Alcohol-Induced Hangover: Prevention

ABSTRACTS

Aleynik MK., 1999. Polyenylphosphatidylcholine opposes the increase of cytochrome P-4502E1 by ethanol and corrects its iron-induced decrease.
Altura BM., 1999. Association of alcohol in brain injury, headaches, and stroke with brain-tissue and serum levels of ionized magnesium: a review of recent findings and mechanisms of action.
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Polyenylphosphatidylcholine opposes the increase of cytochrome P-4502E1 by ethanol and corrects its iron-induced decrease.

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Alcohol Clin Exp Res 1999 Jan;23(1):96-100

Dietary iron overload damages membrane phospholipids and decreases microsomal cytochromes P-450. We wondered whether this might also pertain to cytochrome P-4502E1 (2E1) and whether polyenylphosphatidylcholine (PPC), a 94-96% pure mixture of linoleate-rich polyunsaturated phosphatidylcholines that protects against alcohol-induced liver injury, also affects 2E1, either in the presence or absence of iron. Accordingly, rats were fed for 8 weeks our standard liquid diet containing ethanol (36% of energy) or isocaloric carbohydrates, with either PPC (3 g/1000 Cal) or equivalent amounts of linoleate (as safflower oil). 2E1 was assessed by Western blots and by two of its characteristic enzyme activities: the microsomal ethanol oxidizing system (MEOS), evaluated by the conversion of ethanol to acetaldehyde (determined by head space GC), and p-nitrophenolhydroxylase (PNP) activity, measured by HPLC with UV detection of 4-nitrocatechol. With ethanol (36% of energy) replacing carbohydrates, 2E1 content increased 10-fold, with a corresponding increase in PNP and MEOS activities, but when carbonyl iron (5 g/1000 Cal) was added, the induction was significantly reduced. This iron-induced decrease was corrected by PPC. PPC is rich in linoleate, but when the latter was given as triglycerides (safflower oil), there was no effect, whereas hepatic nonheme iron content was the same in both these groups. It also was found that in the absence of iron, the ethanol-mediated induction of 2E1 and its corresponding enzyme activities were significantly less with PPC (< 0.001) than with safflower oil. In addition, in alcohol-fed animals, PPC decreased the oxidative stress (as determined by F2-isoprostanes), which reflects yet another hepatoprotective effect of PPC.

Association of alcohol in brain injury, headaches, and stroke with brain-tissue and serum levels of ionized magnesium: a review of recent findings and mechanisms of action.

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Alcohol 1999 Oct;19(2):119-30

Although there is general agreement that chronic ingestion of alcohol poses great risks for normal cardiovascular functions and peripheral-vascular homeostasis, a direct cause and effect between the real phenomena of alcohol-induced headache and risk of brain injury and stroke is not appreciated. "Binge drinking" of alcohol is associated with an ever-growing number of strokes and sudden death. It is becoming clear that alcohol ingestion can result in profoundly different actions on the cerebral circulation (e.g., vasodilation, vasoconstriction-spasm, vessel rupture), depending upon dose and physiologic state of host. Using rats, it has been demonstrated that acute, high doses of ethanol can result in stroke-like events concomitant with alterations in brain bioenergetics. We review recent in vivo findings obtained with 31P-NMR spectroscopy, optical reflectance spectroscopy, and direct in vivo microcirculatory studies on the intact brain. Alcohol-induced hemorrhagic stroke is preceded by a rapid fall in brain intracellular free magnesium ions ([Mg2+]i) followed by cerebrovasospasm and reductions in phosphocreatine (PCr)/ATP ratio, intracellular pH, and the cytosolic phosphorylation potential (CPP) with concomitant rises in deoxyhemoglobin (DH), mitochondrial reduced cytochrome oxidase aa3 (rCOaa3), blood volume, and intracellular inorganic phosphate (Pi). Using osmotic mini-pumps implanted in the third cerebral ventricle, containing 30% ethanol, it was found that brain [Mg2+]i is reduced 30% after 14 days; brain PCr fell 15%, whereas the CPP fell 40%. Such animals became susceptible to stroke from nonlethal doses of ethanol. Human subjects with mild head injury have been found to exhibit early deficits in serum ionized Mg (IMg2+); the greater the degree of early head injury (30 min-8 h), the greater and more profound the deficit in serum IMg2+ and the greater the ionized Ca (ICa2+) to IMg2+ ratio. Patients with histories of alcohol abuse or ingestion of alcohol prior to head injury exhibited greater deficits in IMg2+ (and higher ICa2+/IMg2+ ratios) and, unlike the subjects without alcohol, did not leave the hospital for at least several days. Women, for some unknown reason, exhibit a much higher incidence of morbidity and mortality from subarachnoid hemorrhage (SAH) than men. Data on 105 men and women with different types of stroke indicate that, on the average, a 20% deficit in serum IMg2+ is seen; total Mg (TMg) or blood pH is usually near normal. Women with SAH, however, exhibit much lower IMg2+ and higher ICa2+/IMg2+ ratios; the presence of ethanol in the blood is associated with even more depression in IMg2+ in SAH in women. It is possible that prior alcohol ingestion is, in large measure, responsible for a great deal of this unexplained higher incidence of SAH in women. It has recently been reported that the cyclical changes in estrogenic hormones appear to control the serum IMg2+ level in young women. A surge in estrogenic levels prior to SAH could thus precipitate, in part, the SAH. In other human studies, it has been shown that migraines and headache, dizziness, and hangover, which accompany ethanol ingestion, are associated with rapid deficits in serum IMg2+ but not in TMg. The former, and the alcohol-associated headache, can be ameliorated with IV administration of MgSO4. Premenstrual tension-headache (PTH) and its exacerbation by alcohol in women is also accompanied by deficits in IMg2+, and elevation in serum ICa2+/IMg2+; IV MgSO4 corrects the PTH and the serum deficit in IMg2+. Animal experiments show that IV Mg2+ can prevent alcohol-induced hemorrhagic stroke and the subsequent fall in brain [Mg2+]i, [PCr], pHi, and CPP. Other recent data indicate that alcohol-induced cellular loss of [Mg2+]i is associated with cellular Ca2+ overload and generation of oxygen-derived free radicals; chronic pretreatment with vitamin E prevents alcohol-induced vascular injury and pathology in the brain. (ABSTRACT TRUNCATED)

Phospholipid association reduces the gastric mucosal toxicity of aspirin in human subjects.

