The inconvenient corollaries of a convenient antiviral regime

Sir,

We read with interest the article by Verma *et al*. entitled "Effectiveness and safety of oral acyclovir 1 g twice a day for 3 days in the management of genital herpes."[1] The authors evaluated a short course, higher dose acyclovir regimen with the rationale that such a regime would be more convenient and cheaper. While the assumption sounds appealing in theory, certain caveats must be considered.

The fundamental shortcoming of employing acyclovir in a twice-daily antiviral regimen is the short half-life of the drug (2–3 h).[2] Further, the oral bioavailability of acyclovir is merely 15%–30% which further reduces with higher dosage.[2] Any treatment regimen must be based on minimal inhibitory concentration levels of the drug and dosage schedules which can achieve this. The rationale of high dose, less frequent dosing is not justifiable for acyclovir. Most abbreviated regimens have employed longer-acting agents such as valaciclovir and famciclovir.[3,4]

The study recruited cases of clinically active genital herpes. Definitive diagnosis of genital herpes requires laboratory confirmation by viral culture, polymerase chain reaction, direct fluorescence antibody, and type-specific serologic tests. Not all of their patients had the diagnosis confirmed by the relevant laboratory tests. While the syndromic approach justifies clinical diagnosis and management of genital herpes, utilization of laboratory investigations for diagnostic precision is an essential requirement for clinical trials.

The primary goals of antiviral therapy in genital herpes are, reducing the duration of symptoms, early healing of lesions, and limiting viral shedding. In the present study, the duration of symptoms before presentation have not been mentioned, and healing time has been measured from the day of initiation of therapy. Healing time of 3 days in 40.9% of patients suggests a longer duration of disease at the time of recruitment. Effective management of recurrent genital herpes requires initiation of therapy at the earliest, preferably within 1 day of appearance of lesions, therapy is not indicated in patients with a longer duration of symptoms unless the disease is extensive or severely symptomatic. As the duration of episode of untreated recurrent herpes varies from 5 to 10 days, the current regimen (with average healing time of 4.9 days) may not have any added benefit over placebo.[5] As far as primary genital herpes is concerned, it is not justified to treat such patients with 3 days of therapy in view of the severe nature of disease, associated viremia, and possible systemic complications; such patients must be treated for 7–10 days with adequate antiviral dosages.[4]

Finally, an evidence-based regimen of acyclovir 800 mg thrice a day for two days[5] is already available as recommended by European guidelines for recurrent herpes,[6] and it is more economical and shorter than the proposed regimen with equal pill burden. Hence, this new treatment schedule does not seem to have any added benefits over the current guidelines for recurrent genital herpes. Due to the lack of sufficient evidence, purpose and logic behind this new schedule, it would be prudent for clinicians to adhere to the regimens recommended in the WHO/CDC/European guidelines.[4,6]

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