The Use of viable Hepatitis C Organs for Patients with End-Stage Organ Diseases: Medical, Legal and Ethical Perspectives

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Abstract

In the United States, over 115,000 people are presently on the waiting list for a life-saving organ transplant, and many will die while waiting for an organ to become available. Due to the increase in opioid-related deaths caused by accidental overdose, there has been an increase in the number of Hepatitis C infected organs available for potential use. There are currently no vaccinations to prevent hepatitis C but it can be cured with the use of antiviral drugs. This paper addresses the medical, legal and ethical issues associated with the proposal to increase the organ pool by considering the use of hepatitis C organs to save lives of patients with end-stage organ diseases. The use of hepatitis C infected organs will be beneficial both at the individual level and the societal level. For the individual, it would provide life-saving organs to many who would die on the UNOS waiting list and for the families of donors; it might give the death of their loved ones some meaning. On a societal level, it can ultimately decrease the strain on the medical system as more individuals will be given life-saving organs. Ethically, the principles of respect for persons/autonomy, beneficence, justice and the rule of double effects are used to defend the permissibility of the proposed transplant.

INTRODUCTION

Presently, over 115,000 people in the United States are on the waiting list for a life-saving organ transplant[1]. Each day, approximately twenty people die while waiting for an organ transplant. Over fifty percent of those awaiting life-saving transplants are minorities. Eighty percent of patients on the waiting list are in need of a kidney, which the average waiting time to receive one is between three and five[2]. With the increase in demand for organ transplantation, the search for possible solutions has been a major focus in the United States. The growing numbers of patients requiring organ transplantation will require an increase in the number of donors able to supply these organs. Currently, the reliance on organ donors without disease is problematic to fulfilling the number of organs, necessary to meet the demand.

In the United States, morbidity and mortality caused by opioid-related death, has reached epidemic levels[3]. Drug overdose is now the leading cause of accidental death in the United States[4]. Since 2000, the nation's drug overdose rate has more than doubled. In 2000, it was reported that there were more than 20,000 drug related deaths. In 2016, there were approximately 54,000 lethal drug overdoses, caused by opioids. As of 2017, the amount of deaths related to overdose has exceeded 64,000[5]. Opioid addiction is the perpetuating force that is driving this epidemic. Over 20,000 deaths are related to prescription pain medication, and over 12,900 overdoses are caused by heroin[6].

Heroin overdose-related death rates increased by 26% between 2013 and 2014, having more than tripled since 2010[7]. Furthermore, the acute threat is not only from heroin, but also from synthetic opioids, such as fentanyl, acetyl-fentanyl, and carfentanil, which are mixed with or sold as heroin. These drugs, often greater than 50 times more potent than morphine, have seen an unprecedented increase in production and distribution by illegal operations.

Due to the increase in death caused by accidental overdose, there has been an increase in the number of organs available for potential use. Donors who died from drug overdose are more likely to be younger (median age, 31 years), than donors with a cause of death, related to cardiovascular disease (median age, 47 years) or stroke (median age, 52

years)[8]. People, who die of overdose, typically have no other medical comorbidities that would preclude donation, thus making them good candidates for donation. However, they may have contracted Hepatitis C (Hep. C). Hepatitis C is an inflammation of the liver due to a virus called the Hepatitis C virus (HCV). Hepatitis is a contagious disease passed from person to person, through the contact of infected body fluids[9]. Among IV drug users, it is easily passed through the sharing of needles. Currently, there are no vaccinations to prevent Hepatitis C; however, it can be cured with the use of antiviral drugs.

Under these circumstances of acute shortage, it might be possible to increase the pool of donor organs, by considering the use of organs from donors, diagnosed with communicable diseases, such as Hepatitis C.

MEDICAL ISSUES

Organ transplantation is a medical procedure in which an organ is removed from a donor and placed into the body of a recipient. The primary purpose of organ transplantation is to replace a deceased or missing organ. This procedure can consist of organs being transferred from one person to another (allograft) or from one part of the body to another part of the same patient (autograft). Allografts can be transferred from a living donor or cadaveric source. Organs that are commonly and have been successfully transplanted include the heart, kidneys, liver, lungs, pancreas, intestine, and thymus. Tissues such as bone, tendons (both referred to as musculoskeletal grafts), corneas, skin, heart valves, nerves and veins are also commonly used. In the United States, kidneys are the most commonly transplanted organs, followed by the liver[10].