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Am J Gastroenterol 1999 Jul;94(7):1818-22

OBJECTIVE: In previous studies on rats, we have shown that aspirin (ASA)-induced injury to the gastric mucosa is markedly reduced or completely abolished if ASA is chemically associated with the phospholipid, phosphatidylcholine (PC). We have also shown that the protective effect of PC does not influence the ability of ASA to inhibit mucosal cyclooxygenase (COX) activity in the stomach and other tissues. We therefore sought to assess the effect of PC-associated ASA (ASA/PC) on the gastric mucosa of normal volunteers and to compare the results with the use of ASA alone.

METHODS: Sixteen normal healthy subjects were administered ASA or ASA/PC in a randomized, double-blind, crossover study. The subjects received ASA in a dose of 650 mg three times a day for 3 days or an equivalent dose of ASA chemically associated with PC. Endoscopy was performed at baseline and again on the morning of day 4, after the subjects had taken the final dose of the test drug. On both occasions, antral biopsy specimens were obtained for the assessment of mucosal COX activity and prostaglandin concentration.

RESULTS: The number (mean +/- SD) of gastric erosions seen with the ASA/PC formulation was significantly less than when ASA was used alone (8.7 +/- 10.7 vs 2.9 +/- 4.3; $p < 0.025$). A similar trend was seen in the duodenum but the difference was statistically not significant. The antral mucosal COX activity, as well as the level of prostaglandin 6-keto PGF1alpha, were reduced significantly (80-88%) and to a similar extent by both ASA and ASA/PC.

CONCLUSIONS: The present study shows that acute aspirin-induced damage to the gastric mucosa can be reduced by chemically associating ASA with PC. The mechanism of mucosal protection provided by this compound is not related to any alteration in the ability of ASA to inhibit mucosal COX activity. We believe this protection is attributable to the maintenance of the defensive hydrophobic barrier of the gastric mucosa.

Milk thistle (Silybum marianum) for the therapy of liver disease.

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Am J Gastroenterol 1998 Feb;93(2):139-43

Silymarin, derived from the milk thistle plant, Silybum marianum, has been used for centuries as a natural remedy for diseases of the liver and biliary tract. As interest in alternative therapy has emerged in the United States, gastroenterologists have encountered increasing numbers of patients taking silymarin with little understanding of its purported properties. Silymarin and its active constituent, silybin, have been reported to work as antioxidants scavenging free radicals and inhibiting lipid peroxidation. Studies also suggest that they protect against genomic injury, increase hepatocyte protein synthesis, decrease the activity of tumor promoters, stabilize mast cells, chelate iron, and slow calcium metabolism. In this article we review silymarin's history, pharmacology, and properties, and the clinical trials pertaining to patients with acute and chronic liver disease.

[Vitamin B 1 deficiency in chronic alcoholics and its clinical correlation]

Hell D, Six P, Salkeld R

Schweiz Med Wochenschr (Switzerland) Oct 23 1976, 106 (43) p1466-70

50 chronic alcoholics reporting to the medical emergency ward of Basle University Hospital with alcohol-related illness were examined with respect to thiamine nutritional status by means of the transketolase activation test of erythrocytes (ETK). 46% of the chronic alcoholics, compared to only 2% of the control population (1152 healthy adults), had transketolase activation quotients indicating a strong probability of thiamine deficiency (alphaETK greater than 1.25). The most important symptoms associated with the biochemical parameters of thiamine deficiency were: anemia, pathologic liver functions (bilirubin, gamma-globulins), low diastolic blood pressure and Wernicke's encephalopathy. There was a statistically significant correlation (p less than 0.05) between these symptoms and the biochemical parameters for thiamine deficiency. Therefore, when treating chronic alcoholics, these symptoms should direct attention to a possible vitamin B1 deficiency. Since the enzymatic vitamin B1 parameters correlate with the patients' hemoglobin, our results would be consistent with anemia influenced by provision of thiamine.

Leaky gut in alcoholic cirrhosis: a possible mechanism for alcohol-induced liver damage.

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Am J Gastroenterol 1999 Jan;94(1):200-7

OBJECTIVE: Only 30% of alcoholics develop cirrhosis, suggesting that the development of alcohol-induced liver injury requires one or more additional factors. Animal studies have shown that gut-derived endotoxin is one such factor. Because increased intestinal

permeability has been shown to cause endotoxemia, we hypothesized that increased gastrointestinal permeability contributes to the pathogenesis of alcoholic liver disease. This study aimed to measure gastroduodenal and intestinal permeability in alcoholics with and without chronic liver disease and in nonalcoholic subjects with chronic liver disease.

METHODS: Gastroduodenal permeability was assessed by measurement of urinary excretion of sucrose after oral administration. Intestinal permeability was assessed by measurement of urinary lactulose and mannitol after oral administration of these sugars.

RESULTS: Alcoholics with no liver disease showed a small but significant increase in sucrose excretion. Alcoholics with chronic liver disease demonstrated a marked and highly significant increase in urinary sucrose excretion relative to the controls, to the alcoholics with no liver disease, and to the nonalcoholics with liver disease. Alcoholics with chronic liver disease demonstrated a marked and highly significant increase in both lactulose absorption and in the urinary lactulose/mannitol ratio (alcoholics 0.703 vs controls 0.019, p = 0.01). In contrast, alcoholics with no liver disease and nonalcoholics with liver disease showed normal lactulose absorption and normal lactulose/mannitol ratio.

CONCLUSION: Because only the alcoholics with chronic liver disease had increased intestinal permeability, we conclude that a "leaky" gut may be a necessary cofactor for the development of chronic liver injury in heavy drinkers.

Role of oxidative stress and antioxidant therapy in alcoholic and nonalcoholic liver diseases.

