diminished autonomy, which requires that those who are dependent or vulnerable be afforded security against harm or abuse.

Beneficence refers to the ethical obligation to maximize benefits and to minimize harms. *This principle gives rise to norms requiring that the risks of research be reasonable in the light of the expected benefits, that the research design be sound, and that the investigators be competent both to conduct the research and to safeguard the welfare of the research subjects. Beneficence further proscribes the deliberate infliction of harm on persons; this aspect of beneficence is sometimes expressed as a separate principle, non-maleficence (do no harm).*

Justice refers to the ethical obligation to treat each person in accordance with what is morally right and proper, to give each person what is due to him or her. In the ethics of research involving human subjects the principle refers primarily to distributive justice, which requires the equitable distribution of both the burdens and the benefits of participation in research. Differences in distribution of burdens and benefits are justifiable only if they are based on morally relevant distinctions between persons; one such distinction is vulnerability.

"Vulnerability" refers to a substantial incapacity to protect one's own interests owing to such impediments as lack of capability to give informed consent, lack of alternative means of obtaining medical care or other expensive necessities or being a junior or subordinate member of a hierarchical group. Accordingly, special provision must be made for the protection of the rights and welfare of vulnerable persons."

Obligation of non-maleficence: moral dilemma in physician-patient relationship by Peter F Omonzejele in his book - A Peer-review Journal of Biomedical Sciences, June 2005 Vol. 4 No. 1 pp. 22-30:

"The principles and rules of medical ethics are derived from the Hippocratic oath and various declarations

(Declaration of Geneva as amended in Sydney 1968, Declaration of Tokyo 1975, Declaration of Oslo 1970, Declaration of Helsinki 1975, etc.) regulating medical practice. Despite the Hippocratic oath and various declarations, a certain aspect (non-maleficence) of the oath and declaration is sometimes breached in what seems to be in the "interest" of patients in circumstances that constitute moral dilemmas.

The physician-patient relationship is fiduciary. The patient believes and trusts that the physician would apply his professional expertise in his/her (the patient's) interest and benefit. Even more importantly, the patient believes that his/her physicians (based on the principle of non-maleficence) would do nothing to harm him/her. The principle of non-maleficence runs through from the Hippocratic oath to current versions and amendments of medical ethics.

Non-maleficence in general and medical non-maleficence in particular, recommends that one ought not to inflict evil or harm."

Not only has medicine undergone tremendous advancements over the years, the social milieu has changed and the patients have changed as well, which is reflected in the doctor-patient relationship; from "*paternalism*", where doctors were "*parent figures*" taking medical decisions on behalf of their patients to the current "*patient-centric*" where the patient is an "*equal partner*".

Regardless, the core values of the practice of medicine are still based on the principles of non-maleficence, derived from the doctrine of "*primum non-cere*", which means "first do no harm" and its natural corollary, beneficence or "do good", which means doing the right thing for the patient.

Harm reduction is now a new term in non-maleficence. The basic ethical duty of the doctor is to treat on the principle "first do no harm". But doctors will often end up with social determinants of health where they will have to choose between the two devils and in that situation the answer is to choose the lesser devil and this is what is called a harm reduction strategy.

It has been recognized as a public health strategy since the 1980s, when it was first used as an alternative to abstinence-only interventions for adults with substance abuse disorders who were unwilling to quit.

Harm reduction is an umbrella term for interventions aiming to reduce the problematic effects of behavior. Harm reduction has a human rights agenda in that it is committed to bringing effective treatment to groups that have traditionally been denied quality care. It is scientific in that it is committed to the discovery and implementation of evidence-based interventions.

Doctors practice harm reduction every day. To list a few:

- Rational use of drugs and investigations is a harm reduction approach. It requires that "*patients receive medications appropriate to their clinical needs, in doses that meet their individual requirements, for an adequate period of time, and at the lowest cost to them and their community*" (WHO 1985).
- The 'Five Rights' of safe medication administration by the Institute of Healthcare Improvement also promote rational use of drugs: Right patient, Right drug, Right time, Right dose and Right route. Four more 'Rights' have been added to this: Right documentation, Right action (reason for prescribing the medication), Right form and the Right response.
- Antimicrobial stewardship programs, which are being advocated to curb the rising prevalence of antimicrobial resistance.
- The "Choosing Wisely" campaign, an initiative of ABIM (American Board of Internal Medicine Foundation) launched in 2012 encourages a dialogue between the doctor and the patient about "*what is appropriate and necessary treatment"* and helps patients to choose care that is: "*Supported by evidence, not duplicative of other tests or procedures already received, free from harm and truly necessary.*"
- To reduce prescription errors, the Medical Council of India (MCI) has issued guidelines that require a doctor to write in capital letters.
- Vaccination is an established harm reduction strategy.
- Maintaining basic hygiene and hand washing are also ways of harm reduction.

