Efficacy of theophylline in patients with syncope without prodromes with normal heart and normal ECG

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Aim. Patients affected by syncope without or with very short (≤5 s) prodrome with normal heart and normal ECG have been shown to present with low plasma adenosine levels. We investigated whether chronic treatment of these patients with theophylline, a non-selective adenosine receptor antagonist, results in clinical benefit.

Methods and Results. In a consecutive case series of 16 patients (mean age 47±25 years, 9 females), who had had ECG documentation of syncope with asystolic pause/s, we compared the incidence of syncopal recurrence during a period without and with a period with tailored theophylline therapy. During the median 60 months before ECG documentation of the index episode, the patients had had a median of 2 syncopes per year (IQR 0.8; 3). During the 6 months of the study phase without therapy, the patients had a median of 2.6 syncopes per year (IQR 1.8; 10.2), p=0.63. During the 23 months of the study phase with theophylline, the patients had a median of 0.4 syncopes per year (IQR 0.0; 1.1), p=0.005 vs history and p=0.005 vs no therapy. In the 13 patients who had an implantable loop recorder during both study phases, the incidence of asystolic episodes >3 s decreased from 9.6 per year (IQR 2; 16) to 1.1 per year (IQR 0.0; 1.7), p=0.0007. During theophylline treatment, syncope recurred in 1/5 (20%) patients who had an idiopathic AV block as index event versus 9/11 (81%) of patients who had a sinus arrest, p=0.005

Conclusion. Theophylline is effective in reducing syncope burden in patients with syncope without prodromes with normal heart and normal ECG. The efficacy is greater in those with idiopathic AV block.
Syncope

Asystole >3 s

Incidence (per year)

History (60 months) | No therapy (6 months) | Theophylline (22 months)
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3 | 10.2 | 1.1
2 | 2.6 | 0.4
0.8 | 1.8 | 1.7

Incidence (per year)

No therapy (6 months) | Theophylline (23 months)
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16 | 1.7
9.6 | 1.1
2 | 2

p=0.005
p=0.005
p=0.0007
NS (p=0.63)