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Adv Pharmacol 1997;38:601-28

The main pathway for the hepatic oxidation of ethanol to acetaldehyde proceeds via ADH and is associated with the reduction of NAD to NADH; the latter produces a striking redox change with various associated metabolic disorders. NADH also inhibits xanthine dehydrogenase activity, resulting in a shift of purine oxidation to xanthine oxidase, thereby promoting the generation of oxygen-free radical species. NADH also supports microsomal oxidations, including that of ethanol, in part via transhydrogenation to NADPH. In addition to the classic alcohol dehydrogenase pathway, ethanol can also be reduced by an accessory but inducible microsomal ethanoloxidizing system. This induction is associated with proliferation of the endoplasmic reticulum, both in experimental animals and in humans, and is accompanied by increased oxidation of NADPH with resulting H2O2 generation. There is also a concomitant 4- to 10-fold induction of cytochrome P4502E1 (2E1) both in rats and in humans, with hepatic perivenular preponderance. This 2E1 induction contributes to the well-known lipid peroxidation associated with alcoholic liver injury, as demonstrated by increased rates of superoxide radical production and lipid peroxidation correlating with the amount of 2E1 in liver microsomal preparations and the inhibition of lipid peroxidation in liver microsomes by antibodies against 2E1 in control and ethanol-fed rats. Indeed, 2E1 is rather "leaky" and its operation results in a significant release of free radicals. In addition, induction of this microsomal system results in enhanced acetaldehyde production, which in turn impairs defense systems against oxidative stress. For instance, it decreases GSH by various mechanisms, including binding to cysteine or by provoking its leakage out of the mitochondria and of the cell. Hepatic GSH depletion after chronic alcohol consumption was shown both in experimental animals and in humans. Alcohol-induced increased GSH turnover was demonstrated indirectly by a rise in alpha-amino-n-butyric acid in rats and baboons and in volunteers given alcohol. The ultimate precursor of cysteine (one of the three amino acids of GSH) is methionine. Methionine, however, must be first activated to S-adenosylmethionine by an enzyme which is depressed by alcoholic liver disease. This block can be bypassed by SAMe administration which restores hepatic SAMe levels and attenuates parameters of ethanol-induced liver injury significantly such as the increase in circulating transaminases, mitochondrial lesions, and leakage of mitochondrial enzymes (e.g., glutamic dehydrogenase) into the bloodstream. SAMe also contributes to the methylation of phosphatidylethanolamine to phosphatidylcholine. The methyltransferase involved is strikingly depressed by alcohol consumption, but this can be corrected, and hepatic phosphatidylcholine levels restored, by the administration of a mixture of polyunsaturated phospholipids (polyenylphosphatidylcholine). In addition, PPC provided total protection against alcohol-induced septal fibrosis and cirrhosis in the baboon and it abolished an associated twofold rise in hepatic F2-isoprostanes, a product of lipid peroxidation. A similar effect was observed in rats given CCl4. Thus, PPC prevented CCl4- and alcohol-induced lipid peroxidation in rats and baboons, respectively, while it attenuated the associated liver injury. Similar studies are ongoing in humans.

ALCOHOL: its metabolism and interaction with nutrients.

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In the past, alcoholic liver disease was attributed exclusively to dietary deficiencies, but experimental and judicious clinical studies have now established alcohol's hepatotoxicity. Despite an adequate diet, it can contribute to the entire spectrum of liver diseases, mainly by generating oxidative stress through its microsomal metabolism via cytochrome P4502E1 (CYP2E1). It also interferes with nutrient activation, resulting in changes in nutritional requirements. This is exemplified by methionine, one of the essential amino

acids for humans, which needs to be activated to S-adenosylmethionine (SAMe), a process impaired by liver disease. Thus, SAMe rather than methionine is the compound that must be supplemented in the presence of significant liver disease. In baboons, SAMe attenuated mitochondrial lesions and replenished glutathione; it also significantly reduced mortality in patients with Child A or B cirrhosis. Similarly, decreased phosphatidylethanolamine methyltransferase activity is associated with alcoholic liver disease, resulting in phosphatidylcholine depletion and serious consequences for the integrity of membranes. This can be offset by polyenylphosphatidylcholine (PPC), a mixture of polyunsaturated phosphatidylcholines comprising dilinoleoylphosphatidylcholine (DLPC), which has high bioavailability. PPC (and DLPC) opposes major toxic effects of alcohol, with down-regulation of CYP2E1 and reduction of oxidative stress, deactivation of hepatic stellate cells, and increased collagenase activity, which in baboons, results in prevention of ethanol-induced septal fibrosis and cirrhosis. Corresponding clinical trials are ongoing.

Alcoholic liver disease: New insights in pathogenesis lead to new treatments.

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J Hepatol 2000;32 Suppl 1:113-28

Much progress has been made in the understanding of the pathogenesis of alcoholic liver disease, resulting in improvement of prevention and therapy, with promising prospects for even more effective treatments. The most successful approaches that one can expect to evolve are those that deal with the fundamental cellular disturbances resulting from excessive alcohol consumption. Two pathologic concepts are emerging as particularly useful therapeutically. Whereas it continues to be important to replenish nutritional deficiencies, when present, it is crucial to recognize that because of the alcohol-induced disease process, some of the nutritional requirements change. This is exemplified by methionine, which normally is one of the essential amino acids for humans, but needs to be activated to S-adenosylmethionine (SAMe), a process impaired by the disease. Thus, SAMe rather than methionine is the compound that must be supplemented in the presence of significant liver disease. Indeed, SAMe was found to attenuate mitochondrial lesions in baboons, replenish glutathione, and significantly reduce mortality in patients with Child A or B cirrhosis. Similarly, polyenylphosphatidylcholine (PPC) corrects the ethanol-induced hepatic phospholipid depletion as well as the decreased phosphatidylethanolamine methyltransferase activity and opposes oxidative stress. It also deactivates hepatic stellate cells, whereas its dilinoleoyl species (DLPC) increases collagenase activity, resulting in prevention of ethanol-induced septal fibrosis and cirrhosis in the baboon. Clinical trials with PPC are ongoing in patients with alcoholic liver disease. Furthermore, enzymes useful for detoxification, such as CYP2E1, when excessively induced, become harmful and should be down-regulated. PPC is one of the substances with anti-CYP2E1 properties that is now emerging. Another important aspect is the association of alcoholic liver disease with hepatitis C: a quarter of all patients with alcoholic liver disease also have markers of HCV infection, with an even higher incidence in some urban areas but, at present, no specific therapy is available since interferon is contraindicated in that population. However, in addition to antiviral medications, agents that oppose oxidative stress and fibrosis should also be tested for hepatitis C treatment since these two processes contribute much to the pathology and mortality associated with the virus. In addition to antioxidants (such as PPC, silymarin, alpha-tocopherol and selenium), anti-inflammatory medications (corticosteroids, colchicine, anticytokines) are also being tested as antifibrotics. Transplantation is now accepted treatment in alcoholics who have brought their alcoholism under control and who benefit from adequate social support but organ availability is still the major limiting factor and should be expanded more aggressively. Finally, abstinence from excessive drinking is always indicated; it is difficult to achieve but agents that oppose alcohol craving are becoming available and they should be used more extensively.

Hepatic, metabolic, and nutritional disorders of alcoholism: from pathogenesis to therapy.

