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Research article

A new rat model of neonatal bilirubin encephalopathy (kernicterus)

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Nitric acid (PubChem CID: 944)
Methanol (PubChem CID: 887)
Sucrose (PubChem CID: 5988)
Tris (PubChem CID: 6503)
Hydrogen peroxide (PubChem CID: 784)
Paraformaldehyde (PubChem CID: 712)
Xylitol (PubChem CID: 6912)
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ABSTRACT

Introduction: Hemolytic kernicterus, an indirect bilirubin-induced brain dysfunction, is associated with hyperbilirubinemia in mammalian neonates. In this study, a new model of kernicterus has been developed using intra-peritoneal injections of phenyl hydrazine and subcutaneous injections of sulfisoxazole. These drugs can potentially induce kernicterus in neonatal through changes in hemolysis and hypo-albumin.
Methods: For this purpose, 7-day-old male Wistar rats ($n = 72$; mean weight 11 ± 1 g) were used. The animals have been divided into six different groups which received the drugs alone and their combination, and the drugs' solvents and their combination. Biochemical parameters, brain iron and bilirubin, behavioural performance, auditory function and apoptosis were measured using auto-analyser instruments; atomic absorption spectroscopy, Sawasaki, footprint, auditory brainstem response (ABR) and TUNEL test, respectively.
Result: The drug-injected groups showed a significant reduction in serum haematocrit and an increase in the concentration of brain bilirubin, total and indirect bilirubin as well as TUNEL positive cells in basal ganglia. In addition, the obtained results showed that there was a significant increase in behavioural disturbance and auditory dysfunction in the group injected with the combination of two drugs.
Conclusion: This kernicterus-induced rat model could perfectly mimic the common conditions of the hyperbilirubinemia in human neonates. This study offers an easy technique to develop more stable models for follow-up studies.

1. Introduction

Kernicterus, a bilirubin-induced brain dysfunction, is associated with hyperbilirubinemia in mammalian neonates. Accumulation of indirect bilirubin (IB)[1] in brain regions particularly the basal ganglia, cerebellum, brain stem nuclei, and cochlear nucleus causes irreversible neurological damages in neonates (Shapiro, 2003). The clinical features of kernicterus include neurological impairments such as motor-development delay, hearing loss, epilepsy, cerebral palsy, mental retardation, lethargy, and poor nutrition. Since no specific therapeutic strategy exists

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[1] IB (indirect bilirubin): indirect or non-conjugated bilirubin that cannot be excreted from the blood and according to previous studies, increase of this factor in the blood is the main cause of kernicterus.

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