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Key passages

Comparison of treatment effects between animal experiments and clinical trials: systematic review

Pablo Perel¹, Ian Roberts¹, Emily Sena², Philipa Wheble², Catherine Briscoe², Peter Sandercock², Malcolm Macleod², Luciano E Mignini³, Pradeep Jayaram⁴, Khalid S Khan⁴

EDITORIAL by Hackam

¹Crash Trials Coordinating Centre, London School of Hygiene and Tropical Medicine, London WC1E 7HT

²Clinical Neurosciences, University of Edinburgh

³Centro Rosarino de Estudios Perinatales, WHO Collaborative Centre in Maternal and Child Health, Rosario 2000, Argentina

⁴Division of Reproductive and Child Health, Birmingham Women's Hospital, University of Birmingham

Correspondence to: P Perel
pablo.perel@lshtm.ac.uk

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ABSTRACT

Objective To examine concordance between treatment effects in animal experiments and clinical trials.

Study design Systematic review.

Data sources Medline, Embase, SIGLE, NTIS, Science Citation Index, CAB, BIOSIS.

Study selection Animal studies for interventions with unambiguous evidence of a treatment effect (benefit or harm) in clinical trials: head injury, antifibrinolytics in haemorrhage, thrombolysis in acute ischaemic stroke, tirilazad in acute ischaemic stroke, antenatal corticosteroids to prevent neonatal respiratory distress syndrome, and bisphosphonates in the prevention and treatment of osteoporosis.

Review methods Data were extracted on study design, allocation concealment, number of randomised animals, type of model, intervention, and outcome.

Results Corticosteroids did not show any benefit in clinical trials of treatment for head injury but did show a benefit in animal models (pooled odds ratio for adverse functional outcome 0.58, 95% confidence interval 0.41 to 0.83). Antifibrinolytics reduced bleeding in clinical trials but the data were inconclusive in animal models. Thrombolysis improved outcome in patients with ischaemic stroke. In animal models, tissue plasminogen activator reduced infarct volume by 24% (95% confidence interval 20% to 28%) and improved neurobehavioural scores by 23% (17% to 29%). Tirilazad was associated with a worse outcome in patients with ischaemic stroke. In animal models, tirilazad reduced infarct volume by 29% (21% to 37%) and improved neurobehavioural scores by 48% (29% to 67%). Antenatal corticosteroids reduced respiratory distress and mortality in neonates whereas in animal models respiratory distress was reduced but the effect on mortality was inconclusive (odds ratio 4.2, 95% confidence interval 0.85 to 20.9). Bisphosphonates increased bone mineral density in patients with osteoporosis. In animal models the bisphosphonate alendronate increased bone mineral density compared with placebo by 11.0% (95% confidence interval 9.2% to 12.9%) in the combined results for the hip region. The corresponding treatment effect in the lumbar spine was 8.5% (5.8% to 11.2%) and in the combined results for the forearms (baboons only) was 1.7% (-1.4% to 4.7%).

Conclusions Discordance between animal and human studies may be due to bias or to the failure of animal models to mimic clinical disease adequately.

