# EFFECT OF ETHANOL ON GASTRIC SECRETION OF THROMBOXANE $B_2$

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## SUMMARY

*The effects of ethanol on gastric thromboxane $B_2$ was studied in man. A single dose of 20 ml 15% ethanol significantly inhibited the gastric secretion of thromboxane $B_2$ whereas 20 mls of 5% ethanol were without effect. It was concluded that ethanol can suppress gastric secretion of thromboxane $B_2$ psychosis.*

## INTRODUCTION

Ethanol has been found to be a cause of acute gastritis and gastric erosions,[1, 2] and chronic gastritis in man.[3,4,5,6] Studies of the rate of gastric DNA loss has shown that alcohol increases gastric epithelial cell loss[7] and affects the gastric mucosal barrier by reducing transmucosal permeability to hydrogen and potassium ions.[8,9,10]

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Several natural prostaglandins and their synthetic analogues have been shown to have marked effects on gastric function.[11] Prostaglandin $E_2$ and its 15(R) 15 methyl analogue have been shown to be effective in the promotion of gastric ulcer healing.[12–16] Furthermore, several prostaglandins of the A,E,F and I types, either orally or subcutaneously have been effective in preventing gastric mucosal necrosis induced by ethanol in rats.[17] To test the hypothesis that ethanol may have an effect on gastric synthesis of thromboxane $A_2$, we have studied the effects of ethanol administration on thromboxane $B_2$ $TXB_2$ secretion into gastric juice

## MATERIALS AND METHOD

Male volunteers presenting with dyspepsia or peptic ulcer symptoms and between 16 to 70 years old were studied. Only alcohol drinkers were included. Panendoscopy and gastric biopsy were done in all cases prior to the study to determine the pathological changes in the gastric mucosa. Subjects were instructed to cease alcohol, ulcerogenic drugs like salicylates or indomethacin, gastric therapeutic drugs like cimetidine or antacids, and smoking, for at least three days before the test. On the day of study, each subject fasted for six to seven hours, after which a nasogastric tube (Salem) was inserted. The residual gastric juice was aspirated and discarded. Gastric juice samples were collected by continuous suction and after a half-hour basal collection, a single dose of 20 mls of ethanol (5% or

15%) in distilled water was instilled into the stomach via the nasogastric tube. Control subjects were given 20 mls of water instead of alcohol solution. Subsequently two half-hour post-basal samples were collected in all subjects. The gastric juice samples were immediately brought to the laboratory and frozen at -70°C until analysed for $TXB_2$. Titrable acidity was determined in each gastric juice sample, using an automatic titrator and pH meter (Radiometer, Copenhagen).

## Radioimmunoassay of Thromboxane $B_2$

The procedure for the estimation of $TXB_2$ is based on the method of Salmon.[18] In brief, 3H $TXB_2$ was added for the calculation of recovery. Samples were then acidified and extracted with acetone/chloroform and subjected to thin layer chromatography which removed substances interfering with immunoassay of $TXB_2$. The zone corresponding to $TXB_2$ was removed and extracted with MeOH. The MeOH extract was dried, reconstituted in buffer and subjected to radioimmunoassay using $^{125}$I-histamine labelled $TXB_2$. The antibody to $TXB_2$ (from ONO Pharmaceutical Co. Japan) showed low cross reactivity against $PGE_2$, $PGF_{2\alpha}$, 6-keto $PGF_{1\alpha}$ and 6, 15-Diketo $PGF_{1\alpha}$. Each sample was analysed in duplicate. The sensitivity of the assay is 60pg/ml of gastric juice.