Organ donors may be living, brain dead, or dead, via circulatory death (non-heart beating donation)[11]. If the organs are harvested quickly after death, the organs can then be preserved for several hours before transplantation. Kidneys can be preserved for up to thirty hours post-harvest. Pancreas and liver can be preserved for twelve hours or less, and less than six hours for lungs and hearts[12]. The time in which an organ can be stored is dependent on the speed at which deterioration begins in the organs' tissues.

Transplantation medicine is one of the most challenging and complex areas of modern medicine. The most important area surrounding the medical management of organ transplantation is rejection. Transplant rejection represents the attempt by the host to destroy a foreign body. The use of immunosuppressive drugs has decreased the risk of early graft loss due to acute rejection. The problem that arises is when dealing with graft loss caused by chronic rejection of the transplant. Even though acute graft loss has decreased, immunosuppressive protocols have not been able to reduce the risk of chronic rejection. This often leads to an increased risk of life-threatening infections and cancers. Rejection of organs is caused by interactions between the innate and adaptive immune system[13]. The recipient T-cells recognize certain antigens present within the donor organ. When these antigens are detected, the T-cells become activated. The activation of the T-cells results in the clonal expansion, differentiation into effector cells, and migration into the graft. From here, the T-cells begin to destroy the foreign body[14].

Successful human allotransplants have a relatively long history of operative skills that existed, long before the necessities for post-operative survival were discovered. Rejection and the side effects of preventing rejection (infection and nephropathy) were, are, and may always be the key problem in the success of organ transplantation.

End Stage renal failure (ESRD) is caused by multiple factors ranging from certain genetic diseases (polycystic kidney disease), autoimmune disorders (lupus), nephrotic syndrome, and urinary tract problems.[15] Diabetes is the most common cause for ESRD, and is followed by high blood pressure. When the kidneys fail completely, there are two options for treatment, dialysis or kidney transplantation[16].

Liver transplantation is a viable treatment option for End-Stage Liver Disease (ESLD). Increasing waiting times for organ transplantation means that nearly 17% of patients on the transplant wait list die annually[17]. Patients with ESLD have a collection of symptoms and disease-related complications that affect survival and health-related quality of life. When a substance or disease attacks and damages the liver, liver cells are killed and scar tissue is formed. This scarring process is called fibrosis. If the whole liver becomes scarred, it shrinks and becomes hard. Any illness that continuously affects the liver over a long period of time, may lead to fibrosis and may eventually lead to cirrhosis. Some common causes are inherited diseases, heavy drinking, a buildup of fat in the liver, viruses, toxic effects from drugs, and autoimmune diseases. Cirrhosis can be caused by many things. In the United States, heavy alcohol consumption and

Chronic Hepatitis C have been the most common causes of cirrhosis[18]. Obesity is becoming a common cause of cirrhosis, either as the sole cause, or in combination with alcohol, Hepatitis C, or both. Many people with cirrhosis have more than one cause of liver damage.

Heart failure is a chronic long-term condition that gets worse with time. There are 4 stages of heart failure (Stage A, B, C and D). As the condition gets worse, the heart muscle pumps less blood to the organs, and then it progresses toward the next stage of heart failure[19]. Treatment at each stage of heart failure may involve changes to medications, lifestyle behaviors, and cardiac devices. End Stage heart failure, Stage D (ESHD), occurs when there is the presence of advanced symptoms that do not get better with treatment. The usual treatment for ESHD includes heart transplant, ventricular assist devices, heart surgery, continuous infusion of intravenous inotropic drugs, palliative or hospice care.

CURE FOR HEPATITIS C

In 2013 and 2014, Ledipasvir-sofosbuvir (Harvoni), Ombitasvir-paritaprevir-dasabuvir-ritonavir (Viekira Pak), Simeprevir (Olysio), and Sofosbuvir (Sovaldi), were approved by the FDA[20]. These drugs are used to treat and cure hepatitis C. The treatment regimen varies, depending on the type of hepatitis C virus present. The most common strain present in the United Sates is Genotype 1, followed by genotypes 2 and 3. In the U.S., genotypes 4, 5 and 6 are extremely rare. Ledipasvir-sofosbuvir is the first combination pill used to treat hepatitis virus genotype 1 and can be taken without interferon and ribavirin.

