Treatment of hyperglycaemia in acute stroke: results from the Trial of Exenatide in Acute Ischaemic Stroke (TEXAIS) study

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for the TEXAIS investigators.
Post stroke hyperglycaemia (PSH)

Common in acute stroke:

- **On admission**: PSH in 20-50%, 70% in those with diabetes.
- **In hospital**: 30% patients with normal blood glucose on admission - PSH within 48 hours.
  - increased final infarct size; increased sICH.
  - reduced efficacy of thrombolysis and thrombectomy.

Stroke insulin therapy:

- **Variable onset and duration**: start 8 - 15 hours; finish 24 hours - 5 days.
- **Insulin induced hypoglycaemia**: up to 70% of patients, may require dextrose rescue therapy.
- **Resource load**: requires staff training; limited feasibility outside specialty settings (ICU etc…).
- **Clinical outcomes**: no benefit - increased mortality, possibly worse long-term disability.
Phase 2, multi centre, prospective, randomised, open label, blinded end-point (PROBE) trial

\[ n = 528 \text{ patients} \]

**Primary Hypothesis:** Improved neurological outcome: ≥8 point improvement in NIHSS (NIHSS 0-1) at 7 days (or time of discharge).

**Secondary Hypotheses:**
1. reduce the occurrence of post stroke hyperglycaemia (>7mmol/l)
2. improve NIHSS at 90-days
3. improve Modified Rankin Scale (mRS) at 90-days

**TEXAIS Study Design**

Exenatide vs. Standard Care:

5μg subcutaneous injection bd for 5 days - first dose within 9 hours of stroke onset.

- prophylactic anti-emetic treatment (eg. metoclopramide or ondansetron) for 48 hours, then as needed.
- *diabetes patients already on oral agents and/or insulin may continue these in addition to exenatide.*
Treatment with Exenatide did not result in a significant reduction in neurological disability at 7 days in patients with AIS. [96 (56.5%) vs 80 (58.8%)  aOR:1.11 (0.70, 1.77)  p=0.65]

- **Phase 2 trial, with limited power to detect a biological signal**
- Exenatide significantly reduced frequency of hyperglycaemic events
  - no hypoglycaemia, no insulin rescue therapy
- Exenatide was simple and safe to use.
  - subcutaneous auto-injection, no hypoglycaemia, minimal GI adverse events
- TEXAIS results warrant a larger Phase 3 trial.
  - different strata: LVO patients; higher dose Exenatide; imaging analysis