Comparison of urethane/chloralose and pentobarbitone anaesthesia for examining effects of bacterial lipopolysaccharide in mice

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ABSTRACT

Although anaesthetics are widely used to alleviate stress in endotoxaemic animals, these drugs themselves may interfere with the effects of lipopolysaccharide (LPS). The effects of LPS on serum glucose, biochemical markers of hepatic, renal and pancreatic exocrine function, and lung myeloperoxidase (MPO) activity were compared using anaesthesia with either urethane/chloralose or pentobarbitone. Groups of 10–13 of C57B1/6 mice (22.3 ± 0.18 g) were treated with 40 mg/kg LPS or the same volume of saline (10 mL/kg, i.p.) at time 0. Animals were anaesthetized either with urethane (1000 mg/kg) and chloralose (50 mg/kg) or with pentobarbitone (90 mg/kg, i.p.) after 2 h and blood and lung samples obtained after 6 h. In pentobarbitone-anaesthetized mice, LPS caused hypoglycaemia and increased serum levels of alanine aminotransferase (ALT), lipase and creatinine suggesting damage/dysfunction of liver, exocrine pancreas and kidney respectively. Lung tissue MPO activity, an indicator of neutrophil infiltration, was also increased. Urethane/chloralose-treated mice demonstrated hypoglycaemia and enhanced serum levels of ALT and creatinine in response to LPS, but failed to show LPS-induced increases in serum lipase and lung MPO activity. It is concluded that while pentobarbitone may be successfully used in experimental models of endotoxaemia in mice, anaesthesia with urethane and chloralose may protect mice against LPS-mediated damage/dysfunction in the exocrine pancreas and in the lung, and therefore, is not recommended in studies on endotoxaemic mice.

INTRODUCTION

Lipopolysaccharide (LPS), a cell wall component of Gram-negative bacteria, plays a pivotal role in the pathogenesis of sepsis which is a major cause of mortality in humans. LPS is involved in the sepsis-induced complications such as disseminated intravascular coagulation, systemic vascular collapse, vascular leak syndromes and multiorgan failure [1]. Research on septic shock in experimental animals is subject to ethical as well as legal constraints in many countries, because of the marked stress associated with endotoxin-induced shock. Anaesthesia may circumvent these problems, but anaesthetics themselves may influence the effects of LPS [2,3]. Urethane has been widely used as an anaesthetic in laboratory animals alone or together with chloralose. It causes long-lasting unconsciousness of 8–10 h duration with minimal effects on autonomic, cardiovascular and respiratory systems [4,5]. However, urethane may not be suitable for some studies because of its endocrine and renal effects [5]. Alpha-chloralose is similar to urethane in inducing long-term anaesthesia and maintaining cardiovascular and autonomic reflexes [6,7]. However, it should not be used as the sole anaesthetic...