No doctor practices medicine to harm the patient. Yet, patients are exposed to some potential harm.

There are risks of side effects with the prescribed medications; there are implied risks in every intervention or procedure. While a major surgery may be uneventful, sometimes unanticipated accidents can occur even in a minor surgery, despite all care. This makes medicine "a double-edged sword".

Would this be a violation of the principle of non-maleficence?

The **"principle of double effect"** differentiates intended and non-intended effects of an action. The intended

effect is good and primary; however, associated with the intended effect is the necessary but bad and unintended (secondary) effect. To be morally justifiable, it must satisfy certain conditions: (*JMBR*. 2005;4(1):22-30).

- "*The action itself (independent of its consequences) must not be intrinsically wrong (it must be morally good or at least morally neutral).*
- *The agent must intend only the good effect and not the bad effect. The bad effect can be foreseen, tolerated and permitted but must not be intended; it is therefore allowed but not sought.*
- *The bad effect must not be a means to the end of bringing about good effect, that is, the good effect must be achieved directly by the action and not by the way of the bad effect.*
- *The good result must outweigh the evil permitted, that is, there must be proportionality or favorable balance between the good and bad effects of the action.*"

Harm is inflicted when the doctor has a duty of care towards the patient, there is a breach of the said duty and the patient has suffered harm as a consequence of a breach of that duty. This is liable for medical negligence or malpractice claim.

Difference of opinion, error of judgment, medical errors and medical accidents are not medical negligence. Experiencing a bad outcome does not always mean medical negligence. This has also been the position of the Supreme Court of India in its various judgments.

Harm reduction has often invited criticism as seemingly; it is seen to allow subjects to continue with the harmful behavior.

But, harm reduction accepts, without being judgmental, that some individuals are unwilling or averse to the idea of quitting risky health behaviors such as smoking or use of drugs and so takes the view that it is better to reduce the associated harm by some means, rather than pressurizing them to abide by total abstinence.

According to the National Health Care for the Homeless Council (2010), "*harm reduction is not at odds with abstinence; instead it includes it as one possible goal across a continuum of possibilities… Harm reduction neither condones nor condemns any behavior. Instead, it evaluates the consequences of behaviors and tries to reduce the harms that those behaviors pose for individuals, families and communities.*"

Harm reduction currently accommodates a vast array of interventions. It is best exemplified by needle exchange programs for the injection drug users, which aim to prevent HIV transmission and other blood-borne infectious diseases, as well as prevent overdose, including naloxone distribution and opiate substitution treatment (methadone, buprenorphine).

Other examples are prioritizing less risky drinking habits for underage drinkers to reduce the risk of alcohol poisoning, encouraging safe sex and replacing binge eating with healthier alternatives. More extreme interventions would be, for example, providing clean razors for those engaged in self-injurious behavior, or educating intravenous femoral vein injectors how to inject drugs to safer sites.

Some harm reduction techniques have already become a norm (e.g., opiate substitution treatment), while others remain highly controversial (e.g., educating injecting users on how to properly inject drugs in order to minimize health consequences).

India is the world's second largest consumer and third largest producer of tobacco. According to WHO, India is home to 12% of the world's smokers. Tobacco is an important "modifiable" risk factor for non-communicable diseases. India also has the highest oral cancer rates globally. Tobacco therefore is a major preventable cause of premature morbidity and mortality. Around 9 lakh people die every year due to diseases attributable to tobacco use (*Press Information Bureau*, March 1, 2016). This makes tobacco a major public health issue and tobacco control of great importance. Hence, harm reduction strategy should also be applied to tobacco.

While the duty and obligations of physicians to their patients remain unequivocally that of beneficence and non-maleficence, patient autonomy has now come to the forefront. The patients' choices about their treatment should be respected as should be their right to make decisions about their health. This also forms the basis of "informed consent", which is not only an ethical, but also a legal requirement today.

