



Effects of Buprenorphine and Hepatitis C on Liver Enzymes in Adolescents and Young Adults

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INTRODUCTION

➤ There are few efficacy or safety data for buprenorphine in adolescents (Marsch et al., 2005), and limited clinical experience.

➤ The potential of buprenorphine for liver toxicity has not been fully evaluated.

➤ Liver safety is of particular concern in opioid addicts due to the high prevalence of Hepatitis C (Hep C) (Murrill et al, 2002).

➤ Hep C prevalence among younger opioid addicts is less well known.

OBJECTIVES

➤ Here we report on liver safety and Hepatitis C data from a trial of buprenorphine adolescents and young adults (George Woody, PI) recently completed through the NIDA Clinical Trials Network.

➤ The aims of the study are 1) to describe the liver function and hep C status of this population, and 2) to evaluate the effects of buprenorphine and Hepatitis C on liver function in this population.

METHODS

➤ Baseline data were available for 152 subjects at 6 sites who sought treatment for opioid dependence who were randomized to 2 week detoxification with buprenorphine/naloxone (DETOX) or 12 weeks buprenorphine/naloxone (BUP).

➤ 111 participants had at least one set of LFTs during treatment and were included in analyses of treatment effects.

➤ Mean age was 19.1 years, and mean duration of opioid dependence was 1.5 years.

➤ 76% used heroin, 56% used prescription opioids, and 50% injected drugs.

➤ Liver function tests (LFTs) were evaluated prior to treatment and at 4, 8, and 12 weeks, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl transferase, lactate dehydrogenase, Total Bilirubin, and alkaline phosphatase.

➤ Any value above the upper limit of normal was considered abnormal.

➤ Hep C antibody was determined at baseline and at 12 weeks.

RESULTS

➤ 24.5% of participants had one or more abnormal LFTs at baseline, and 31.5%, 29.1%, and 24.1% at 4, 8, and 12 weeks respectively, excluding from the denominator those with missing data.

➤ Two individuals in the DETOX group and 2 in the BUP group developed markedly elevated LFTs (greater than 5 times the upper limit of the normal range).

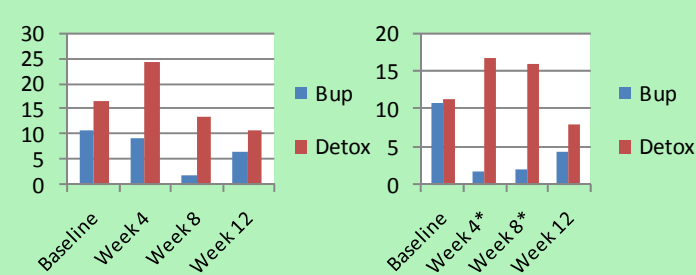
➤ 18% of participants were Hep C positive at baseline and 4 seroconverted within 12 weeks, 2 in each group.

➤ There were highly significant differences in rates of Hep C by site ($p < .0005$).

Average rates of LFT and transaminase abnormalities by treatment group and Hep C status

	Bup	Detox		HC+	HC -	
Any LFT Abnormal	0.364 (n = 59)	0.526 (n = 51)	U = 1365.5 Z = -.912 p = .362	0.675 (n = 20)	0.387 (n = 90)	U = 732.0 Z = -1.425 p = .154
AST or ALT Abnormal	0.050 (n = 60)	0.162 (n = 51)	U = 1282 Z = -2.309 p = .041	0.246 (n = 20)	0.0695 (n = 91)	U = 640.0 Z = -2.878 p = .004

% ALT and AST abnormalities by treatment group and week



* $p < .05$, Fisher's exact. Two-sided. Number of subjects: baseline bup = 74, detox = 78; week 4 bup = 54, detox = 41; week 8 bup = 51, detox = 37; week 12 bup = 46, detox = 37.

Logistic Regressions controlling for baseline transaminase values and Hep C status (N = 111)

ALT

	B	S.E.	Wald	df	Sig.	Exp(B)
Baseline Hep C	-.903	.598	2.279	1	.131	.405
Baseline ALT	.008	.005	2.649	1	.104	1.008
BUP vs. DETOX	.667	.522	1.629	1	.202	1.948
Constant	-1.500	.666	5.076	1	.024	.223

AST

	B	S.E.	Wald	df	Sig.	Exp(B)
Baseline Hep C	-1.313	.648	4.102	1	.043	.269
Baseline AST	.004	.010	.159	1	.690	1.004
BUP vs. DETOX	1.362	.635	4.595	1	.032	3.902
Constant	-1.800	.800	5.062	1	.024	.165

Baseline Hep C status and transaminase value entered in block 1, treatment condition entered in block 2.

DISCUSSION

➤ No evidence was found for any hepatotoxicity of buprenorphine in this sample. If anything, transaminase values were less likely to be abnormal in patients treated with Bup for 3 months. These differences were not clinically significant and should be interpreted cautiously due to multiple comparisons and the post-hoc nature of the findings specific to the transaminases and AST in particular.

➤ Hepatitis C was present in a significant minority of participants and predicted transaminase elevation. The high rate of seroconversion points to the importance of effective treatment and prevention in this population, which could include longer-term agonist treatment.

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