RECOMMENDATIONS FOR ADMINISTRATION OF IMMUNOSUPPRESSANTS VIA ENTERAL FEEDING TUBE ACCORDING TO THEIR IN-VITRO ADMINISTRATION

AUTHORS

Kristína Lajtmanová[1], Kristína Szmicseková[1], Slávka Porubcová[1' 2]

[1] Hospital Pharmacy, National Institute of Cardiovascular Diseases, Bratislava, Slovakia
[2] Department of Organisation and Management in Pharmacy, Faculty of Pharmacy, Comenius University, Bratislava, Slovakia

BACKGROUND

Immunosuppressants (IS) are used in the treatment and prevention of graft rejection after solid organ or tissue transplantation (1). Their administration via an enteral feeding tube (EFT) is problematic regarding their narrow therapeutic index, cytotoxic, teratogenic potential, and occupational hazard. Incomplete absorption due to incorrect administration via EFT may lead to life-threatening graft rejection (2). Appropriate drug forms of IS for administration via EFT are missing in Slovakia.

AIM AND OBJECTIVES

Despite multiple published guidelines for the administration of medicines via EFT, available drug forms differ between countries. Our aim was to create local guidelines for the safe administration of IS via EFT reflecting the available drug forms in Slovakia, while preventing EFT occlusion and preserving optimal effect of IS.

METHODS

A literature search was aimed to determine a site of absorption of IS, timing according to feeding, measures to decrease the occupational hazard when intact capsules or tablets are crushed, and to optimize the treatment. The practical part consisted of dissolving tablets, capsules' content, and their administration via different types of EFTs of diameters 10, 8, and 6 French. The maximum monitored time for dissolution was 2 minutes due to the practical aspect of the procedure for nurses. The administration of different IS was realized by the adapted protocol by White et al., 2017 (3). A rate of dissolution, a disintegration of tablets, and a potential to occlude EFT was observed.
As the most suitable IS for administration via EFT we have considered the one that dissolved or disintegrated in a closed system and passed by EFT without causing its occlusion.

RESULTS

Table 1: Guidelines for administration of IS via EFT.

ACTIVE SUBSTANCE	MEDICATION	BEFORE ADMINISTERING	TUBE ENDING IN			DIAMETER OF TUBE			OTHER
			STOMACH	DUODENUM	JEJUNUM	10 Fr	8 Fr	6 Fr	
Tacrolimus (immediate release)	GECROL cps dur 1 mg	suspend the content of capsule in the water	✓ (*)	✓ (4)	✓ (4)	✓	✓	✓	stop feeding 1 hour before administration or restart feeding after 2 hours, incompatible with PVC (*), use PPE (2), TDM (3)
	PROGRAF cps dur 1 mg; 5 mg								
	MODIGRAF gru por 0,2 mg; 1 mg	suspend 1 g of tacrolimus in 2 ml of water (*)						✗	
Tacrolimus (prolonged release)	ADVAGRAF cps pld 0,5 mg; 1 mg; 3 mg; 5 mg	do not administer via EFT							
	DAILIPORT cps pld 0,5 mg; 1 mg; 3 mg; 5 mg								
	TACFORIUS cps pld 0,5 mg; 1 mg; 3 mg; 5 mg								
Ciclosporin	CICLOSPORIN MYLAN cps mol 25 mg; 50 mg; 100 mg	do not administer via EFT							
	EQUORAL cps mol 25 mg; 50 mg; 100 mg								
	EQUORAL sol por 100 mg/ml	dilute 1:1 with water (2)	✓ (3, 6)	✓ (6)	✗	✓	✓	✓	administer consistently in relation to feeding, incompatible with PVC (*), use PPE (2), TDM (3)
	SANDIMMUN NEORAL cps mol 25 mg; 50 mg	do not administer via EFT							
	SANDIMMUN NEORAL sol por 100 mg/ml	dilute 1:1 with water (2)	✓ (3, 6)	✓ (6)	✗	✓	✓	✓	administer consistently in relation to feeding, incompatible with PVC (*), use PPE (2), TDM (3)
Mycophenolate sodium	MYFORTIC tbl ent 180 mg; 360 mg	do not administer via EFT							
Mycophenolate mofetil	CELLCEPT cps dur 250 mg	do not administer via EFT							
	CELLCEPT tbl flm 500 mg								
	CELLCEPT plu por 200 mg/ml	administer without dilution (3)	✓ (*)	✓ (4)	✗ (4)	✓ (*)	✓ (*)	✗	administer consistently in relation to feeding, teratogenic potential, contains sorbitol (*)
	MYFENAX tbl flm 500 mg	do not administer via EFT							
	MYKOFENOLÁT MOFETIL SANDOZ tbl flm 500 mg	suspend a tablet in a syringe with 10 ml of water while shaking for 2 min	✓ (3)	✓ (4)	✗ (4)	✓	✓	✗	administer consistently in relation to feeding, teratogenic potential - use PPE (*)
Azathioprine	IMASUP tbl flm 25 mg; 50 mg	do not administer via EFT							
	IMMUNOPRIN tbl flm 100 mg	suspend a tablet in a syringe with 10 ml of water while shaking for 15 s	✓ (3)	possible increased BD ✓ monitor adverse effects (4)	possible increased BD by 67% ✓ monitor adverse effects, adjust dosage (4)	✓	✓	✗	stop feeding 1 hour before administration or restart feeding after 3 hours, teratogenic potential - use PPE (*)
	IMURAN tbl flm 25 mg; 50 mg	suspend a tablet in a syringe with 10 ml of water while shaking for 1,5 min						✓	
Everolimus	CERTICAN tbl 0,25 mg; 0,75 mg	crush tablet	✓ (5)	✗	✗	✓	✓	✓	administer consistently in relation to feeding (*), use PPE, TDM (2)
Sirolimus	RAPAMUNE tbl obd 1 mg	crush tablet	✓ (6)	✓ (4, 6)	✗ (4, 6)	✓	✓	✓	administer consistently in relation to feeding (*), use PPE
Prednisone	PREDNISON tbl 5 mg; 20 mg	crush tablet	✓ (7)	✓ (7)	✓ (7)	✓	✓	✓	administer after feeding (*), use PPE

* according to Summary of Product Characteristics available at www.sukl.sk

abbreviations:
BD – biodisponibility; **cps dur** - hard capsule; **cps mol** – modified-release capsule; **cps pld** – prolonged-release hard capsule; **Fr** - French; **gru por** – granules for oral suspension; **PPE** – personal protective equipment; **PVC** – polyvinylchloride; **sol por** – oral solution; **tbl** – tablet; **tbl ent** – gastro-resistant tablet; **tbl flm** – film coated tablet; **tbl obd** – coated tablet; **TDM** – therapeuric drug monitoring

CONCLUSION

Our recommendations are summarised in Table 1. Only four of the studied tablets disintegrated in a set time. All the other tablets need to be crushed. Crushing IS or opening capsules is not the most appropriate method of administration via EFT, however, those are the only possibilities due to the lack of more appropriate drug forms in Slovakia. If crushing (tablets) or opening (capsules) is necessary, using personal protective equipment is always needed. We observed important differences in disintegration of mycophenolate mofetil and azathioprine tablets of different brands. The occlusion of EFT was observed in EFT of diameter 6 Fr. Not all studied IS can be administered by EFT.

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CONTACTS

PharmDr. Kristína Lajtmanová
kristina.lajtmanova@nusch.sk
Hospital Pharmacy, National Institute of Cardiovascular Diseases, Pod Krásnou hôrkou 1, 833 48 Bratislava, Slovakia

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