The Revised Declaration of Geneva adopted on October 17, 2017, now called the "Physician's Pledge" also puts the patients' interests and well-being foremost and in keeping with the changing times, has emphasized on patient autonomy.

- "*THE HEALTH AND WELL-BEING OF MY PATIENT will be my first consideration;*
- *I WILL RESPECT the autonomy and dignity of my patient;*
- *I WILL SHARE my medical knowledge for the benefit of the patient and the advancement of health care.*"

Doctors should also respect the principle of justice in health care, where justice means fairness of access to treatment.

"Do no harm" is a utopian concept as medicine is not an exact science; it is an art based on science. No two patients are alike and clinical decisions are tailored to individual patients. Probability and uncertainty are part of the practice of medicine where complications are bound to occur and accidents are inevitable.

In a Guest Editorial published in the journal *Advances in Chronic Kidney Disease*, Kellerman PS writes, "*On a daily basis, we physicians weigh the benefits against the risks in almost everything we do, both diagnostically and therapeutically*" (*Adv Chronic Kidney Dis*. 2012; 19(3):127-8).

As Harvard Health Publishing also writes in its Blog "*The fact is that when difficult, real-time decisions must be made, it's hard to apply the "first, do no harm" dictum because estimates of risk and benefit are so uncertain and prone to error.*"

While quitting the harmful behavior is the optimal goal, the patient ought to be given the option of harm reduction.

But, despite the apparent conflict between "Do no harm" and "harm reduction" and the ethical dilemma it poses, it is important to remember that doctors should act in the best interest of the patient, i.e., "*Salus aegroti suprema lex*".

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Effect of Nasal and Plasma SARS-CoV-2 RNA Levels on Symptom Duration

Levels of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA in the plasma and respiratory tract may explain why some patients with acute coronavirus disease 2019 (COVD-19) quickly recover, while others take longer, suggests a recent study published in *Clinical Infectious Diseases*.[1]

Researchers from the United States set out to examine the correlation between the plasma and nasal SARS-CoV-2 RNA concentrations and symptom duration in 559 untreated, non-hospitalized adult patients with confirmed COVID-19 with onset of symptoms since ≤10 days and ongoing symptoms 48 hours before enrollment. The symptom score (median) at baseline was 10. They included the placebo recipients in the phase II/III multicenter Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)-2/A5401 platform trial between August 2020 and July 2021 when the ancestral strain, Alpha and Delta variants were the predominant circulating strains. The trial was conducted in the outpatient setting. Majority of the study subjects were unvaccinated and just 7% of them had taken the vaccine; 86% patients aged ≥55 years and those with comorbid conditions such as chronic lung disease, moderate to severe asthma, body mass index (BMI) >35 kg/m^2, diabetes, hypertension, heart disease or chronic kidney/liver disease were at higher risk of progressing to severe infection.

SARS-CoV-2 was detected in plasma in 467 subjects at baseline, while 523 had anterior nasal SARS-CoV-2 RNA. Eighty-nine of the 467 patients in whom plasma RNA was detected presented with more severe symptoms when the study began. Participants with baseline anterior nasal RNA of ≥6 $\log_{10}$ copies/mL took 16 days for symptom improvement versus patients with ≤2 $\log_{10}$ copies/mL, whose symptoms improved in 9 days. Their symptoms also took longer time to resolve (25 vs. 15 days). When the association of anterior nasal RNA and symptoms of acute COVID-19 was examined, resolution of cough and shortness of breath were delayed in patients with anterior nasal RNA of ≥6 $\log_{10}$ copies/mL with adjusted hazard ratio (aHR) of 0.63. However, fatigue or body ache resolved without delay. Among patients with detectable plasma SARS-CoV-2 RNA, resolution of cough (aHR 0.67), shortness of breath (aHR 0.67) and body pain (aHR 0.74) was delayed. No such association was observed for fatigue.

This analysis shows that resolution of acute COVID-19 symptoms is delayed in patients with SARS-CoV-2 viremia and high anterior nasal RNA levels. According to the authors, these findings suggest the potential use of nasal and plasma SARS-CoV-2 RNA levels as prognostic markers to assess duration of symptoms and predict recovery in acute COVID-19 patients being managed as outpatients.

Reference

1. Li Y, et al. Nasal and plasma SARS-CoV-2 RNA levels are associated with timing of symptom resolution in the ACTIV-2 trial of non-hospitalized adults with COVID-19. Clin Infect Dis. 2022 Oct 10;ciac818.