

Gastroprotective Effects Of Effervescent Alendronate Formulation Shown By Scintigraphic and Gastric pH Monitoring

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Purpose.

This study evaluated gastric emptying and gastric pH after administration of Fosamax® tablets, a novel effervescent alendronate (ALN) formulation (EX101) and an effervescent ALN comparator. EX101 was designed to reduce the dosing restrictions and GI side effects of ALN.

Methods.

This was a single centre, open label, randomised, three-way crossover study in twelve fasted healthy female volunteers. pH probes were inserted via the nasogastric route to monitor pH from 2 hours pre-dosing. Fosamax® 70mg tablets were radiolabelled with 4MBq [^{99m}Tc]-DTPA at time of dose using a drill and fill procedure and were administered with 240ml water. Effervescent EX101 and a comparator, both with 70mg ALN, were administered in 100ml radiolabelled water (4MBq [^{99m}Tc]-DTPA at time of dose). Scintigraphy was performed immediately after dosing and then every 5 minutes until complete gastric emptying was observed. pH was monitored until 4 hours post-dose.

Results.

The solutions and tablet rapidly entered the stomach after ingestion. There was considerable variability in gastric emptying after ingestion of all three formulations, and no clear trend was observed across the treatments. Mean pH at gastric emptying T_{50%} was significantly higher in EX101-treated subjects compared to those treated with Fosamax® (3.5±1.3h vs 1.9±0.5h; p=0.008). At T_{90%}, the mean pH values were comparable over the three treatments.

Conclusion.

There were no statistically significant or physiologically relevant differences in gastric emptying time between Fosamax® and the effervescent formulations. Mucosal exposure to bisphosphonates at pH less than 3 is irritating to oesophageal tissue, but is benign at pH above 3. There were highly significant differences between the effervescent formulations and Fosamax® in terms of gastroprotection. Fosamax® provided no pH protective effects, while EX101 was superior in providing pH protection.

Ingestion of Fosamax® resulted in ALN being present in the stomach at a pH below 3 within minutes of dosing. EX101 minimised the possibility of exposing the stomach and oesophageal mucosa (in case of reflux) to acidified ALN, for in no subject were the stomach contents below pH 3 during the crucial 30 minute post-dose fasting period.