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How We Process Alcohol

UNDERSTANDING THE PHARMACOLOGY OF ETHANOL

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Basic Pharmacology of Ethanol

Ethyl alcohol (ethanol, ETOH) or just alcohol has been described as the "perfect" drug. It is soluble in water, the major constituent of all bodily fluids and tissues, not charged, a small molecule and not subject to changes in molecular structure as a result of changes in the acidity (pH) of the body fluids. Because ETOH is uncharged, it is also soluble in fatty substances (i.e., lipids) and passes easily through the lipid membrane barriers in the body (e.g., from the stomach into the blood or from the intestines into the blood).

Ethanol, like all drugs undergoes four scientific or pharmacokinetic processes in the body:

1. ABSORPTION
2. DISTRIBUTION
3. METABOLISM
4. EXCRETION

These four processes occur contemporaneously until (1) all the alcohol is absorbed from the GI tract, and there is no more absorption phase, and (2) all the alcohol has been metabolized, and there is no more metabolism of ETOH and it is no longer detectable in the blood.

In order to simplify the pharmacokinetic model, many authors refer to a "plateau" phase instead of a "peak" blood level, a diffusion-equilibrium phase instead of a distribution phase, and an elimination phase which combines the processes of metabolism and excretion.

Absorption

Absorption is the process by which alcohol is made available to the fluids of distribution of the body (e.g., blood, plasma, serum, aqueous humor, lymph, etc.). Approximately 80% of orally ingested ETOH is absorbed from the small intestines, and the remainder is absorbed from the stomach.

In the fasting state, the majority of alcohol (i.e., >50%) will be absorbed within 15 minutes and a "peak" or maximum blood level will occur in approximately 20 minutes, with 80-90% complete absorption achieved within 30-60 minutes.

The RATE of absorption of alcohol and subsequent appearance of alcohol in the blood is dependent on the following factors:

1. The rate of consumption (Chugging vs. sipping),
2. The volume consumed (1 shot, ~1.25 oz. vs. a 12 oz. beer),
3. The concentration or proof of ethanol (ETOH) in the drink(Beer = ~3.5%, wine = ~12%, whiskey = ~43% or 86 proof),
4. The presence or absence of carbonation (e.g., champagne vs. wine, or scotch and soda vs. scotch and water, carbonation increases the rate of absorption, but absorption of alcohol from beer is delayed).
5. The presence or absence of food in the stomach (Food delays absorption).
6. Is the person taking any medication(s) that can interfere with gastrointestinal (GI) motility (e.g., Reglan slows, Aluminum antacids slow, drugs like atropine or scopolamine used for ulcers or "queasy stomachs" slow GI motility keeping the alcohol in the stomach slowing absorption, while drugs like Tagamet, Zantac and Pepcid-AC decrease gastric acid production increasing the rate of gastricemptying and increasing the rate of ETOH absorption (see DiPadova, et al., Effects of Ranitidine on Blood Alcohol Levels After Ethanol Ingestion. Comparison With Other H-2 Receptor Antagonists. JAMA, Vol. 267: 83-86, Jan.1, 1992).

Distribution

Once a drug has been absorbed from the stomach and/or intestines (GI Tract) into the blood, it is circulated to some degree to all areas of the body to which there is blood flow. This is the process of distribution.

The police know that the absorption of alcohol from the GI tract into the blood and the distribution of alcohol from the blood into the brain (central nervous system, CNS) takes time. This is why some jurisdictions have adopted a policy of taking individuals suspected of DWI to the police station to conduct a breathalyzer test, rather than doing it at the site where the citizen is stopped for the alleged infraction.

Citizens are usually made to wait at least 20 minutes before the "breath test" is done in order to give any alcohol that could be in the individual's GI tract sufficient time to be absorbed into the bloodstream. Distribution of alcohol to the brain (CNS) would then potentially cause the citizen to exhibit signs or symptoms of impairment and the citizen would be more likely to fail a field sobriety test at the "station" rather than at the site where he/she was stopped for the alleged infraction.

Metabolism

Alcohol in the blood and tissues must be inactivated and excreted from the body. This process is initiated by altering the chemical structure of the alcohol in such a way as to promote its excretion. The transformation of the alcohol molecule into a chemically related substance that is more easily excreted from the body is called metabolism or detoxification.