Patients who are infected with chronic HCV genotype 1 are prescribed the Viekira Pak multi-pill. This medication stops the growth of hepatitis C. The suggested treatment involves taking two ombitasvir, paritaprevir, ritonavir tablets once daily (in the morning) and one dasabuvir tablet twice daily (morning and evening) for at least 12 weeks. Viekira has a 91 - 100% cure rate. Simeprevir is taken with interferon and ribavirin. This combination of medication clears the hepatitis C virus in about 80% of people who take it[21]. Sofosbuvir is able to be used without interferon for people with some types of hepatitis C. Sofosbuvir is meant to be taken for 12 weeks, once per day. It is effective in curing up to about 90% of the patients who use it and comes in an easy once-a-day pill[22].

In 2015, ombitasvir, paritaprevir and ritonavir (Technivie) was approved to be used in conjunction with ribavirin. It is the first treatment option for genotype 4 infections that does not require interferon. It can achieve 100% cure rates. That same year, daclatasvir (Daklinza) was approved to treat genotype 3 infections. This drug is given with sofosbuvir (Sovaldi), and has been able to cure up to 98% of patients[23]. In 2016, the FDA approved elbasvir and grazoprevir (Zepatier), to be used with or without ribavirin, for the treatment of genotype 1and 4. Zepatier is a single tablet that is a combination of Harvoni and Viekira Pak. It is primarily being used in treatment for cases of genotype 1 that do not require interferon. Its cure rates in genotype 1 are 94-97%, while for genotype 4, it could achieve 100% cure rates[24].

LEGAL ISSUES

There are many legal issues surrounding the procurement of organs from donors. One of the main concerns of obtaining organs is the time in which it is possible to harvest the donor's organs. The dead donor rule was put in place to create a standard that stipulates when organs are allowed to be taken. This rule states that a patient's vital organs should only be taken from patients who are dead[25]. The issue that arises revolves around the different definitions of death. There are two types of "dead" donors- donation after brain death and donation after circulatory death (non-heart beating donation). Brain death is the irreversible cessation of all brain activity. The brain dies from lack of blood/oxygenation. Circulatory death is the irreversible cessation of all circulatory and respiratory function. In most cases, organ donation occurs after brain death. In many cases, the family will be asked for permission to take the patient's organs. If the patient was not registered as a donor, the family is able to make an informed decision based on what they believe the patient would have wanted. If a signed organ donation card is present, the organ procurement organization (OPO) will still seek the family's informed consent to proceed with donation. The Uniform Anatomical Gift Act of 1968 (revised 1987), established that a signed organ donation card is sufficient to proceed with donation. It has been confirmed that such documents function legally as advance directives. Due to fear of ligation, it is still customary for the OPO to request permission from the next-of-kin [26].

All 50 states have adopted the 2006 Revised Uniform Anatomical Gift Act (UAGA) or enacted similar legislation giving individuals the "First Person Authorization" (FPA) to consent to organ donation after death. This is done via a

signed donor card or driver's license or by enrollment in a donor registry. When the living and the deceased don't agree on organ donation, this legislation ensures that the family cannot override an individual's documented desire to be an organ donor. This law is based on the strong belief that the donor's wishes should be adhered to.

ETHICAL ISSUES

The main ethical problem arises from concerns over disease transmission (HIV, hepatitis B, and hepatitis C virus), hence the reasons these donors are under-used by the transplant community. Approximately 500 HIV-infected, but otherwise healthy, deceased donors are discarded every year, because use of organs from HIV-infected donors has, until recently, been prohibited by the National Organ Transplant Act[27]. With the passage of the HIV Organ Policy Equity Act (HOPE Act) in November 2013, transplant centers may transplant HIV infected donors into HIV-infected recipients, under specific research studies. Deceased donors, who are HIV positive, represent a potentially novel source of organs for HIV-infected transplant candidates that could decrease waitlist deaths and even reduce the national waitlist[28]. Modern antiretroviral therapy has made organ transplantation a safe, effective, and cost-saving modality for treating HIV-infected patients, who develop end-stage organ failure[29].

