Toxicology Findings as a Predictor of Reactive Serology in a Cornea Donor Population

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ABSTRACT

Prevention of disease transmission by corneal transplantation remains an ongoing concern for eye banking professionals in evaluation of suitability and viral risk assessment. This retrospective study of 588 cornea donors from a single county medical examiner's office examines the correlation, if any, between findings of positive toxicology screening and reactive serology in this donor population. Population demographics were consistent with the normal donor population except as relates to manner of cause of death which excludes most individuals with prior hospitalization. Donors with prior, usually immediate post mortem, conditions were excluded as toxicology is not a routine in general medical conditions and these donors are not routinely medical examiner cases. Twenty-five of the potential donors were reactive for one or more serologies. 294 donors had positive toxicology findings and an equal number had negative toxicology findings. Toxicology does not, in this population, appear to be an indicator of disease risk transmission.

Transmission of an infectious disease via allograft transplantation remains a concern although incidence of transmission from tissue is rare given the volume of allograft transplants occurring annually.[1] Risk for infectious disease is potentially increased in individuals using drugs, especially IV,(intravenous), drugs due to increased high risk behaviors, according to the Centers for Disease Control, CDC.[2] These risks include but may not be limited to shared needles, unprotected sex, and sharing items and contact with individuals who are known to be infected with virus, i.e. infectious hepatitis or HIV. Donor screening seeks to exclude from the recovery or release of allografts the high risk populations through a combined donor suitability determination of medical /social history screening and infectious disease testing. To document the correlation of the drug use as found by toxicology screening and infectious disease test reactivity, this retrospective study looks at the success of this screening and the correlation of positive toxicology results and reactive serologic results in cornea donors over a three-year period in a medical examiner population where toxicology is routinely performed and where cornea donation and transplantation occurred. This subset of the donor population, 588 donors from a total population of 2759,was selected as the only group in which toxicology screening was routinely performed.

METHOD

All donors of corneal tissue for transplantation between 2015 and 2017 which fell under the jurisdiction or were referred to the medical examiner for a single county were reviewed for the presence of positive toxicology screens and reactive serology testing. Serology testing included HIV1/HCV/HBV Nat, HIV1/2 plus O antibody, Hepatitis B Antigen, Hepatitis Bc antibody, Hepatitis C antibody, RPR, and West Nile NAT.[3,4,5] Toxicology screening was performed utilizing a standard toxicology methodology of ELISA, liquid chromatography and high resolution mass spectrometry which detected the presence of a variety of drugs including opioids, cannabis, codeine and methamphetamine. Table one shows the total type of drug isolates on screening without qualification as to route of administration or possible therapeutic treatment.

RESULTS

In 2015 there were 178 recovered donors which were also medical examiner cases. In 2016 there were 203 donors and in 2017 there were 207 donors. Total medical exam-

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Funding Support: Funded in part by unrestricted grant from Research to Prevent Blindness, New York, NY.)

iner donors of 588 of which 25 had a reactive serology test as seen in Table two. There were within this population of medical examiner cases 563 donors with non-reactive serologies but with 279 positive toxicology findings. The drug findings with in these two groups showed more non-reactive serologies with drug findings on toxicology screening than reactive serologies with drug use as seen in Figure 1. Toxicology findings were equally divided between negative

Table 1: *Drugs found during toxicology testing*

5F-ADB*	Cocaine	Hydromorphone	Oxycodone
AB-CHMINACA*	Codeine	Ketamine	Oxymorphone
ADB-CHMINACA*	Cyclobenzaprine	Levamisole	PCP (phencyclidine)
ADB-FUBINACA*	Diazepam	Lorazepam	Phenobarbital
AKB-48-N*	Difluoroethane	Meprobamate	Temazepam
Alprazolam	Ethanol	Metaxalone	THC (tetrahydrocannabinol)
Amphetamine	Etizolam	Methadone	Tramdadol+
Carisoprodol	Fentanyl	Methamphetamine	U-47700 (opioid analgesic)
Chlordiazepoxide	Heroin	Methylphenidate	Zolpidem
Clonazepam	Hydrocodone	Morphine	

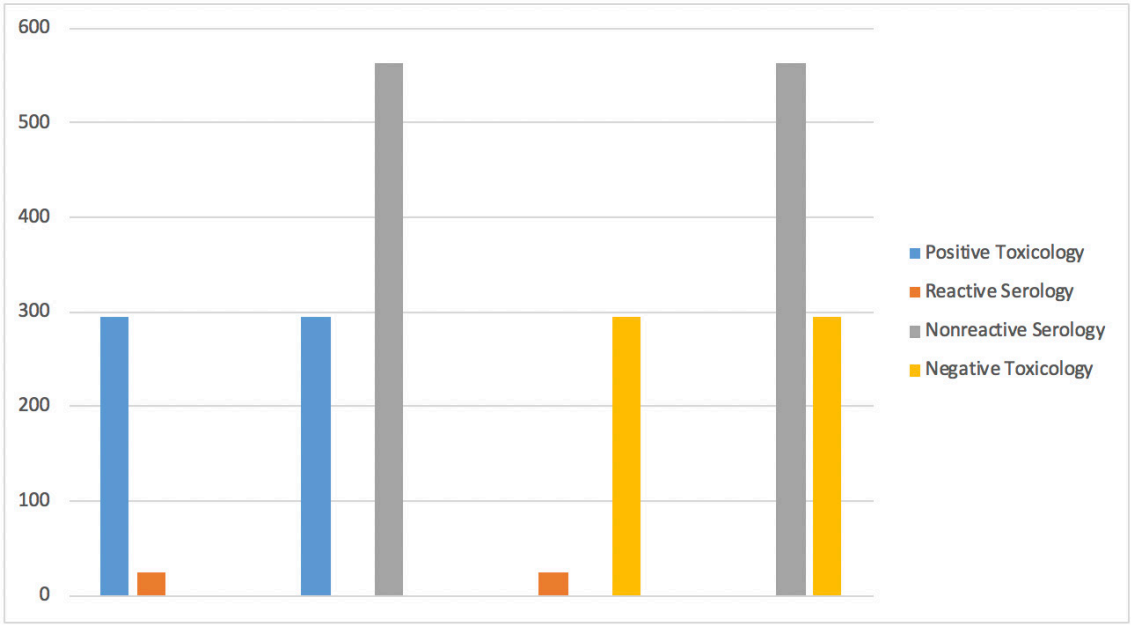
*Indicates drug is a synthetic cannabinoid.