In the case of ETOH, the alcohol is metabolized in the liver by the enzyme alcohol dehydrogenase, to acetaldehyde which causes dilatation of the blood vessels and, after accumulation, is responsible for the subsequent hangover which ensues. The acetaldehyde is subsequently metabolized by the enzyme aldehyde dehydrogenase to acetate, a substance very similar to acetic acid or vinegar. In fact, measurement of blood serum acetate levels may be an indicator of "problem or chronic drinking"

Certain drugs can inhibit the alcohol dehydrogenase enzyme responsible for the first step in metabolizing ETOH. Inhibition of this enzyme causes an increase in the blood alcohol level. Some of these drugs are probably known to you. Antabuse is used for the treatment of alcoholism. People taking this drug can get very sick from ingesting just a small amount of ETOH. Chloral hydrate is a sleeping pill that when put into someone's drink is known as a "Mickey Finn". Some orally administered antidiabetic drugs like Diabinese also cause an "Antabuse-like" reaction and the inhalation of the solvent trichloroethylene can also inhibit alcohol metabolism.

Subjects exposed to these drugs can ingest 1-2 drinks and have a blood alcohol level 2-3 times higher than one would expect based on classical prediction models described later in this presentation. Although these individuals may test "drunk" on the breathalyzer or by blood alcohol determination, they may have only ingested one or two alcoholic drinks. *(REALLY!)*

Excretion

Excretion is the process by which a drug is eliminated from the body. In the case of ETOH, the kidney and lungs excrete only 5-10% of an absorbed dose of ethanol unchanged (unmetabolized). The rest must be metabolized prior to excretion.

In order to determine the rate of excretion of ETOH from blood, one must first be certain that all the ETOH in the subject's GI tract has been absorbed. If not, calculation of a rate of excretion would be confounded be the ongoing absorption of more ETOH. Once all ETOH has been absorbed, this is called the post-absorptive, or distributive stage. At this time, serial (multiple) blood level determinations should show a decline with time. The slope of the line is indicative of the rate of excretion.

In most individuals, the rate of excretion ranges from 0.01% (10 mg/100 ml) to 0.025% (25 mg/100 ml) per hour, with a mean of 0.0175 (frequently rounded off to 0.017 or 0.018).

Note that the units of concentration are a percent indicating a weight of ETOH dissolved in a volume of blood. By definition, percent means grams per 100 ml. However, BAC may also be expressed as mg/100 ml or mg/dl (a "dl" is a deciliter, or 100 ml), in which case the decimal point on the value expressed as a percent is moved 3 places to the right, (e.g., 0.025% = 25 mg/100 ml or 25 mg/dl).

Try to think of percent as teaspoons of sugar per cup of coffee. A teaspoonful of sugar weighs approximately 4 grams and 100 ml equals approximately 3.3 ounces of volume or half a cup. Therefore a cup of coffee 6-7 ounces with two teaspoonfuls of sugar (8 grams) would have a concentration of approximately 4% sugar (4 grams/100 ml or half cup).

Breathalyzer Testing for Ethanol

Only air in the deepest portion of the lungs, the alveolar sacs is in equilibrium with blood alcohol. Therefore the amount of ETOH in the lungs of individuals undergoing "breath testing" is very small and has been estimated at a ratio of 1:2100 to blood. Because this is a general estimate or average and all people are different, "Breath Tests" may overestimate BACs.

Quick Estimates of Blood Alcohol Concentrations

There are some very easy techniques for estimating blood alcohol concentrations (BACs). First of all, you should be able to determine how much alcohol is in a drink. This is accomplished by obtaining the percent or proof of alcohol in the drink from the label of the beverage and multiplying that percent by the volume of the beverage in the drink.

Calculating Percent of Alcohol in a Beverage

Example: Beer = ~4.2%, Wine = ~12%, Whiskey = 43% (86 proof),

Vodka could be 80 proof (40%) or 100 proof (50%), and brandys, rums, malt liquors, and European or "special calls" can have various proofs.

Let's start with a Beer:
4.2% is written 0.042. A can of beer is 12 oz.
0.042 x 12 oz. = 0.50 oz.of pure ethanol per can of beer.

One Shot of Whiskey:
43% x one shot, or approximately 1.25 oz.
0.43 x 1.25 oz. = 0.54 oz. of pure alcohol per "shot",
regardless of how much "mixer" is added.

One glass of wine:
12% x 4 oz. (the approximate volume of a wine glass).
0.12 x 4 oz. = 0.48 oz. of pure alcohol per "glass" of wine.

The "Bottom Line" is that one can of beer, one glass of wine and one "shot" of whiskey all have similar alcohol concentrations.

