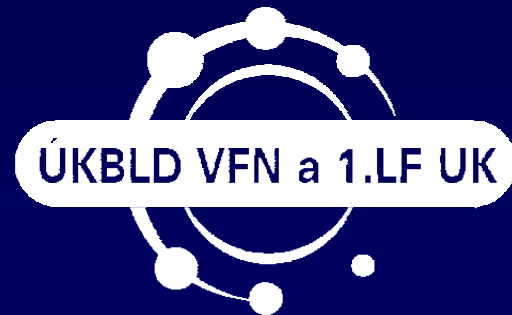


Biological markers for abuse and addiction

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Denial is the feature of the alcoholism

- Patient's history.
- Family
- Psychologic examination
- Laboratory markers of alcohol abuse.

Conventional laboratory markers of alcohol abuse

- **GGT.**
- **AST/ALT ratio.**
- **mean erythrocytes corpuscular volume (MCV).**

sensitivity	27-52%
specificity	85-90%

Innovative markers of alcohol abuse

- **Sialic acid deficient protein:**
transferrin, α -acidglycoprotein
- **Enzymatic systems:**
phosphatidylcholine hydroperoxide (PCOOH)
- **Direct ethanol metabolites**
 - fatty acid ethyl ester
 - ethyl glucuronide
 - phosphatidyl ethanol
 - ethyl sulfate

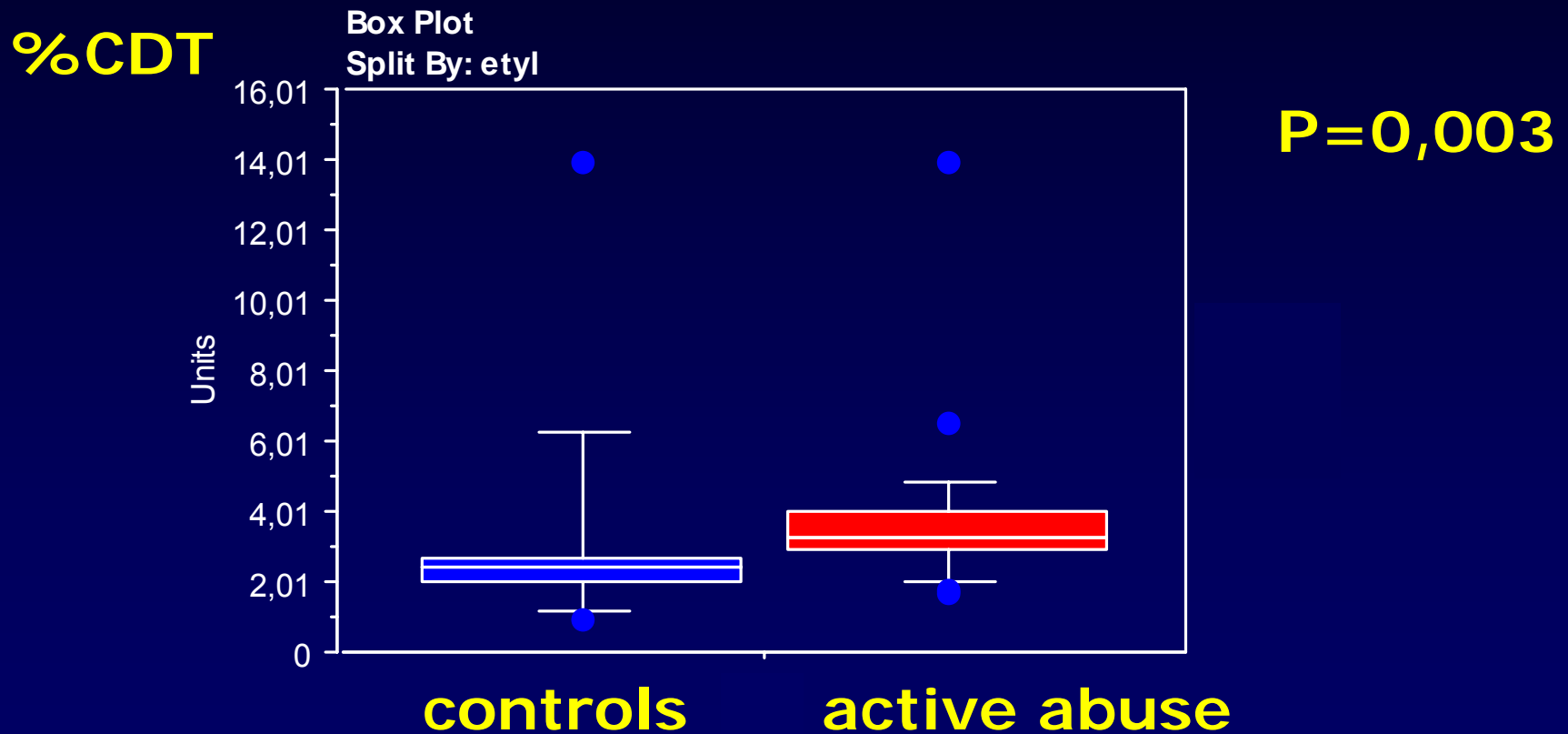
Carbohydrate-deficient transferrin - CDT