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Crit Rev Clin Lab Sci 2000 Dec;37(6):551-84

Much progress has been made in the understanding of the pathogenesis of alcoholic liver disease, resulting in an improvement in treatment. Nutritional deficiencies should be corrected when present but, because of the alcohol-induced disease process, some of the nutritional requirements change. For instance, methionine, one of the essential amino acids for humans, must be activated to S-adenosylmethionine (SAMe), but, in severe liver disease, the activity of the corresponding enzyme is depressed. Therefore, the resulting deficiencies and associated pathology can be attenuated by the administration of SAMe, but not by methionine. Similarly, phosphatidylethanolamine methyltransferase (PEMT) activity, which is important for hepatic phosphatidylcholine (PC) synthesis, is also depressed in alcoholic liver disease, therefore calling for the administration of the products of the reaction. Inasmuch as free radical generation by the ethanol-induced CYP2E1 plays a key role in the oxidative stress, inhibitors of this enzyme have great promise and PPC, which is presently being evaluated clinically, is particularly interesting because of its innocuity. In view of the striking negative interaction between alcoholic liver injury and hepatitis C, an antiviral agent is eagerly awaited that, unlike Interferon, is not contraindicated in the alcoholic. Antiinflamatory agents may also be useful. In addition to steroids, down-regulators of cytokines and endotoxin are being considered. Finally, anticraving agents such as naltrexone or acamprosate should be incorporated into any contemplated therapeutic cocktail.

Glutathione prevents ethanol induced gastric mucosal damage and depletion of sulfhydryl compounds in humans.

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Gut (England) Feb 1993, 34 (2) p161-5

Whether parenteral administration of reduced glutathione prevented ethanol induced damage to and depletion of sulfhydryl compounds in the human gastric mucosa was investigated. Ten healthy volunteers underwent endoscopy on three separate occasions. Gastric mucosal damage was induced by spraying 80% ethanol on to the gastric mucosa through the biopsy channel of the endoscope. The gastric mucosal score, total sulfhydryls, glutathione, and cysteine were evaluated in basal conditions and after ethanol administration with and without pretreatment with parenteral glutathione. Glutathione significantly decreased the extent of ethanol induced macroscopic injury to the mucosa of the gastric body and antrum. Glutathione's protective effect is associated with appreciable inhibition of ethanol induced depletion of gastric sulfhydryl compounds. This is the first report of protection against ethanol induced gastric mucosal damage by a sulfhydryl containing agent in humans.

Improvement of hemorheological abnormalities in alcoholics by an oral antioxidant.

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Hepatogastroenterology 2001 Mar-Apr;48(38):511-7

BACKGROUND/AIMS: It has been shown that alcohol impairs erythrocyte (red blood cell) membrane fluidity and lipid composition. The aim of this study was to test the effect of a novel acid-resistant antioxidant on the hemorrheology in alcoholics.

METHODOLOGY: Thirty alcoholics (25 males, 5 females; mean age: 42 years; range: 31-54; 150 g ethanol/day for 3-5 years) were enrolled into the study. Patients were randomly and double-blindly allocated into 2 groups which were given, for a 2 week period, 18 g/day of Bionormalizer (obtained from biofermentation of carica papaya, pennisetum purpureum, sechium edule, Osato Res. Foundation, Gifu, Japan) dissolved in 5 mL of water at bedtime and 3 hours prior to examination. Placebo consisted of flavored sugar. Healthy teetotalers served as control. On the examination day, blood samples were taken for testing: routine tests, plasma glutathione, ascorbic acid, selenium, plasma lipid hydroperoxides and alpha-tocopherol. Erythrocytes were separated and tested for red blood cell malonyldialdehyde and glutathione content. The hemorheological studies were as follows: blood and plasma viscosity, whole blood filterability, red blood cell membrane fluidity by electron spin resonance, red blood cell aggregation index by photometric rheoscopy and red blood cell deformability by ektacytometry.

RESULTS: As compared to healthy controls, alcoholics on placebo treatment showed no change of plasma viscosity but a significantly higher red blood cell malonyldialdehyde, blood viscosity ($P < 0.05$) and lower plasma glutathione, whole blood filterability and red blood cell fluidity ($P < 0.01$). No relationship appeared between biochemical tests and red blood cell membrane fluidity. Bionormalizer group showed a significant recovery to control values of either blood viscosity and whole blood filterability ($P < 0.01$) and a partial, although significant, improvement of red blood cell membrane fluidity, red blood cell malonyldialdehyde and plasma glutathione ($P < 0.05$). As compared to healthy control, red blood cell aggregation decreased in alcoholics ($P < 0.05$) and was not affected by Bionormalizer. However, Bionormalizer significantly improved the reduced red blood cell deformability ($P < 0.05$ vs. alcoholics) and this parameter correlated with red blood cell malonyldialdehyde ($r: 0.62$. $P < 0.05$).

CONCLUSIONS: These preliminary data suggest that an effective antioxidant supplementation is able to improve the hemorrheology in alcoholics either by directly affecting the ethanol-related lipoperoxidation and xanthine oxidase system activation and/or by modifying red blood cell membrane characteristics.

"S-Adenosylmethionine and the Liver"

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The Liver: Biology and Pathobiology, 3rd Edition, 1994; 27:461-470

In the adult 6 to 8 gm of S-adenosylmethionine (SAM) is produced daily. Most of it is produced in the liver where it is utilized. The methionine cycle and trans-sulfuration pathways are impaired in human liver disease. One or more of these abnormalities may be responsible for some of the clinical manifestations of liver cirrhosis. The increased breakdown in methionine at the expense of methylation reactions is generated by a need to synthesize hepatic GSH to offset the damaging oxidant effects of ethanol. Paracetamol (acetaminophen) can result in fetal liver damage in overdosed individuals. Two forms of cytochrome P450 convert paracetamol into a reactive metabolite that depletes liver reduced glutathione. Reduced glutathione is a tripeptide containing

glycine, glutamic acid and cysteine. It is the most important cellular thiol. N- acetylcysteine, in an hepatic toxic condition resulting from paracetamol overdose can, if given in time, improve survival and reduce liver damage. Different studies have shown SAM to be effective in symptomatic treatment of intrahepatic cholestasis of the liver and of pregnancy. SAM has also been reported to improve liver function in various chronic liver diseases including alcoholic and nonalcoholic cirrhosis. This article also notes that the trans-sulfuration pathway, which can lead to homocystinuria/homocysteinemia,is dependent on enzymes that are cofactors with vitamin B12, folic acid, B6, choline and betaine hydrochloride. Homocysteine is believed to be an independent risk factor for the development of coronary artery disease in man. The molecular basis for homocysteine playing a role in cardiovascular function is not known, but it may be related to its interference.

