Effect of spinal anaesthesia on plasma concentrations of glutathione S-transferase

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Background. Plasma glutathione S-transferase (GST) concentration measurement is a sensitive and specific index of hepatocellular injury. GST concentration increases after anaesthesia with most volatile anaesthetic agents, but not after propofol. Such increases are thought to result from reduced liver blood flow. The effect on GST concentration of spinal (subarachnoid) anaesthesia, which might also reduce liver blood flow, is not known.

Methods. We studied the effects of spinal anaesthesia on GST concentrations measured by specific radioimmunoassay in 33 patients undergoing intermediate orthopaedic, general or gynaecological surgery. GST concentrations were measured before anaesthesia and 3, 6 and 24 h after induction of anaesthesia. Hypotension (systolic blood pressure <70% of pre-induction value) was rapidly corrected with i.v. ephedrine.

Results. Mean duration of surgery was 41 min (range 11–80). No increase in GST concentration was observed at any time, but at 24 h GST concentration was significantly reduced (P<0.05). One patient in whom hypotension was not treated developed a greatly increased GST concentration at 3 h.

Conclusion. We found no association between spinal anaesthesia and disturbance of hepatocellular integrity when hypotension does not occur or is rapidly corrected.


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Subclinical hepatic injury after anaesthesia continues to provoke interest, particularly with newer, more sensitive methods of assessment such as measurement of plasma glutathione S-transferase (GST) concentration. GST is rapidly released into the circulation after hepatic damage and its short plasma half-life (<90 min) allows early detection of hepatic injury and its resolution. Using such assessment, various workers have shown minor disturbances of hepatocellular integrity after anaesthesia with halothane, enflurane, sevoflurane and desflurane but not propofol. Isoflurane anaesthesia has been shown by several workers to have no effect on plasma GST concentration but this has been contested. Reduced liver blood flow is believed to be responsible for the observed increases in GST concentration after anaesthesia. Spinal (subarachnoid) anaesthesia may also reduce liver blood flow but it is not known whether spinal anaesthesia may induce subclinical hepatic injury. We have therefore assessed the effect of spinal anaesthesia on hepatocellular integrity using a well-validated technique for measurement of plasma GST concentration.

**Methods and results**

After obtaining approval from the local ethics committee, written informed consent was obtained from 34 randomly selected adult patients (ASA I or II) who were to have intermediate orthopaedic, general or gynaecological surgery which was expected to last 30–120 min. Exclusion criteria included previous liver disease, general anaesthesia within the preceding 3 months, contraindications to spinal anaesthesia, alcohol intake >3 u day−1 and body weight >20% above ideal weight. Patients receiving medications likely to interfere with liver function were also excluded.

Premedication was with an oral benzodiazepine 1 h before surgery. Spinal anaesthesia was induced in the lateral position at the L3/4 interspace, using either 2% lidocaine, 0.5% bupivacaine or 0.5% bupivacaine in 8% dextrose (‘heavy’ bupivacaine) as indicated clinically. Midazolam was given intravenously for sedation if required. Patients received i.v. Ringer lactate solution 500–1000 ml during surgery. Arterial pressure was measured every 5 min throughout anaesthesia; heart rate and oxygen saturation were monitored continuously. Hypotension, defined as systolic blood pressure <70% of pre-induction value for >5 min, was corrected with i.v. ephedrine.

Blood was sampled into heparin tubes immediately before induction of anaesthesia and 3, 6 and 24 h later for measurement of plasma GST B1 concentration (or α class GST) by specific radioimmunoassay. The reference range for GST B1 concentration is 0.5–4.8 μg litre−1.

Data were analysed by Friedman’s test for repeated measurements. The Wilcoxon signed rank test was used to examine changes in GST concentration from before anaesthesia to 3, 6 and 24 h after induction of anaesthesia. Analysis was performed with Minitab for Windows (version 12).