More than 500 high- quality kidneys from deceased donors with Hepatitis C virus are discarded annually[30]. Similarly, 1,000 donor hearts infected with Hep. C are unused annually[31]. Current medical advances allow for better management of HCV and potentially the ability to cure HCV, using direct-acting antiviral agents. The shortage of organs within the U.S. is at crisis levels. If nothing is done, more people will continue to die. In order to save lives, new measures need to be taken. Many organs from hepatitis C patients go to waste. The overarching ethical question here becomes: is it ethical to infect a patient with a very serious disease (Hep.C), in order to cure him/her of a different ailment?

In medicine, the risk/burden calculus always demands that the potential benefits of a procedure be weighed against its risks and disadvantages. Besides the possible complication that may arise from this procedure (transplant), there are no guarantees that the patient will be cured of Hep C. There is up to 98% chance of cure with the approved drugs. What if the patient is not cured, is this a violation of the ethical principle of “do no harm”? In addition, the recipient may need to be on immunosuppression medication for a long time. Immunosuppression drugs have inherent side effects, which include diminished immunoresponse, propensity to dispose patients to opportunistic infections, organ damage, diabetes, and lymphoma [32] [33] [34]. In the light of these risks, these questions come to mind: Are the benefits of receiving a healthy organ commensurate with the risks of potentially contracting Hep.C? Is it justified for the medical professionals to offer such a procedure to patients with end-stage liver disease, considering the inherent risks and complications? Yes. A case could be made for the permissibility of such transplants, based on the ethical principles of respect for persons/autonomy, beneficence, justice and rule of double effect.

Respect for persons entails the right of a person to freely exercise self-determination and to be treated with fundamental dignity and respect. The principle of respect for persons has two integral but separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy (The Belmont Report, 1979). In other words, “to respect autonomous agents is to acknowledge their right to hold views, to make choices, and to take actions based on their personal values and beliefs”[35]. Competent patients have a common-law and constitutional right, to decide whether to accept or refuse a proposed treatment. This right extends to full and active participation in health decisions that affect their lives, even if those decisions may be wrong or counterproductive. Every competent adult, including patients with end-stage organ failure, have this right of autonomy. If informed consent is obtained from the potential recipients, which details the benefits and risks of the procedure, including the understanding that they may not be cured of Hep. C, then the transplant should proceed. Typically for every procedure, the surgeons will fully disclose the risks and benefits in a manner that the patient understands, in order for the patient to make informed decision to consent or to refuse therapy. It is the gold standard in clinical practice and biomedical research that competent adults choose or decide in any form of medical procedure (including experimental procedures and clinical trials) available to them. End-stage organ patients should not be denied this right of self-determination.

The principle of beneficence entails the moral obligations to confer benefits and prevent, remove or minimize harm and risk to others. It also incorporates weighing an action’s

possible goods against its costs and possible harms[36]. Beneficence, whose focus is the promotion and enhancement of the good of others, encompasses nonmaleficence, which specifically prohibits the infliction of harm, injury or death upon others. This ethical principle traces its roots to the Hippocratic Oath that stipulates "Above all, do no harm" (primum non nocere). In clinical practice and biomedical research, this principle demands that as moral agents, physicians have an ethical responsibility to treat their patients in a way that will maximize benefits and minimize harm. These diseased organs have the potential to save many lives with little to no harm caused to the patient. New medications make it possible to effectively treat and cure Hep C. The new FDA approved medications for the cure of Hep C have a 98% cure rate, making this viable option for organ transplantation is hepatitis C negative patients. Over 116,000 people in the United State on the waiting list for a lifesaving organ transplant, and approximately twenty people who die while waiting for an organ transplant have the potential of a better quality of life, through this transplant[37].