Protective action of ascorbic acid and sulfur compounds against acetaldehyde toxicity: implications in alcoholism and smoking.

Sprince H, Parker CM, Smith GG, Gonzales LJ

Agents Actions (Switzerland) May 1975, 5 (2) p164-73

Acetaldehyde is a toxic substance common to heavy drinking of alcohol and heavy smoking of cigarettes. It has been implicated thereby in diseases of the cardiovascular, respiratory, and central nervous systems. Protection against acetaldehyde toxicity (i.e. anesthesia and lethality) was studied in rats by oral intubation of test compounds 30-45 minutes prior to oral intubation of a standardized oral LD 90 dose (18 millimoles/kilogram) of acetaldehyde. Animals were monitored for anesthesia (loss of righting reflexes) and lethality for 72 hours. A total of 18 compounds was tested. L-ascorbic acid at 2 millimoles/kilogram (mM/kg) showed moderate protection against anesthesia and marked protection against lethality. Greatest protection against anesthesia and lethality was obtained at 2 m M/kg with each of the following: L-cysteine, N-acetyl-L-cysteine, thiamin-HCl, sodium metabisulfite, and L-cysteic acid. A combination of L-ascorbic acid with L- cysteine, and thiamin-HCl at reduced dose levels (2.0, 1.0 and 0.3 mM/kg, respectively) gave virtually complete protection. A detailed literature review is presented of the rationale and significance of these findings. Our findings could point the way to a possible build-up of natural protection against the chronic body insult of acetaldehyde arising from heavy drinking of alcohol and heavy smoking of cigarettes.

Alcohol and brain damage.

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Hum Toxicol (England) Sep 1988, 7 (5) p455-63

1. The safe limits of alcohol intake are difficult to define because of individual variations in susceptibility to damage. The present recommendations are based largely on epidemiological studies of liver damage.

2. Recent investigations indicate that alcoholic brain damage is much more common than previously suspected. More information is required about its natural history and the characteristics of individuals most likely to suffer damage.

3. Thiamin (vitamin B1) deficiency has long been associated with brain damage and may result from a number of additive causes in the alcoholic patient. New information indicating damage to the protein moeity of some of the thiamin-using enzymes has been reviewed, as have possible mechanisms of brain cell necrosis.

"N-Acetylcysteine for Lung Cancer Prevention"

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Nico Chest May 1995;107(5):1437-1441

In 1981 it was estimated by Doll and Peto that of all cancer deaths in the United States 30% were due to tobacco, 3% to alcohol and 35% to diet and other causes. Twelve percent of lung cancers were not attributable to tobacco and dietary factors were implicated in the causation of cancer in tissues other than the gastrointestinal tract. Damage to cellular DNA not only occurs from environmental mutagens but also from the endogenous production of oxidants which damage DNA and other mechanisms related to the conversion of food, in particular fats to energy. Inflammation and the healing process can also result in damage. Dietary antioxidants have also been shown to prevent this oxidative cellular DNA damage; these include vitamin A, the carotene family, vitamin C, E and selenium. In reviewing approximately 200 published studies there was overwhelming evidence that the consumption of fruit and vegetables is associated with reduced cancer incidence. Cigarette smoke contains oxidants as well as several precarcinogens. Metabolism of carcinogens and the steps of carcinogenesis are a balance between forces such as metabolic activation and detoxification, formation and scavenging of radicals and DNA damage and repair. This suggests that carcinogenic compounds can initiate tumor growth only when they saturate detoxification pathways. Glutathione plays a role in the

detoxification of xenobiotics. N-acetylcysteine which is an amino thiol and precursor of intracellular cysteine and glutathione has been shown not only to be an efficient antidote in acetaminophen poisoning but also has important chemopreventive properties. N-acetylcysteine appears to exert its chemopreventive effects by multiple mechanisms and may provide protection against different mutagens and carcinogens in different stages of carcinogenesis. N-acetylcysteine has reached the Phase III trial stage in chemoprevention in Europe and has been used in clinical practice for more than 30 years. In large groups of patients with chronic obstructive lung disease N-acetylcysteine has turned out to be a safe agent with minor effects even when prescribed for a prolonged period of time. N- acetylcysteine is well tolerated when taken continuously in a dose of 600 mg per day. Dyspepsia has been reported as a mild side effect. N-acetylcysteine holds promise and it may turn out to be effective in preventing secondary tumors. It may have a wider use in chemopreventive purposes.

N-acetyl cysteine attenuates ethanol induced hypertension in rats.

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Artery 1995;21(6):312-6

All known pathways of ethanol metabolism result in the production of acetaldehyde, a highly reactive compound. N-acetyl cysteine, an analogue of the dietary amino acid cysteine, binds acetaldehyde, thus preventing its damaging effect on physiological proteins. This study examined the effect of oral N-acetyl cysteine on the increased blood pressure, platelet cytosolic free calcium, blood acetaldehyde and adverse renal vascular changes induced by chronic ethanol treatment in rats. Twenty-four male Wistar-Kyoto (WKY) rats, age 7 weeks were divided into four groups of six animals each. Animals in group I were given water and group II 5% ethanol in water for the next 14 weeks. Animals in group III were given 5% ethanol + 1% N-acetyl cysteine for 4 weeks followed by 5% ethanol + 2% N-acetyl cysteine for the next 10 weeks. Animals in group IV were given 5% ethanol for 7 weeks; at that time ethanol was withdrawn and animals were placed on water with 2% N-acetyl cysteine for the next 7 weeks. After 14 weeks systolic blood pressure and platelet cytosolic free calcium were all significantly higher (< 0.001) in rats given ethanol as compared to rats in other groups. N-acetyl cysteine treatment, along with ethanol, significantly (< 0.001) attenuated the increased blood pressure and platelet cytosolic free calcium and adverse renal vascular changes. Discontinuation of ethanol treatment for 7 weeks along with N-acetyl cysteine supplementation also significantly lowered the blood pressure and platelet cytosolic free calcium and attenuated adverse renal vascular changes. There was no significant difference in aortic malonaldehyde among four groups. Increase in blood acetaldehyde with ethanol treatment was significantly attenuated with N-acetyl cysteine treatment. These results suggest that acetaldehyde may be the cause of ethanol-induced hypertension and elevated cytosolic free calcium and renal vascular changes.

The alcohol hangover.