Of the 34 patients studied, one was excluded from analysis because of lost samples. Data from the remaining 33 (18 male; mean age 57 (range 22–81) yr) were analysed. This sample size gave the study a power of 78% for a change in GST concentration >0.7 μg litre−1. Sixteen patients had orthopaedic surgery such as knee arthroscopy, tendon repair or fixation of lower limb fractures; 12 patients had general surgical procedures such as inguinal hernia repair or haemorrhoidectomy, and the remaining five patients had pelvic floor repair. Mean duration of surgery was 41 (range 11–80) min. Five patients received 2% lidocaine (mean 3.75 ml), 10 received 0.5% plain bupivacaine (mean 3.25 ml) and 18 received 0.5% ‘heavy’ bupivacaine (mean 3.04 ml). Twenty-one patients received midazolam (mean dose 4.4 (range 2–10) mg).

Median (interquartile range) GST concentrations (μg litre−1) were: before anaesthesia, 2.25 (1.7, 2.9); 3 h, 2.1 (1.8, 3.4); 6 h, 2.0 (1.5, 3.85); 24 h, 1.8 (1.4, 2.95). Significant temporal changes in GST concentration occurred after anaesthesia (P<0.05). No increase in GST concentration was observed, but at 24 h GST concentration was significantly less than that found before anaesthesia (Fig. 1). Three patients (9%) developed GST concentrations >4.8 μg litre−1 during the study period; one patient had a greatly increased (more than twice the upper limit of the reference range) GST concentration at 24 h. Three patients had GST concentration >4.8 μg litre−1 in blood samples obtained before anaesthesia. The mean maximum (range) reduction in systolic blood pressure during spinal anaesthesia was 27 (0–57)%.

Seven patients required correction of hypotension with i.v. ephedrine (total dose 6–12 mg). Two of these patients had received 2% lidocaine, one had received 0.5% plain bupivacaine and four had received 0.5% ‘heavy’ bupivacaine. One further patient developed hypotension (52% reduction in systolic blood pressure)
which inadvertently was not corrected with ephedrine; GST concentration increased greatly at 3 h in this patient (7.2 µg litre\(^{-1}\) compared with 1.8 µg litre\(^{-1}\) before anaesthesia). Overall changes in GST concentration were not related to hypotension, type of local analgesia used for spinal anaesthesia or administration of midazolam.

**Comment**

We have shown that plasma GST B\(_1\) concentration does not increase after spinal anaesthesia. In contrast, GST concentration is known to increase after anaesthesia with halothane, enflurane, sevoflurane\(^1\) and desflurane.\(^2\) Such increases are thought to result from a reduction in hepatic blood flow. The lack of change in GST concentration in the present study appears to agree with the known effects of spinal anaesthesia on liver blood flow. Liver blood flow is reduced in spinal anaesthesia but this is related to systemic hypotension.\(^4\) If hypotension does not occur,\(^6\) or if it is corrected with ephedrine,\(^7\) liver blood flow is not reduced. Seven patients in our study developed hypotension which was rapidly corrected with administration of ephedrine. GST concentrations did not increase in these patients suggesting that liver blood flow was maintained. One further patient developed hypotension which was not corrected. The large increase in GST concentration observed at 3 h in this patient suggests that liver blood flow was significantly reduced. As hypotension did not occur in the remaining 26 patients it is unlikely that liver blood flow was adversely affected and hence why increased GST concentrations were not observed. The finding that GST concentrations at 24 h were significantly lower than before anaesthesia is thought to reflect changes in hydration status.\(^8\) A similar explanation may account for the finding of increased GST concentrations in three patients before anaesthesia.\(^9\) The mechanism of the secondary increases in GST concentration observed at 24 h is not known. In conclusion, the findings from this study suggest that disturbance of hepatocellular function does not occur after spinal anaesthesia when hypotension does not occur or is rapidly corrected with ephedrine.

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**References**