The principle of beneficence demands we offer the procedure to these sick patients and the concomitant treatment regimen for the cure of Hep C. The potentials, prospects and positivity, expressed by the medical community show that curability of Hep. C lessens the concerns about increase in mortality. A clinical trial by Penn Medicine, started in the spring of 2016 and funded in part by Merck, who manufactured the Hep C drug Zepatier, indicate that all the 30 patients who received diseased organs and started a 12-week dose of Zepatier, have become virus free[38]. Not giving end-stage organ patients, who might likely die without a transplant the option of this procedure, is a violation of the principle of beneficence. The efforts by the surgical team to minimize the risks of the procedure pass the test of nonmaleficence.

Finally, the principle of justice recognizes that each person should be treated fairly and equitably, and be given his or her due. Distributive justice requires that everyone receives equitable access to the basic health care, necessary for living a fully human life[39]. End-stage organ diseases are devastating for the individuals, families and society at large. There are lost wages for those affected, because the disease imperils the ability to work and pay taxes for the common good. Justice demands that these individuals who are now at the mercy of their disease and may likely die without a transplant, be offered a redeeming procedure (though experimental). To deny them of this opportunity is a violation of the principle of justice.

PRINCIPLE OF DOUBLE EFFECT

Society, in general, has always recognized that in our complex world there are times when we are faced with situations that have two consequences--one good and the other evil. The time-honored ethical principle that has been applied in these situations is called the principle of double effect. As the name itself implies, the human action has two distinct effects. One effect is intended and good; the other is unintended and harmful. As an ethical principle, it was never intended to be an inflexible rule or a mathematical formula, but rather it is to be used as an efficient guide to prudent moral judgment in solving difficult moral dilemmas.[40] This principle focuses on the agent in terms of intentions and accountability, not just contingent consequences. The principle of double effect specifies four conditions, which must be fulfilled for an action with both a good and a harmful effect to be ethically justified:

1. The action, considered by itself and independently of its effects, must not be morally harmful. The object of the action must be good or indifferent.
2. The harmful effect must not be the means of producing the good effect.
3. The harmful effect is sincerely not intended, but merely tolerated.
4. There must be a proportionate reason for performing the action, in spite of the harmful consequence[41].

The principle of double effect is applicable to the issue of use of viable Hepatitis C organs for patients with end-stage organ failure, because it has two effects, one good and the other harmful. The good effect is that these organs have the potential to save lives and decrease health care expenses in the long-term. The harmful effect is that hepatitis C infected organs are being placed in patients who will become infected with hepatitis C. This could violate the medical maxim of "do no harm." To determine if transplanting hepatitis C organs into non-infected recipients is ethical, this issue will be examined in light of the four conditions of the principle of double effect.

The first condition allows for the transplantation of hepatitis C organs because the object of the action, in and of itself, is good. The moral object is the precise good that is freely willed in this action. The moral object of this action is to save lives by providing an effective and alternative treatment for individuals on the waiting list for end-stage organ

disease. The immediate goal is not to expose recipients to a hepatitis infected organ that would lead the recipient to being infected. Rather, the direct goal is offer an effective alternative treatment for those individuals on the UNOS waiting list for a vital organ who meet the criteria for the program, in order to save the lives of those who would die because of a lack of viable organs. Over 116,000 people in the United States are presently on the waiting list for a life-saving organ transplant[42].

The second condition permits making hepatitis C organs available as an alternative treatment for end-stage organ diseases because the good effect of offering a transplantable organ that can save lives is not produced by means of the harmful effect. The two effects are completely independent. Making hepatitis C organs available to recipients who understand the risks, benefits, alternatives and consequences of this action has no intention of causing direct harm to the recipients. In fact, the opposite is true. To argue that transplant surgeons are causing direct harm to their patients is illogical. This is "like suggesting that air bags and seatbelts encourage unsafe driving"[43].

The third condition is met because the direct intention of making hepatitis C organs available is to protect and preserve human life and to encourage those on the waiting list who might die before an organ becomes available. The direct intention of this program is not to place potential recipients in harm's way by infecting them with hepatitis C, but to preserve the lives of the most vulnerable that is, those on the UNOS organ waiting list who will die because of a lack of organs. The foreseen but unintended consequence of this may be the belief by some that the surgeons are causing direct harm by infecting potential recipients to hepatitis C. As long as potential recipients give informed consent and one of the four potential life-saving drugs for hepatitis C (are made available to the recipients that will cure their hepatitis C, then one can ethically allow for the foreseen but unintended consequence[44].