Table 2: *Serology and toxicology results for 25 donors with reactive serology*

DONOR	***REACTIVE SEROLOGY RESULTS***	***TOXICOLOGY RESULTS***
A	HCV Ab, HBc Total, HCV NAT	Ethanol, THC
B	HBc Total, HBV NAT	None
C	HBc Total, HBV NAT	Ethanol
D	HBc Total	None
E	RPR(STS)	THC
F	HCV Ab, HBc Total, HCV NAT	Cocaine, Tramadol, Codeine
G	HBc Total	AB-CHMINACA
H	RPR(STS)	None
I	HBc Total	None
J	HBc Total	Cocaine
K	RPR(STS)	THC, Levamisole
L	HCV Ab, HBc Total, HCV NAT	Amphetamine/Methamphetamine
M	HCV Ab, HCV NAT	Cocaine, THC
N	RPR(STS), CAPTIA (Treponemal Syphilis)	None
O	HCV Ab, HCV NAT	None
P	HBc Total	ADB-FUBINACA, ADB-CHMINACA
Q	HTLV I/II Ab	Cocaine
R	HTLV I/II Ab	PCP, Cocaine, Ethanol
S	HCV Ab	Ethanol
T	RPR(STS)	None
U	HCV Ab, HBc Total	Tramadol, Hydrocodone
V	HBc Total	Chlordiazepoxide, Diazepam
W	HBc Total	None
X	HBc Total	None
Y	HBc Total	None

Ten donors with reactive serology had no positive toxicology findings.

Figure 1: *Relationship of reactive and nonreactive serology to the positive or negative toxicology screens*



Of the 588 screened for serology and toxicology, 294 had positive toxicology results (50%),and 294 had negative toxicology,(50%) results. In addition,25(4.25%) of the total cases had reactive serology and 563(95.75%) had a negative serology.

and positive toxicology findings with 294 of each. Only 15 of the reactive serologies had positive toxicology screens while 284 of the non-reactive donors had positive toxicology screens. Toxicology also identified the presence of alcohol which may be considered to have a different level of risk for infectious disease but may in some cases correlate with hepatitis findings.[6,7] In the reactive serology group there were only 4 identified for alcohol and in the non-reactive group there were 128 positive toxicology findings of alcohol. Of the four with alcohol two had addition drug findings and two did not.

DISCUSSION

Based on the data from 588 donors of corneal tissue and examination of drug toxicology and reactive serologic screening, drug use does not appear to be a reliable indicator of the risk of communicable disease transmission. The population of this study had an age range from 2 years to 74 years with 404 males and 184 females. The cause of death was representative of those case referred to the medical examiner for cause and manner of death determinations.[8] This included motor vehicle accidents, homicides, suicides, deaths of unknown causes, deaths hospitalized for less than twenty-four hours where death was not expected by prior history or admission findings and others as may be referred by a corner or justice of the peace or agreed to by special request.

These cases are comprised of donations which were not found on medical social history screening to have identifiable risk factors to exclude their suitability as donors. There were in total referrals, medical examiner and non-medical examiner, 915 cases of prior rule out for possible high risk behavior as defined by FDA, Food and Drug Administration. This population, eliminated on initial history, had no testing and therefore the positive serology confirmation of documented disease transmission potential cannot be determined. In addition, there were 15 cases where serologies were obtained prior to recovery and determined not suitable for recovery and not included in this data. The 588 medical examiner cases are a portion of 2759 total ocular donors of the three-year time period. The age and sex is similar to that of hospitalized donors but the cause or manner of death does not reflect the majority of health related illness of the hospitalized population normally contained in donations and for which no medical examiner referral is necessary. In the hospitalized donor significant prior medical history may be available but autopsy finding as seen in the medical examiner cases is not routine. Therefore, determining suitability of ocular tissue for transplantation must continue to rely on a combination of information

and documented findings, medical /social history, serology testing, and other tests as available. Donors should not be assumed to be suitable or unsuitable based on any single factor which is not specifically defined in FDA regulations as a contraindication to donation.[9,10] FDA unequvilely defines the reactive serology parameters which deem a donor unsuitable ,while other medical history findings may require further clarification or investigation.[11] The presence of drugs alone, especially when the route of administration cannot be documented to be intravenous, does not appear to correlate with risk of communicable disease as indicated by serology reactivity. Serology and toxicology results for 25 donors with reactive serology.

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