Adjusting Blood Alcohol Concentrations For Body Weight

Most "estimate" calculations of BACs are based on an individual weighing 150 lbs. (~70 kg, a kg = 2.2 lbs). However, we all know that most women weigh less thanthis and most of the men I know weigh more! But 150 lbs is a standard or basis towhich we can compare the rest of the population, and is an acceptable starting place.

The "Rule of Thumb" is that one mixed drink will produce a peak BAC of approximately 0.02 g/100 ml (same as percent) in a 150 lb. man. For wine, a littleless, and for beer, still less, because wine and beer contain less pure alcohol perserving (see calculations above). If the subject's body weight is greater, the BAC willbe less, if the subject's body weight is less, the BAC would be higher (e.g., 0.025- 0.04).

Obviously, there is great inter-subject variation. If the subject is eating with thealcohol, the peak BAC would be lower, and shifted to the right (i.e., take longer to be achieved).

Since the mean (average) "burnoff" rate is 0.017 per hour, this is the origin of the "old addage" that you can drink one drink an hour without getting drunk (actually, without increasing BAC).

Back Extrapolation

Based on the "burnoff" rate, one should be able to back-extrapolate from a BACknown at a certain time to a BAC at an earlier time. This procedure is based on theassumption that an individual will eliminate a constant amount of ETOH from his/herblood per unit time.

Since the "burnoff" rate or elimination rate ranges from 0.01 to 0.025 per hour, the most valid indicator of prior BACs would be to construct a "best case" and "worse case" scenario using both values. You could then be virtually certain that the "true" value resided within the range, between the two extremes.

Example:

A man leaves a bar at midnight. He gets into an automobile accident at 1 am, and at 2 am at the hospital, his blood is drawn. The BAC value of the blood sample is determined to be 0.12. What were his BACs at 1 am and at midnight?

Best Case Scenario:

Assume a slow burnoff rate of 0.01/hr. Then if the BAC were 0.12 at 2 am, it would have been 0.13 at 1 am and 0.14 at midnight.

Worst Case Scenario:

Assume a fast burnoff rate of 0.025/hr. Then if the BAC were 0.12 at 2 am, it would have been 0.145 at 1 am and 0.170at midnight.

Using The Mean Value:

Assume a mean burnoff rate of 0.0175/hr. Then if the BAC were 0.12 at 2 am, itwould have been 0.137 at 1 am and 0.155 at midnight.

Actual Value For The Burnoff Rate:

The only way to know the subject's actual burnoff rate would be to have obtained two blood samples at least 30, and preferably 60 minutes apart and determine thedifference between the two. *It does take two points to determine a straight line!*

Correlating BAC With Impairment

A statutory level for the presumption of DWI is just that, an arbitrary standard. Any

BAC level, whether 0.10% or 0.08%, speaks only to a legal standard, and not ascientific (physiological) standard.

If an individual is accustomed to having 2-3 (or more) alcoholic drinks per day, with dinner or while watching TV after work, it is quite likely that they will have developed some tolerance to the intoxicating properties of alcohol and might not show signs of intoxication even at BACs over 0.10%. On the other hand, an individual who drinks infrequently would have developed no tolerance and might show signs of intoxication at BACs below the statutory level.

Conversion Of Plasma Or Serum Levels To BACs

What is serum? When whole blood (usually obtained from a patient by venipuncture) is left in a test-tube without an anti-coagulant, it clots. If you "spin it down" in a cetrifuge, the clot goes to the bottom of the tube taking all of the red blood cells and most of the white blood cells with it. The clear fluid remaining at the top is serum.

What is plasma? When whole blood is obtained from a patient, and the blood sample is mixed with an anticoagulant like heparin, citrate, or oxalate or a chemical that interferes with clotting like EDTA (more on EDTA) and the red blood cells are separated by centrifugation, the remaining clear fluid on top is plasma. Plasma and serum differ in that the white blood cells are still present in plasma. After centrifugation, they can be seen as a thin coating on top of the red blood cells.

When "blood" samples are drawn in the hospital and subjected to BAC analysis, it is important to know that analyses conducted on serum and plasma must be reduced by 16-18% in order to convert the serum or plasma value to "whole blood" levels, which are usually the way legal statutes are written.

