OBSERVATIONAL COMPARISON OF THREE TREATMENT REGIMENS FOR LATE LATENT/UNKNOWN STAGE SYPHILIS

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Background:
CDC guidelines recommend treating latent syphilis of unknown duration (LSUD) with 3 doses of benzathine penicillin (BPG) or 28 days of doxycycline. This recommendation is based on expert opinion, and optimal treatment is uncertain.

Methods:
We conducted a retrospective cohort study to evaluate the association of a two-titer drop in RPR (serological cure) with three treatment regimens: 1 dose of BPG, 3 doses of BPG, and 28 days of doxycycline. Subjects included persons reported with LSUD in King County, Washington, USA, from 2007-2020 with an initial RPR ≥1:2 and any follow-up RPR reported ≤36 months following diagnosis. Analyses used RPR results from public health surveillance. We used chi-squared tests to assess the association of treatment regimen with serological cure, stratifying cases into high (≥1:32) or low (<1:32) initial titer groups, and Cox proportional hazards to compare regimens.

Results:
The study population included 761 cases. Median age was 35, 62% were cisgender MSM, and 38% had HIV. Mean time to cure or most recent RPR was 341 days (SD=295). Of 483 high-titer cases, serological cure occurred in 36 (88%) of 41 cases that received 1 dose of BPG, 330 (88%) of 376 that received 3 doses of BPG, and 58 (88%) of 66 that received doxycycline (p=1.00). Among 278 low-titer cases, 4 (31%) of 13 treated with 1 dose of BPG, 114 (49%) of 235 treated with 3 doses of BPG, and 14 (47%) of 30 treated with doxycycline had serological cure (p=0.458). Controlling for initial RPR, serological cure did not differ significantly between cases receiving 1 and 3 doses of BPG (hazard ratio: 0.87; 95% CI: [0.63, 1.21]).

Conclusion:
Based on serological outcomes, the three regimens were similarly effective in treating high-titer LSUD. Many high-titer LSUD cases are likely early infections treatable with 1 dose of BPG.

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