Generic mycophenolate mofetil in heart transplant recipients: implementation of active pharmacovigilance

L. Calixto[1], T. Laranjeira[1], A. Mirco[1], M.J. Rebocho[2], F. Falcão[1].
[1] Hospital Pharmacy, [2] Heart Transplant Unit,
Centro Hospitalar Lisboa Ocidental, EPE – Lisboa, Portugal

Centro Hospitalar de Lisboa Ocidental E.P.E.
HOSPITAL DE SANTA CRUZ
18th Congress of eahp european association of hospital pharmacists

Background

Immunossupression drugs have an important role in prophylaxis of transplant rejection, as they are considered "critical dose drugs". Use of a generic immunosuppressant represents a significant cost savings to the medical system. Since safety data for new medicines are always limited, a post-marketing surveillance is essential to determine medicines' safety in real life use. With the introduction of generic Mycophenolate Mofetil (MMF) in CHLO,EPE–HSC, pharmaceutical services (PHS) implemented a MMF active pharmacovigilance program (APP) for heart transplant (HT) recipients.

Purpose

This study aim to describe and quantify suspected adverse drug reactions (ADRs) identified during the APP.

Material and Methods

Between November 2011 and September 2012, all adult HT recipients who switched from innovator to the generic MMF were included in MMF APP. This substitution was made under medical supervision and the pharmacist provided all necessary explanations to patients. Afterwards, pharmaceutical assessment of suspected ADRs was made by applying a questionnaire (personally or by phone). Data collection also included demographic information and concomitant treatment.

Results

Demographics

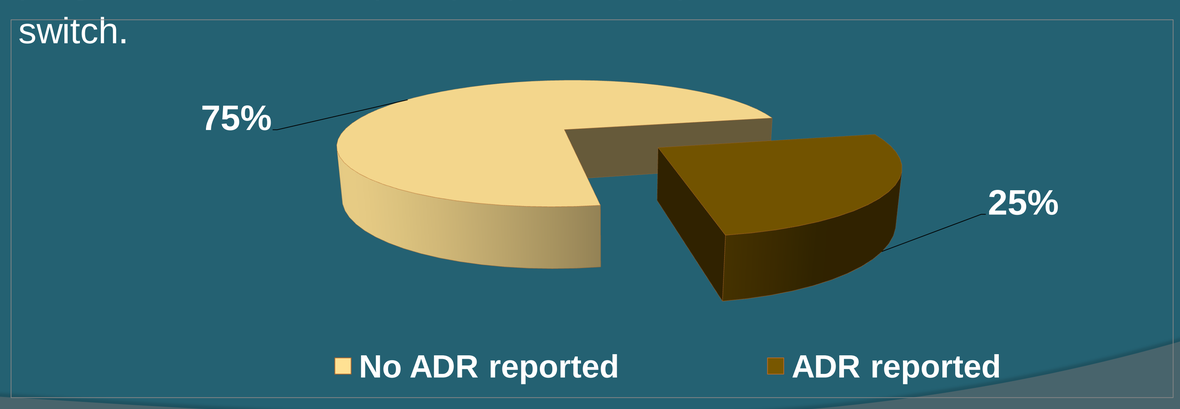
The program included 55 patients who switched from innovator to the generic MMF; 78% were male and the average age was 55 ± 13 years with a range between 22 -76 years.

Patients Number	Gender		
Age(years)	Male	Female	Total
20-29	2	0	2
30-39	1	2	3
40-49	5	1	6
50-59	12	4	16
60-69	18	5	23
70-80	5	0	5
Total	**43**	**12**	**55**

Table 1 – Patients distribution by gender and age.

ADRs Classification

Fifty-five (55) patients were included in MMF active pharmacovigilance program, of which 14 (25%) reported suspected ADRs after MMF switch.



Graphic 1 - Patient distribution by reported ARDs

Results

Twenty-three (23) ADRs were reported, with an average of 1,6 ADRs per patient. All ADRs notifications were reported to the Portuguese National Pharmacovigilance Unit (PNPU) and are sumarized in table 2:

ADR description	ADR %	SPC manifestation	Causality assessment (PNPU)
Diarrhea	22%	D	PR
Asthenia	13%	D	PR/PSB
Stomachache	13%	D	PR
Rash	9%	D	PR
Tachycardia	4%	D	PR
Insomnia	4%	D	PR
Abdominal pain	4%	D	PR
Lower limb oedema	4%	ND	PSB
Constipation	4%	D	PR
Cramps	4%	D	PR
Headaches	4%	D	PR
Lack of appetite	4%	ND	PR
Muscular pain	4%	ND	PSB
Flatulence	4%	D	PR

Table 2 – Characterization of reported ADRs. Legend: SPC - summary of product characteristics; D- Described; ND-Not Described; PR- Probable/likely; PSB- Possible.

The most common ADRs identified were diarrhea (n=5), stomachache (n=3) and asthenia (n=3). Of the reported events, 21% were not described in the SPC and are considered unexpected ADRs. Regarding causality assessment of suspected ADRs by PNPU, 87% were considered "probable" and 13% "possible" according WHO Probability Scale.

From all the patients who reported ADRs, only one patient discontinued generic MMF. After a 2 months period, the innovator drug was again switched to the generic without recurrence of ADRs. At present time, the 55 patients maintain therapy with generic MMF.

Discussion/Conclusion

Most of suspected ADRs identified correspond to MMF´s profile ADRs described in the summary of product characteristics. The switch from innovator to generic drug should be accomplished with a surveillance strategy that includes medical and pharmaceutical monitoring, patient education and the contribution of all healthcare professionals involved in patient care. The pharmacovigilance active program implemented in patients with immunosuppressive regimen allows early detection of adverse drug reactions and safer user of generic drugs.

References

Abajo, Francisco J. de; Improving pharmacovigilance practice beyong spontaneous reporting; WHO Drug Information Vol 18, No. 3, 2004
Comoglio, Raquel Herrera; Pharmacovigilance Update; WHO Drug Information Vol 22, No. 4, 2008
Goldberg, Laurence A; Risk management in pharmacotherapy; HPE, January/February, 2005
Goméz, Ernesto Sánchez et al.; Active pharmacovigilance in a hospital pharmacy department; EJHP Vol 15, 2009/4
Rath, Thomas; Generic Immunosuppressive Drugs in Kidney Transplantation; Transplantation, 2011
Alloway Rita R. et al.; Report of the American Society of Transplantation Conference on Immunosuppressive Drugs and the Use of Generic Immunosuppressants; American Journal of Transplantation; 2003, 3: 1211-1215
European Society for Organ Transplantation Advisory Committee on Generic Substitution of Immunosuppressive Drugs; March, 2011

Contacts: lcalixto@chlo.min-saude.pt ; tlaranjeira@chlo.min-saude.pt

GRP-077