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Ann Intern Med 2000 Jun 6;132(11):897-902

PURPOSE: To review the cause, pathophysiologic characteristics, cost, and treatment of alcohol-induced hangover.

DATA SOURCES: A MEDLINE search of English-language reports (1966 to 1999) and a manual search of bibliographies of relevant papers.

STUDY SELECTION: Related experimental, clinical, and basic research studies.

DATA EXTRACTION: Data in relevant articles were reviewed, and relevant clinical information was extracted.

DATA SYNTHESIS: The alcohol hangover is characterized by headache, tremulousness, nausea, diarrhea, and fatigue combined with decreased occupational, cognitive, or visual-spatial skill performance. In the United States, related absenteeism and poor job performance cost $148 billion annually (average annual cost per working adult, $2000). Although hangover is associated with alcoholism, most of its cost is incurred by the light-to-moderate drinker. Patients with hangover may pose substantial risk to themselves and others despite having a normal blood alcohol level. Hangover may also be an independent risk factor for cardiac death. Symptoms of hangover seem to be caused by dehydration, hormonal alterations, dysregulated cytokine pathways, and toxic effects of alcohol. Physiologic characteristics include increased cardiac work with normal peripheral resistance, diffuse slowing on electroencephalography, and increased levels of antidiuretic hormone. Effective interventions include rehydration, prostaglandin inhibitors, and vitamin B6. Screening for hangover severity and frequency may help early detection of alcohol dependency and substantially improve quality of life. Recommended interventions include discussion of potential therapies and reminders of the possibility for cognitive and visual-spatial impairment. No evidence suggests that alleviation of hangover symptoms leads to further alcohol consumption, and the discomfort caused by such symptoms may do so. Therefore, treatment seems warranted.

CONCLUSIONS: Hangover, a common disorder, has substantial morbidity and societal cost. Appropriate management may relieve symptoms in many patients.

Suggested Reading

Acute ethanol poisoning and the ethanol withdrawal syndrome.

Adinoff B, Bone GH, Linnoila M Laboratory of Clinical Studies, National Institute on Alcohol Abuse and Alcoholism, Bethesda.

Med Toxicol Adverse Drug Exp (New Zealand) May-Jun 1988, 3 (3) p172-96

Ethanol, a highly lipid-soluble compound, appears to exert its effects through interactions with the cell membrane. Cell membrane alterations indirectly affect the functioning of membrane-associated proteins, which function as channels, carriers, enzymes and receptors. For example, studies suggest that ethanol exerts an effect upon the gamma-aminobutyric acid (GABA)-benzodiazepine-chloride ionophore receptor complex, thereby accounting for the biochemical and clinical similarities between ethanol, benzodiazepines and barbiturates. The patient with acute ethanol poisoning may present with symptoms ranging from slurred speech, ataxia and incoordination to coma, potentially resulting in respiratory depression and death. At blood alcohol concentrations of greater than 250 mg% (250 mg% = 250 mg/dl = 2.5 g/L = 0.250%), the patient is usually at risk of coma. Children and alcohol-naive adults may experience severe toxicity at blood alcohol concentrations less than 100 mg%, whereas alcoholics may demonstrate significant impairment only at concentrations greater than 300 mg%. Upon presentation of a patient suspected of acute ethanol poisoning, cardiovascular and respiratory stabilisation should be assured. Thiamine (vitamin B1) and then dextrose should be administered, and the blood alcohol concentration measured. Subsequent to stabilisation, alternative aetiologies for the signs and symptoms observed should be considered. There are presently no agents available for clinical use that will reverse the acute effects of ethanol. Treatment consists of supportive care and close observation until the blood alcohol concentration decreases to a non-toxic level. In the non-dependent adult, ethanol is metabolised at the rate of approximately 15 mg%/hour. Haemodialysis may be considered in cases of a severely ill child or comatose adult. Follow-up may include referral for counseling for alcohol abuse, suicide attempts, or parental neglect (in children). The ethanol withdrawal syndrome may be observed in the ethanol- ependent patient within 8 hours of the last drink, with blood alcohol concentrations in excess of 200 mg%. Symptoms consist of tremor, nausea and vomiting, increased blood pressure and heart rate, paroxysmal sweats, depression, and anxiety. Alterations in the GABA-benzodiazepine-chloride receptor complex, noradrenergic overactivity, and hypothalamic-pituitary-adrenal axis stimulation are suggested explanations for withdrawal symptomatology.

[Severe somatic complications of acute alcoholic intoxication]

Billy I, Lejonc JL Services d'urgences-medecine generale, hopital Henri-Mondor, Creteil. Rev Prat (France) Oct 15 1993, 43 (16) p2047-51

Acute alcohol ingestion can affect life expectancy and is directly responsible for 3,500 deaths per year. Acute lung diseases are mainly caused by pneumococci, Gram negative bacilli and anaerobic germs, and are often due to multiple microbes. In this case, evolution toward abscess can be feared. Septicaemia and enterobacterial peritonitis are frequently observed in cirrhotic patients. Ethanol, hypokaliemia and hypophosphoraemia also lead to rhabdomyolysis. Rhabdomyolysis can be complicated with acute renal failure and hyperkaliaemia. Alcoholic ketoacidosis and the hypoglycaemia favored by prolonged inadequate nutrition, are corrected by infusion of glucose solutions. Hyponatraemia can be complicated by convulsions and central pontine myelinolysis. Minor forms of alcoholic hepatitis remiss after stopping alcohol intoxication. The major forms can evolve toward fatal encephalopathy; treatment with corticosteroids improves the prognosis in severe hepatitis. The cardiac failure with lactic acidosis in shoshin beriberi rapidly evolves to collapsus; treatment is based on emergency administration of vitamin B1. Management of patients in acute alcohol episodes requires great vigilance. Careful clinical examination and biological tests should eliminate severe somatic complications before concluding to simple alcoholic intoxication.

[The therapeutic approach in optic neuropathy due to methyl alcohol]

Buzna E, Cernea D Clinica Oftalmologica, Craiova.

Oftalmologia (Romania) Jan-Mar 1991, 35 (1) p39-42

The paper reports on the case of a 44-year-old patient suffering from toxic optic neuropathy produced by ingestion of a drink brought at second hand. The eye examination revealed the installment of bilateral blindness without the perception of light and with alteration of the general state. After the treatment with 3 perfusions/day with 22 ml ethylic alcohol, 90 degrees, in 250 ml glucosed serum 10%, 200 mg vitamin B1, 500 mg vitamin B6, nicotined xanthnol, vials II for six days, the evolution was good: VOD = 2/3 n.c.; VOS = 1/8 n.c.

