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STABILITY OF TENECTEPLASE SYRINGES AFTER FRACTIONATION

M.T. GOMEZ SANCHEZ, M. SANCHEZ VALERA, R. GAZQUEZ PEREZ,
A.M. GARCIA AGUILERA, M.G. DÍAZ LÓPEZ, F. SIERRA GARCIA
H.U TORRECÁRDENAS, PHARMACY, ALMERIA, SPAIN

Background

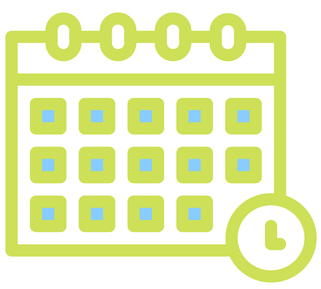
Tenecteplase is a recombinant plasminogen activator protein indicated in adults for the thrombolytic treatment of suspected myocardial infarction within 6 hours of symptom onset. Recently, the Spanish Agency of Medicines and Health Products reported a shortage of tenecteplase. Therefore, a tenecteplase fractionation protocol was developed in our pharmacy service based on a study that analyzed the stability and bioactivity of frozen syringes (-20ºC or -70ºC) for a month, admitting up to 6 freeze/thaw cycles. No studies exploring stability and bioactivity beyond this have been performed.

Objective

To evaluate the physical and chemical stability of frozen syringes of reconstituted tenecteplase over a 2-month period using proton nuclear magnetic resonance (1H-NMR).

Material and Methods

Tenecteplase was reconstituted and fractionated in 5mg/1mL syringes. They were stored at -20°C and evaluated at days 0, 30, 45 and 60. Physical parameters were monitored: turbidity and color. Chemical stability was evaluated by 1H-NMR spectroscopy. The spectroscopic signals were interpreted and assigned to the chemical structure of Tenecteplase and subsequently compared with the spectra at days 30,45 and 60. All spectra were acquired using a Bruker Avance DRX 500 MHz spectrometer.



Results

In terms of physical parameters there appears to be no difference between the syringe at day 0 and at days 30, 45 and 60. Regarding chemical stability, the spectrum resulting from the syringe at day 30 does not show significant differences compared to the reference spectrum. However, when comparing the spectrum of the syringe at day 45 with the reference spectrum, there do appear to be significant changes that call into question the stability and bioactivity of the fractionated reconstituted Tenecteplase. Therefore, the study was stopped and the spectrum at day 60 wasn't compared with the reference spectrum.

Conclusion

This study seems to confirm the stability (physical and chemical) and bioactivity of Tenecteplase syringes frozen at -20ºC for a month. However, it doesn't seem to maintain chemical stability at 45 days, so it is assumed that at 2 months it has no stability.

Junta de Andalucía

TORRECÁRDENAS Hospital Universitario

eahp european association of hospital pharmacists