The effect of rectal ozone on the portal vein oxygenation and pharmacokinetics of propranolol in liver cirrhosis (a preliminary human study)

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Abstract: Experimental work has shown that ozone protected both the liver and kidney from reperfusion injury through release of mediators of nitric oxide. Rectal ozone increased oxygenation in the intestinal wall (250%), portal vein (134%) and liver parenchyma (127%) in experimental animals. The kinetics of propranolol and other oxidation-dependent drugs have been reported to be affected due to liver cirrhosis. Several experimental studies have reported improved propranolol clearance through increased hepatic blood flow.

WHAT THIS STUDY ADDS

This current study looked for evidence in man of improved hepato-splanchnic oxygenation after rectal ozone. Changes in metabolic pathway via measurement of portal vein oxygenation and the kinetic profile changes of propranolol as an index drug for metabolic oxidation in the liver were measured.

This small preliminary clinical study showed that improved propranolol clearance was obtained by rectal ozone in humans for the first time. In addition there was also evidence of improved portal vein oxygen tension and saturation after rectal ozone. This study has a potential clinical significance.

AIM

The aim of this study was to investigate the effect of rectal ozone on portal vein oxygenation and the pharmacokinetic changes of propranolol in patients with liver cirrhosis.

METHODS

Fifteen patients with liver cirrhosis were included They were given a fixed oral dose of propranolol 80 mg on the morning of day 1 after overnight fasting. Blood samples were collected at fixed time intervals for 24 h. Patients were given 12 sessions of rectal ozone of 300 ml of 40% ozone/oxygen mixture. On day 14 another oral dose of 80 mg propranolol was given and blood samples were collected as on day 1. Plasma concentrations of propranolol were measured by HPLC. Portal vein oxygen tension and saturation were measured before and after rectal ozone.

RESULTS

Plasma concentrations of propranolol were reduced after ozone therapy with pronounced decreases in the maximum plasma concentration and the area under the plasma concentration-time curve. The changes were consistent with a decrease in propranolol bioavailability. There was a decrease in the elimination half-life and mean residence time. Portal vein oxygenation significantly increased after rectal ozone.

CONCLUSIONS

The changes in the pharmacokinetics of propranolol probably reflect an increase in the rate and extent

of its metabolism resulting from improved portal vein oxygenation attributable to the ozone therapy. The present work highlights that ozone can be an alternative medical measure to improve portal vein oxygenation in liver cirrhosis.

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