Does orally dissolving formulation of clobazam provide clinical advantage over its standard formulation

Sir,

Oral formulation with modified drug delivery is usually designed to address some clinical concern such as difficulty in swallowing or overcome pharmacological limitations of the drug such as improving bioavailability or speeding the onset of action.\(^1\) Orally dissolving tablet has potential to improve onset of action or convenience of administration which in turn may improve patient compliance.\(^2\)

Orally dissolving tablet of clobazam has been recently developed to facilitate drug administration in children.\(^2\) Before knowing whether the new formulation facilitates drug administration in children, one needs to understand whether the drug administration is really a problem.

In a recently published study, clobazam in stable dosage was effective for Lennox–Gastaut syndrome resulting in drop seizure and total seizure improvements consistently for >3 years. This clinical trial included children above 2 years of age and adults up to 60 years of age. Some patients even received treatment up to 6 years.\(^3\) With availability of such long-term efficacy and safety data, compliance does not seem to be a major problem. The innovator’s clobazam tablet is available in the market since close to four decades,\(^4\) and neither major concerns regarding compliance or convenience have been reported regarding oral administration of standard tablet of clobazam or need for orally dissolving tablet has been stressed in the literature. Standard formulation of clobazam has been successfully used in children with different types of epilepsy.\(^5\)

The other objective of preparing orally dissolving formulation of clobazam is to control the epileptic attack in shortest possible time.\(^2\) During the seizure attack, it is highly unlikely that clinician will use orally dissolving tablet. Injection of benzodiazepine becomes the choice in urgent situation to control ongoing seizures.

In regards to the onset of action, clobazam standard formulation also has a fast onset of action.\(^6\) The question whether mouth dissolving tablet provides clinically meaningful faster onset of action compared to standard tablet has to be answered by conducting a comparative clinical trial. Currently, to the best of my knowledge, there are no published clinical trials with orally dissolving formulation of clobazam to show its efficacy and safety in epilepsy patients. Pharmacokinetic study in animal\(^2\) needs to be replicated in human beings because orally dissolving tablet may not be bioequivalent to the conventional oral tablet.\(^3\) Unless bioequivalence study versus innovator’s clobazam tablet and a clinical trial with new formulation in epilepsy patients are conducted, it is difficult to comment on its clinical advantage over standard formulation.

Coming to the facilitation of drug administration in children; orally dissolving tablet needs to be placed on the patient’s tongue. The disintegration time of optimized mouth dissolving formulation of clobazam is 24 (±5) sec.\(^3\) Practical question arises whether the child will be able to keep tablet for 24 sec on his/her tongue? The parents of children with epilepsy have concerns regarding health of children because of the disease. The impact of disease is not just limited to child, but it affects all members of the family.\(^7\) In fact, epilepsy and parent stress have been described as the chicken and the egg dilemma.\(^8\) Usually, mothers are the primary caretakers of children, and it has been shown that mothers of children with epilepsy are at risk of depression.\(^9\) If the child spits given orally dissolving tablet before it is completely disintegrated, it will further add concerns about inadequate dosage or need of readministration of the drug.

Does orally dissolving formulation of clobazam provide a clinical advantage over the standard formulation of clobazam? The answer to this question at the moment is not known. To summarize, a new drug formulation (new drug delivery system) is usually prepared to address certain unmet clinical needs with existing formulation. New drug formulation should overcome the limitations of an existing product, provide a significant clinical advantage over existing option, must be effective and safe and convenient for the use in the targeted population for whom it is designed. A well-designed clinical trial comparing orally disintegrating tablet of clobazam versus standard tablet of clobazam should address these questions.

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Nil.

**Letters to the Editor**

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Conflicts of Interest
There are no conflicts of interest.

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