Finally, the argument for the ethical justification of making hepatitis C organs available by the principle of double effect focuses on the fourth condition of whether there is a proportionately grave reason for allowing the unintended possibility of scandal and the possibility of increased drug usage. Proportionate reason is the linchpin that holds this complex moral principle together.

Proportionate reason refers to a specific value and its relation to all elements in the action[45]. The specific value in allowing for the transplant of hepatitis C infected organs is to preserve human life to the most vulnerable members of society. The harm, which may come about by trying to achieve this value, is the foreseen but unintended possibility that some may view this as condoning the direct harm on a patient by infecting them with hepatitis C. The ethical question is whether the value of preserving human life outweighs the harm of the foreseen, but unintended, possibility of infecting patients with hepatitis C that can be cured? To determine if a proper relationship exists between the specific value and the other elements of the act, ethicist Richard McCormick, S.J. proposes three criteria for the establishment of proportionate reason:

1. The means used will not cause more harm than necessary to achieve the value.
2. No less harmful way exists to protect the value.
3. The means used to achieve the value will not undermine it[46].

The application of McCormick's criteria to making hepatitis C organs available as an alternative treatment supports the argument that there is a proportionate reason for allowing this program. First, according to various studies mentioned above, the use of hepatitis C infected organs can decrease the numbers of patients on the UNOS organ transplant waiting list from dying and this new process would be cost effective in the long run. The cost of the life-saving hepatitis C drugs would be much cheaper than continuing patients on long term dialysis or other supportive therapies.

Second, at present, there does not appear to be an alternative that is as effective as using hepatitis C infected organs to save the lives of those on the UNOS organ transplant waiting list. It is true that other means of treatment exist such as cadaver and living organ donors, but according to statistics twenty people die every day waiting for an organ transplant. If using hepatitis C infected organs is effective clinically in saving the lives of those who would die on the organ transplant list and other organs are not available, then this program needs to be initiated in the United States immediately before more lives are lost.

Third, using hepatitis C infected organs does not undermine the value of human life. One can argue convincingly that the intention of making these organs available to those recipients in the UNOS waiting list is to save human lives. The purpose of making these organs available to the most vulnerable people on the waiting list is to save lives and from the current data there are no viable options for these

individuals. This is a public health issue that must be addressed because innocent lives are being lost. It seems clear that there is a proportionate reason to allow hepatitis C infected organs to be made available in the United States. Saving the lives of potential recipients contributes to the well-being of these individuals and society as a whole because it has the potential to preserve their lives and to decrease health care costs in the United States. Therefore, it is ethically justified under the principle of double effect to allow for hepatitis C infected organs to be made available to those individuals on the UNOS waiting list who give informed consent and are well-aware of the risks, benefits, alternatives and consequences of their action. They must also be assured that the life-saving drugs to cure hepatitis C are made available to them as well. Ethically, the greater good of recipients and the common good of society are advanced by medically and ethically supporting the use of hepatitis C infected organs in the United States.

CONCLUSIONS AND RECOMMENDATIONS

Organ donation is clearly a life and death issue, as the supply of organs remains static in our country and the demands seems to be growing yearly. Organ donation affects thousands of lives and costs society billions of dollars each year. From all the information gathered it appears that the use of hepatitis C infected organs will be beneficial both at the individual level and the societal level. For the individual, it would provide life-saving organs to many who would die on the UNOS waiting list and for the families of donors; it might give the death of their loved ones some meaning. On a societal level, the use of hepatitis C infected organs can ultimately decrease the strain on the medical system as more individuals will be given life-saving organs.
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Based on the information provided the following are practical recommendations:

It is clear that the use of hepatitis C infected organs can and will save lives. If we as a society value human life, we must increase access to this new form of donation. A comprehensive approach that includes a preventative strategy and a treatment strategy could serve as a new paradigm to guide our decisions regarding organ donation worldwide. We cannot allow the fear of infection that can be effective treated to stand in the way of proven scientific evidence. Human lives are hanging in the balance.

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