Why do serum and plasma levels have to be "corrected" mathematically? Just think of the old child's tale about the crow who tried to drink from a pitcher of water while perched on its edge. When the crow put his beak in the pitcher, the water level was too low for him to drink. He then obtained a number of pebbles and dropped them in the pitcher. As more pebbles were dropped into the pitcher, the water level rose and eventually, the crow was able to drink from the pitcher. The red blood cells have the same effect in blood. They artificially increase the volume of fluid in whole blood just as putting ice in a glass of water is likely to cause the water to overflow. Therefore, the alcohol in plasma and serum alcohol samples are "more concentrated" than blood because the red blood cells have been removed and the values must be "corrected" to represent a value that would have been obtained from whole blood.

Remember, BAC stands for Blood Alcohol Concentration, and concentration is described in percent which is defined as weight per volume. Percent means part per 100. A 1% solution of any substance contains 1 gram dissolved in 100 ml. For blood alcohol, a 0.10% level would mean 1/10th of a gram (100 mg) dissolved 100 ml blood.

Just for fun, how sweet is a cup of coffee? A standard coffee cup probably holds about 6-8 oz. So 7 is a good estimate. An ounce equals about 28 ml.So 7 oz. x 28 ml/oz. = 196 or approximately 200 ml. A teaspoonful of sugar weighs about 4 grams. So 1 teaspoonful of sugar = 4 grams/200 ml or 2 gms/100 ml, 2%. If you use two teaspoonfuls of sugar, your coffee is 4%. If you drink out of a coffee mug, try someone else's homepage.

More on EDTA

EDTA, the one that got all the hype in the OJ trial stands for ethylenediamine tetraacetic acid. The coumpound is used medically (usually as the disodium salt) as a treatment for poisoning with heavy metals like lead. A chelating agent binds other molecules. In a blood collection tube, (see next page) the EDTA binds calcium ions which have two positive charges (Ca^{++}). Becuase calcium ions are required for normal clotting to occur, chelation or binding of calcium inhibits clot formation.

During the OJ trial, people bagan refering to EDTA as a preservative, which means that it stops bacteria from growing or living tissue (blood) from decaying or putrefying. Preservative is a misnomer. Even EDTA treated blood samples can decompose. A preservative would be sodium fluoride, fluoride is a metabolic poison, like cyanide, to humans and human tissues.

The other "anticoagulatnts" used in various color-topped blood collection tubes are: heparin, oxalate (calcium binder) and citrate (calcium binder).

Cross-Examining BACs

Regardless of the source of the BAC value you are discussing, there will always be some variability in the procedure used to determine that particular value. One reason why two readings are done for the breathalyzer is to demonstrate reliability and reproducibility of the method.

That is also why there are "controls" or standards built into the system. One control is usually a "Blank" (or Air Blank in Breathalyzers) and contains no alcohol and, of course, should give a BAC reading of 0.00. The other standard is called a positive control or calibration test and is frequently 0.15 or 0.20.

Any BAC level or Breathalyzer test which was not "run against a blank" and which did not include a positive control or a series of positives which described a "standard curve" are scientifically invalid and should be subject to being suppressed.

You might also wish to ask about when the chemical solutions were made up for the machine. They need to be fresh to be accurate. The last time the machine was certified for calibration by any official state or county agency. The qualifications of the operator.

Statistics

When reviewing BAC results with three numbers to the right of the decimal point, make certain to ask about "rounding off". Generally, in science, any number ending in 5 or greater gets rounded off up to the next number, while anynumber less 5 is rounded down. However in fairness to a defendant, the law usually demands that the last number be dropped and not "rounded up".

For example by scientific convention, 0.075 would be rounded off as 0.08, and 0.074 would be rounded off as 0.07, whereas in a court of law, both 0.074 and 0.075 would both be presented as 0.07. The sensitivity of the breathalyzer to differentiate between a BAC of 0.075 and 0.074 is very speculative *(unlikely)*.

For laboratory or breathalyzer values, ask for the Quality Control and Quality Assurance data. If there are none, you've made your point, if they produce them, give them to your expert for review and analysis. Determine if the hospital's laboratory passed its last certifying tests, and if those tests were conducted "blinded" or not. Blinded means the laboratory did not know the value of the unknown sample.

Ask about the Coefficient of Variation of the assay. It should be between 5-10% to be acceptable. If it wasn't calculated, ask them how they can be certain that the result they're reporting is a correct result.

Ask about the Standard Deviation (SD) of the assay, another indicator of variability. For example, if a result is reported as 0.08 and the SD=+0.002 (read "plus or minus 0.002), then the reported value has the same probability of being 0.078 as 0.082.

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