- CDT – one of the most sensitive and specific laboratory markers of alcohol abuse.
- Alcohol causes deficiency of sialic acid - measurement of this defect is marker of alcohol abuse.
- Half-time: 12 days
cut-off value: 2.5% – 3% of CDT

CDT – characteristics

- **Specificity 70-80%**
- **False positivity 20-30%**
- **Stability in serum 4C – week -20C 6 months**
 - Serum separated - preferably during 4 hr
- **RIA, HPLC, turbidimetry**
- **CDT – more specific than GGT**
- **CAVE - genetic variation, congenital disorders of glycosylation**
- **Disorders with transferrin increase – pregnancy, oestrogen use, contraceptive use, iron deficiency anemia, anti-epileptic drug therapy – hepatic drug affects**

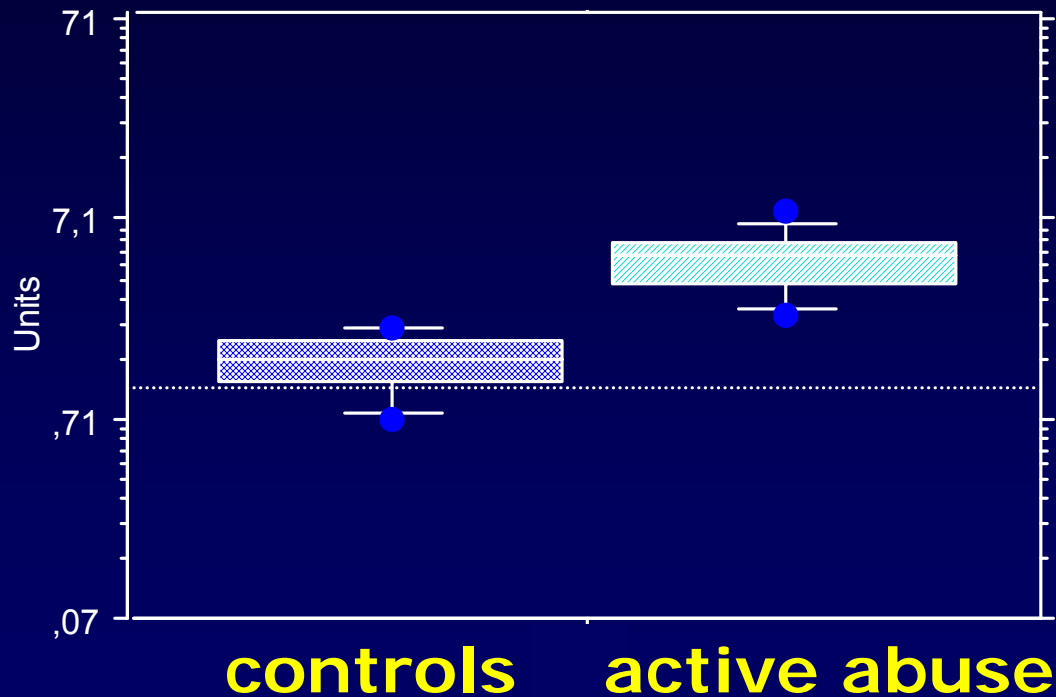
%CDT in cirrhotic patients active alcohol abuse, control patients with cirrhosis