Protection against toxic effects of formaldehyde in vitro, and of methanol or formaldehyde in vivo, by subsequent administration of SH reagents.

Guerri C, Godfrey W, Grisolia S

Physiol Chem Phys (United States) 1976, 8 (6) p543-50

Rapid and progressive inactivation in vitro of both alcohol dehydrogenase and aldehyde dehydrogenase by low concentrations of acetaldehyde or formaldehyde is illustrated. This inactivation can be prevented or reversed by glutathione or other SH reagents. Those effects led to investigations in vivo. Rats and mice were injected with concentrations that would result in death in approximately 10 h (methanol) and approximately 4 h (formaldehyde). When 2,3-dimercaptopropanol (BAL), cysteine, or mercaptoethanol was injected (10 min to 3 h) after administration of methanol or formaldehyde, approximately 70% of the animals survived indefinitely; the remaining 30% showed substantial increase in survival time. The findings indicate the possibility of using reagents such as BAL for human therapy and suggest that the toxicity of methanol and formaldehyde is due in part to effects other than acidosis.

Clinical signs in the Wernicke-Korsakoff complex: a retrospective analysis of 131 cases diagnosed at necropsy.

Harper CG, Giles M, Finlay-Jones R

J Neurol Neurosurg Psychiatry 1986 Apr;49(4):341-5

A recent necropsy study has shown that 80% of patients with the Wernicke-Korsakoff syndrome were not diagnosed as such during life. Review of the clinical signs of these cases revealed that only 16% had the classical clinical triad and 19% had no documented clinical signs. The incidence of clinical signs in this and other retrospective pathological studies is very different from that of prospective clinical studies. This discrepancy may relate to "missed" clinical signs but the magnitude of the difference suggests that at least some cases of the Wernicke-Korsakoff syndrome may be the end result of repeated subclinical episodes of vitamin B1 deficiency. In order to make the diagnosis, clinicians must maintain a high index of suspicion in the "at risk" group of patients, particularly alcoholics. Investigations of thiamine status may be helpful and if the diagnosis is suspected, parenteral thiamine should be given.

Reduction of lower motor neuron degeneration in wobbler mice by N-acetyl-L-cysteine

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Journal of Neuroscience (USA), 1996, 16/23 (7574-7582)

The murine mutant wobbler is a model of lower motoneuron degeneration with associated skeletal muscle atrophy. This mutation most closely resembles Werdnig-Hofmann disease in humans and shares some of the clinical features of amyotrophic lateral sclerosis (ALS). It has been suggested that reactive oxygen species (ROS) may play a role in the pathogenesis of disorders such as ALS. To examine the relationship between ROS and neural degeneration, we have studied the effects of agents such as N-acetyl-L-cysteine (NAC), which reduce free radical damage. Litters of wobbler mice were given a 1% solution of the glutathione precursor NAC in their drinking water for a period of 9 weeks. Functional and neuroanatomical examination of these animals revealed that wobbler mice treated with NAC exhibited (1) a significant reduction in motor neuron loss and elevated glutathione peroxidase levels within the cervical spinal cord, (2) increased axon caliber in the medial facial nerve, (3) increased muscle mass and muscle fiber area in the triceps and flexor carpi ulnaris muscles, and (4) increased functional efficiency of the forelimbs, as compared with untreated wobbler littermates. These data suggest that reactive oxygen species may be involved in the degeneration of motor neurons in wobbler mice and demonstrate that oral administration of NAC effectively reduces the degree of motor degeneration in wobbler mice. This treatment thus may be applicable in the treatment of other lower motor neuropathies.

Prevention and treatment of liver fibrosis based on pathogenesis.

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Alcohol Clin Exp Res 1999 May;23(5):944-9

Multiple agents have been proposed for the prevention and treatment of fibrosis. S-adenosylmethionine was reported to oppose CCl4-induced fibrosis in the rat, to attenuate the consequences of the ethanol-induced oxidative stress, and to decrease mortality in cirrhotics. Anti-inflammatory medications and agents that interfere with collagen synthesis, such as inhibitors of prolyl-4-

hydroxylase and antioxidants, are also being tested. In nonhuman primates, polyenylphosphatidylcholine (PPC), extracted from soybeans, protected against alcohol-induced fibrosis and cirrhosis and prevented the associated hepatic phosphatidylcholine (PC) depletion by increasing 18:2 containing PC species; it also attenuated the transformation of stellate cells into collagen-producing transitional cells. Furthermore, it increased collagen breakdown, as shown in cultured stellate cells enriched with PPC or pure dilinoleoyl PC, the main PC species present in the extract. Because PPC and dilinoleoyl PC promote the breakdown of collagen, there is reasonable hope that this treatment may be useful for the management of fibrosis of alcoholic, as well as nonalcoholic, etiologies and that it may affect not only the progression of the disease, but may also reverse pre-existing fibrosis, as demonstrated for CCl4-induced cirrhosis in the rat and as presently tested in an ongoing clinical trial.

Effect of S-adenosyl-L-methionine administration on red blood cell cysteine and glutathione levels in alcoholic patients with and without liver disease.

Loguercio C, Nardi G, Argenzio F, Aurilio C, Petrone E, Grella A, Del Vecchio Blanco C, Coltorti M Cattedra di Gastroenterologia, Facolta di Medicina, II Universita di Napoli, Italy.

Alcohol Alcohol (England) Sep 1994, 29 (5) p597-604

We measured glutathione and cysteine concentrations in erythrocytes of chronic alcohol misusers with (20 subjects) and without liver cirrhosis (20 subjects). Glutathione levels were decreased, whereas those of cysteine were increased in all patients. Parenteral treatment with S-adenosylmethionine (SAME); (2 g daily in 250 ml 0.15 M NaCl for 15 days) corrected the erythrocyte thiol alterations. We conclude that parenteral treatment with SAME affects the metabolism of SH compounds in erythrocytes of alcoholic patients.

A possible protective role for sulphydryl compounds in acute alcoholic liver injury.

Macdonald CM, Dow J, Moore MR

Biochem Pharmacol (United States) Aug 15 1977, 26 (16) p1529-31

No abstract.

Hypoxic neuronal injury in tissue culture is associated with delayed calcium accumulation.

Marcoux FW, Probert AW Jr, Weber ML. Parke-Davis Pharmaceutical Research Division, Warner-Lambert Company, Ann Arbor, Mich 48105.