## RESULTS

There were six control subjects, eight given 5% alcohol and seven given 15% alcohol. Mean ages were 51, 47 and 44 years respectively. At gastric biopsy chronic gastritis was present in all subjects in the control and 15% alcohol groups, and in seven out of the eight subjects in the 5% alcohol group. Individual values of $TXB_2$ in gastric juice are shown in Fig. 1. The mean (±SD) $TXB_2$ output in the basal and post-basal gastric juice samples of the control group were 65.5 (±105.7), 51.4 (±59.6) and 49.0 (±55.2) ng/30 mins, respectively. The mean (±SD) $TXB_2$ output in the basal and post-alcohol gastric juice samples of the 5% alcohol group were 23.8 (±28.0), 25.3 (±34.2) and 19.3 (±17.1) ng/30 mins, respectively. Analysis by the paired t test showed that the post-basal or post-alcohol $TXB_2$ outputs were not significantly different from basal in these two groups ($p > 0.2$). The mean (±SD) $TXB_2$ outputs in the basal and post-alcohol samples of the 15% alcohol group were 18.6 (±11.4), 11.6 (±7.5) and 18.4 (±13.2) ng/30 mins, respectively. Analysis by paired t test showed that the first post-alcohol $TXB_2$ outputs of the 15% alcohol group were significantly lower than basal, with six of seven of the subjects showing a reduction over this period of time ($p < 0.01$). The percentage changes of post-basal $TXB_2$ outputs from basal values in the two alcohol groups were compared to the control group by the Wilcoxon Rank Sum test and again showed a significant decrease for the first alcohol sample of the 15% ethanol group ($p < 0.05$). No significant change was seen in the 5% alcohol group. Analysis of acid outputs in all the gastric juice samples showed no significant difference between post-basal or post-alcohol values and basal, in all three groups ($p > 0.2$).

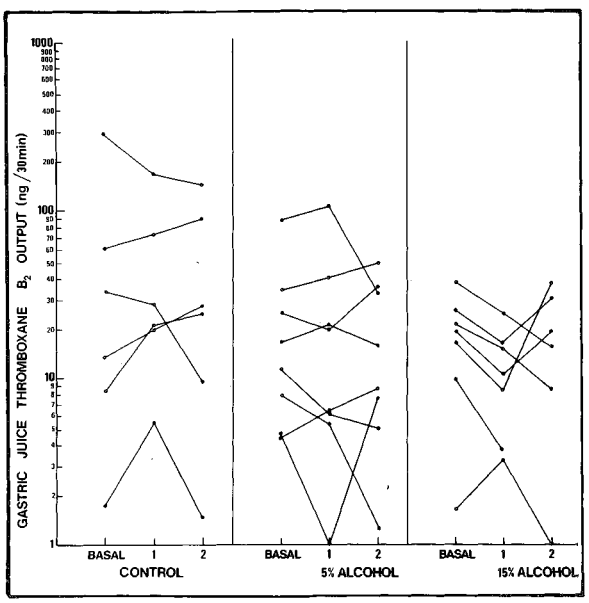


**Fig. 1 Basal and post-basal or post-alcohol gastric thromboxane $B_2$ outputs in the control, 5% alcohol and 15% alcohol groups. The $TXB_2$ outputs of the first post-alcohol samples in the group given 15% alcohol were significantly lower than basal levels. This change was significantly different from the control group.**

## DISCUSSION

$TXB_2$ has been shown to be synthesised by the gastric mucosa of the dog[19] and the rat.[20] Little is known about the physiological role of its immediate precursor thromboxane $A_2$[21] in the stomach, except that Whittle *et al.*, have shown that endogenous formation of $TXB_2$ in the gastric artery of dogs produces strong vasoconstriction and aggravates the effects of acidified taurocholate on the gastric mucosal barrier.[22] More recently, Konturek *et al.*, have reported that selective inhibition of thromboxane biosynthesis by OKY-1581 can prevent taurocholate-induced gastric necrosis but not ethanol-induced gastric necrosis.[23] Of great interest was their finding that gastric necrosis was reduced by 80% when 20% ethanol was administered prior to the administration of 100% ethanol.[23] Our present finding that 15% ethanol significantly inhibits gastric secretion of $TXB_2$ suggests that the protective effect of 20% ethanol reported by Konturek *et al.*, may be closely associated with secretory inhibition of $TXB_2$ by ethanol solutions of 15 – 20%.

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