



Arrhythmias

INFLUENCE OF ZOLEDRONIC ACID ON ATRIAL ELECTROPHYSIOLOGICAL PARAMETERS ASSOCIATED WITH RISK OF ATRIAL FIBRILLATION

Poster Contributions

Poster Sessions, Expo North

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Background: Bisphosphonates have been associated with an increased risk of serious atrial fibrillation (AF). We determined the effects of zoledronic acid (ZA) on atrial measures associated with AF.

Methods: Ex vivo study: Hearts from Dunkin-Hartley (D-H) guinea pigs (n=12) were excised and randomized to perfusion with modified Krebs-Henseleit (K-H) buffer and ZA 0.07 mg/kg or K-H without ZA. Left atrial monophasic action potentials (MAPs) were recorded at 240 bpm for 20 minutes.

In vivo chronic ZA: D-H guinea pigs (n=32) were randomized to intraperitoneal injections every 2 weeks in one of 4 groups: ZA 0.007 mg/kg (low), ZA 0.07 mg/kg (therapeutic), ZA 0.7 mg/kg (high dose), or placebo. Hearts were excised at 8 weeks and perfused with modified K-H. Left atrial MAPs and effective refractory periods (ERP) were measured.

Results: Ex vivo study: ZA-perfused hearts showed a decrease from baseline in atrial action potential duration at 90% repolarization (APD90) vs controls (-23.2% ± 5.1% vs -2.1% ± 9.1%, p < 0.0001) and APD30 (-18.8% ± 4.9% vs -1.9% ± 8.7%, p < 0.0001).

In vivo chronic ZA: Atrial ERP and APD30 were decreased by ZA (Table; data are mean ± SD). There were significant differences in ERP between placebo and therapeutic dose groups and between placebo and high dose groups. There were significant differences in APD30 between the placebo and high dose group; low and high dose group; and therapeutic and high dose group.

Conclusion: ZA shortens left atrial APD and ERP, which may result in an increased risk of AF.

Effects of ZA on Atrial Electrophysiology

| | Placebo | Low Dose ZA | Therapeutic Dose ZA | High Dose ZA | p |
|------------|--------------|-------------|----------------------|---|---------|
| ERP (ms) | 106.0 ± 15.9 | 94.4 ± 12.4 | 83.1 ± 7.8* | 87.1 ± 10.6* | 0.004 |
| APD90 (ms) | 90.1 ± 13.0 | 90.1 ± 10.4 | 85.4 ± 9.6 | 77.2 ± 9.6 | 0.08 |
| APD30 (ms) | 59.2 ± 6.9 | 62.6 ± 6.4 | 57.2 ± 7.5 | 46.7 ± 6.4*† | <0.0001 |
| | | | *p < 0.05 vs placebo | *p < 0.05 vs placebo †p < 0.05 vs low and therapeutic dose | |