%CDT in patients without cirrhosis -active alcohol abuse, control patients

Box Plot
Split By: etyl

%CDT

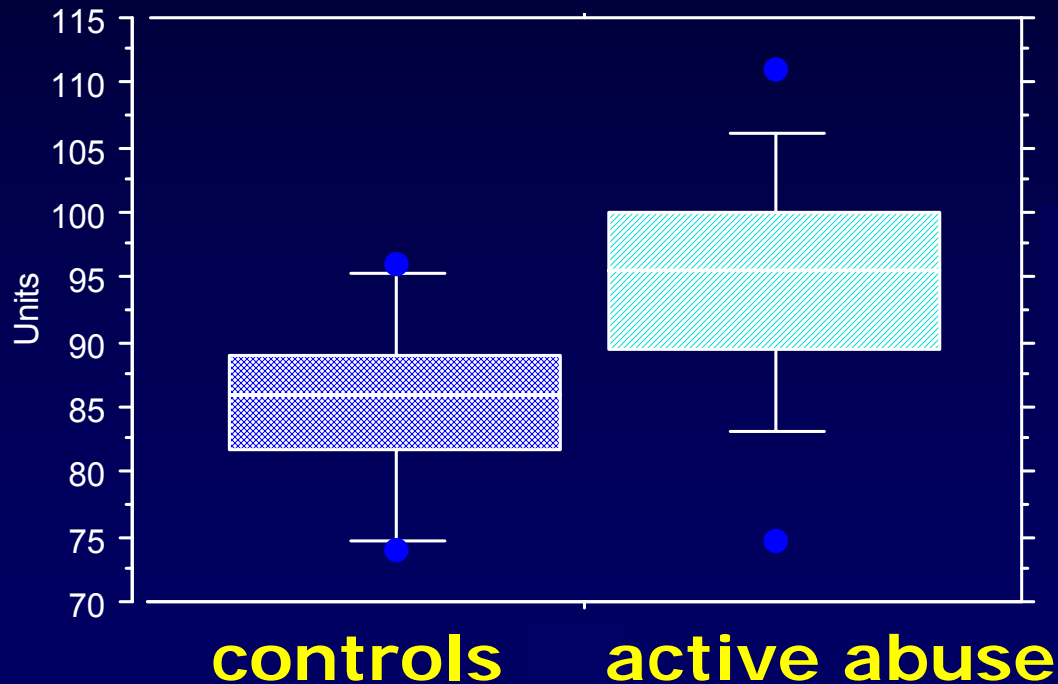


P= 0,0009

MCV in patients without cirrhosis -active alcohol abuse, control patients

Box Plot
Split By: etyl

MCV

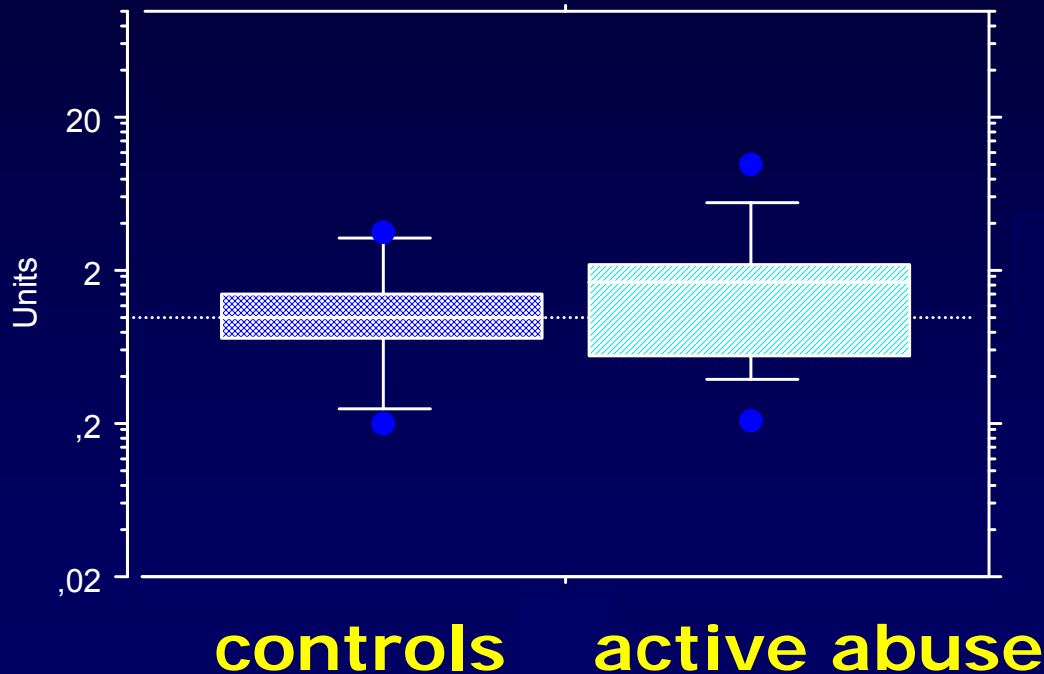


$P = 0,0348$

GMT in patients without cirrhosis -active alcohol abuse, control patients

Box Plot
Split By: etyl

GMT



P = n.s.
(0,5802)