Stroke 1990 Nov;21(11 Suppl):III71-4

Calcium accumulation and neuronal injury were studied after hypoxia in cerebrocortical cell cultures in vitro. Neuronal injury was associated with a delayed calcium accumulation, which was greatest 5-7 hours after hypoxic exposure. Antiexcitotoxic treatments with tetrodotoxin and magnesium chloride or the selective N-methyl-D-aspartate antagonist (+/-)-4-(3-phosphonopropyl)-2-piperazinecarboxylic acid prevented hypoxic calcium accumulation and neuronal injury even when added 3 hours after hypoxia, during reoxygenation. Rescue of the neurons after hypoxia by blocking the delayed calcium accumulation in this cell culture preparation suggests a "therapeutic window" determined by calcium entry.

Sulfur amino acid metabolism in hepatobiliary disorders.

Martensson J, Foberg U, Fryden A, Schwartz MK, Sorbo B, Weiland O Dept. of Clinical Chemistry, University Hospital, Linkoping, Sweden.

Scand J Gastroenterol (Norway) May 1992, 27 (5) p405-11

Sulfur amino acid metabolism was studied in patients with mild to severe forms of liver dysfunction and compared with that of healthy controls. Patients with mild liver dysfunction (for example, Gilbert's syndrome) had a normal sulfur amino acid metabolism. With increased inflammatory activity and cirrhosis (for example, chronic active hepatitis, alcohol-induced cirrhosis, and hepatic coma) a decreased ability to metabolize methionine (to cysteine, with cystathionine accumulation) and cysteine (to inorganic sulfate, with thiosulfate and N-acetylcysteine accumulation) was found. In contrast, transaminative metabolism of sulfur amino acids was preserved in patients with advanced forms of liver dysfunction, suggesting that transamination of sulfur amino acids is performed not only in the liver but also in extrahepatic tissues. Some implications of these findings are discussed.

Nimodipine improves the disruption of spatial cognition induced by cerebral ischemia.

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Physiol Behav 2000 Jul 1-15;70(1-2):19-25

The direct neuroprotective effect of nimodipine, a central Ca antagonist, was investigated in in vitro experiments. Also, in in vivo experiments, the effects of nimodipine and amlodipine, a noncentral Ca antagonist, on rat cerebral ischemia models developing by different mechanisms were compared. In an in vitro ischemic model using acidotic and hypoglycemic rat cerebellar granule cells, nimodipine directly protects against brain neuronal cell damage. In in vivo models of single (one 10-min, four-vessel occlusion) and repeated rat cerebral ischemia (two 10-min, four-vessel occlusions; a 50-min interval), the impairment observed 24 h after the single ischemic procedure was likely to be prevented by nimodipine (0. 1-5mg/kg, i.p.). At 7 days after the repeated cerebral ischemia, the disruption of spatial cognition was significantly prevented by nimodipine (5 mg/kg, i.p.) but not amlodipine (5 mg/kg, i.p.), which was given after each ischemia. These results indicated that nimodipine may protect neuronal cells by a more persistent mode of action, that is, nimodipine may enter into the cell and control the intracellular Ca ion cascade by inhibiting excessive Ca(2)+ influx into the mitochondria.

Effects of amino acids on acute alcohol intoxication in mice--concentrations of ethanol, acetaldehyde, acetate and acetone in blood and tissues.

Tsukamoto S, Kanegae T, Nagoya T, Shimamura M, Mieda Y, Nomura M, Hojo K, Okubo H Department of Legal Medicine, Nihon University School of Medicine.

Arukoru Kenkyuto Yakubutsu Ison (Japan) Oct 1990, 25 (5) p429-40

Condensation reactions between some SH-amino acids (L-and D-cysteine 1%) and acetaldehyde (50 microM) were studied in vitro experiment. In the aqueous solution, free acetaldehyde was reduced to 41.3% by L-cysteine and to 36.4% by D-cysteine. In the reaction with human blood medium, after the medium was deproteinized with perchloric acid reagent, acetaldehyde was reduced to 47.0% by L-cysteine and to 43.8% by D-cysteine. D-Cysteine appears to have great stability of reacting acetaldehyde. In vitro experiment reactability for D-cysteine exhibited 3-8% higher than that for L-cysteine. Next, effects of some amino acids on alcohol metabolism were studied in male ICR mice. The animals were given ethanol through a gastric catheter at a dose of 2 g/kg and they were intraperitoneally injected L- cysteine (300 mg/kg), D-cysteine (300 mg/kg), L-alanine (300 mg/kg) and control (saline), respectively in the period of one hour before the injection of ethanol. Blood and tissues samples were analyzed for ethanol, acetaldehyde, acetate and acetone during alcohol intoxication in mice by head space gas chromatography. In the groups administered D-cysteine and L- cysteine, the mice showed a definitely faster oxidation and disappearance of ethanol. Especially in the D-cysteine group, ethanol levels in blood, liver and brain remained lower than that in the other groups (p less than 0.01). Acetaldehyde levels in blood, liver and brain remained low by L- cysteine. Ethanol metabolites during alcohol oxidation by chemical reactabilities of L- and D-cysteine showed different distribution in the mice, respectively. In the mice received L-alanine, acetate and acetone levels in blood, liver and brain were distinctly reduced (p less than 0.01). L-Alanine is reported to supply an abundance of pyruvic acid that performs the NAD-generating system. NAD produced is introduced to alcohol metabolism and the TCA cycle. It was thus presumed that the L- or/and D- cysteine, and L-alanine was effective in acute alcohol intoxication by heavy drinking.

Thiamine status of institutionalised and non-institutionalised aged.

Vir SC, Love AH

Int J Vitam Nutr Res (Switzerland) 1977, 47 (4) p325-35

Thiamine status of 196 institutionalised (in hospital, residential accommodation and sheltered dwelling) and non-institutionalised Caucasian aged subjects was assessed by combined dietary, biochemical and clinical studies. Fourteen subjects (7.1 per cent) consumed less than two-thirds of recommended vitamin B1/DAY. Erythrocyte transketolas activity coefficient (a) test indicated biochemical deficiency of thiamine in 17.6 per cent males and 12.5 per cent females. The incidence of deficiency was highest in subjects of sheltered dwelling. Multivitamin supplementation failed to raise the biochemical thiamine status to normal in 2.9 per cent subjects. No characteristic clinical features of thiamine deficiency were noted, though extreme loss of appetite was reported by 3 subject with activity coefficient greater than 1.30. Dietary intake was not always associated with deficient biochemical indices. The possible factors such as alcohol intake and low folate status affecting the biochemical status of thiamine are discussed.

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