Alcoholic hepatitis

- **Alcoholic hepatitis diagnosis**
 - Physical examination
 - ALT, AST, bilirubin elevated
 - Na, albumin low
 - INR and leukocytes elevated

New markers I

- **Fatty acid ethylester**
 - Non-oxidative metabolites of esterification of ethanol with free and bound fatty acids GC-MS
 - FAEEs separate social drinkers from heavy
 - Detection serum up to 24 hrs (hairs – months)
- **Ethylglucuronide**
 - Direct metabolite of ethanol
 - Detection urine up to 8 hrs (hairs – months)
- **Phosphatidylethanol**
 - Ethanol-phosphatidyl adduct via action with phospholipase D

New markers II

- **5-OH-tryptophol**
 - Minor metabolite of serotonin
- **Sialic acid**
 - Total and Free sialic acid in serum increase
- **Beta-hexosaminidase**
- **Blood acetate**
- **Acetaldehyde adducts**
 - MS/MS methods for acetaldehyde modified Hb
- **Dolichol**

CDT and EtG

- **CDT and EtG – established indicators of chronic alcohol abuse**
 - Positivity 40-60 g EtOH per day
 - 1-2 weeks increase CDT
 - In 50-60% heavy drinkers
 - Increasing to 70-80% in alcoholics

Other biochemical parameters

GGT – WHO project increases 58% alc dependent,

- **Not sensitive to screen**
- **IgA increase 69% alcohol liver diseases**
- **Lipids – HDL, TG 80% increase heavy drinkers**
- **Uric acid**

Usefull parameters

- **Combination GGT and CDT – most useful**
- **CDT – more specificity**
- **GGT – low senzitivity**
- **Specitficity – negative test – negative diagnosis**

TP

—————

TN + FP

0,95 very good, higher 0,7 acceptable

- **Sensitivity – positive test - positive diagnosis**

TP

—————

TP + FN

Drug abuse analysis I

- **Basic laboratory parameters**
 - Sodium, potassium, creatinine, glucose, creatine kinase etc.
- **Toxicological analysis**
 - Only in some drugs
 - Metabolites

Drug abuse analysis II

- Saliva, Urine, Blood, Hair
- Point-of care testing
 - Oriented, not analytically precise

Hair analysis I

- **Diagnosis of drug abuse**
- **Control of treatment**
- **Dopping control**

Hair analysis I /

- **Hair analysis for drug and alcohol abuse**
 - **Canabis – THC**
 - **Morphine – heroine**
 - **Codeine – heroine**
 - **Methadon**
 - **Cocaine – benzoylecgonine**
 - **Crack – AEME**
 - **Amphetamine**
 - **LSD**
 - **GHB**
 - **Ethanol – FAEE, Etg**

Candidate genes and alcoholic diseases

Mechanisms

- Alcohol toxicity
- ROS
- Immune response/
inflammation
- Activation of stellate cells
- Collagen – synthesis /degradation

Candidate genes

- ADH, AIDH, CYP2E1
- CYP2E1, GST, MPO, MnSOD
- TNF α , INF γ , IL-10, IL-1 β , CD14
- TGF β , leptin, CTGF, angiotensinogen
- TIMP-1, MMP-3,9

*Results conflicting - Not reproduceable data
Initial euphoria has faded*

Stickel 2006

Signal transduction and ethanol toxicity

Signal transduction mechanisms of ethanol toxicity are not well understood

Central role of MAPK and NF- κ B

- Differentiation
- Development
- Apoptosis
- Inflammation
- Proapoptotic – JNK, c-jun, p38 via AP-1
- Antiapoptotic – ERK, NF- κ B (IAP-inhibitory apoptosis protein)

Proteomics

- Biomarkers – 24 studies MALDI or SELDI-TOF MS
- Alcohol abuse
 - Increase fibrinogen α chain
 - Decrease apolipoprotein A-I and AII
 - Nomura et al 2004
- Hepatocellular carcinoma
 - Decrease des-Ala-fibrinopeptid A
 - Orvisky et al 2006

Conlusions

- **%CDT is the most suitable biochemical marker of alcohol abuse in routine practice and combination with basic biochemistry and hematological examination can increase its credibility.**

Abstinence from alcohol

- The knowledge of an abstinence is a basic information for decision in the treatment strategy.



- The prognosis in long term sobriety is excellent.

Thank you for your attention

