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ANALYSIS OF THE EPIDEMIOLOGICAL PROFILE AND EFFECTIVENESS OF THE USE OF DUAL THERAPY IN HIV PATIENTS AT THE INFECTOLOGY OUTPATIENT OF HOSPITAL SANTA CASA DE MISERICÓRDIA DE VITÓRIA/ES

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Abstract: Objective: The objective of the work is to evaluate the effectiveness of using dual therapy in HIV treatment and the epidemiological profile of patients at the Infectious Diseases Outpatient Clinic of Hospital ``*Santa Casa de Misericórdia de Vitória*``. **Method:** This is an observational, analytical and descriptive study. The initial sample was selected from a list of patients undergoing HIV treatment at the infectious disease outpatient clinic and selection of patients on dual therapy. Information on the epidemiological profile was collected and efficacy was defined by the suppression of the viral load within a period of 6 months to 1 year after the start of dual therapy. **Results:** A total of 120 patients met the study inclusion criteria and 95 remained after the exclusion criteria. 63 patients were using dual therapy with DTG + DRV/r, 26 were using DTG + 3TC and 6 patients were using DRV + 3TC. The main reason for changing therapy was due to toxicity from the triple regimen. The average age of the sample was 60.6 years. Efficacy of dual therapy was achieved in 87 patients (91.6%). **Conclusion:** It is possible to verify the high effectiveness of dual therapy in suppressing viral load, which makes it an appropriate alternative for cases with contraindications or intolerant to the triple regimen.
Keywords: HIV. Dolutegravir. Darunavir.

INTRODUCTION

Despite scientific advances in recent years, the Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) still have an important impact on health systems due to the large number of people affected and their serious consequences when treatment is not carried out properly.

The triple antiretroviral therapy (ART) regimen demonstrated great efficacy and became a reference in the world in 1996 (CAHN et al., 2017). Its standard therapy consists of two nucleoside reverse transcriptase inhibitors (NRTI) associated with another drug: a protease inhibitor with ritonavir booster (PI/r), a non-nucleoside reverse transcriptase inhibitor (NRTI) or an integrase (II). In Brazil, the therapeutic plan is established by the three first-choice medications: Tenofovir (TDF), Lamivudine (3TC) and Dolutegravir (DTG) (BRAZIL,2017).

HIV treatment is currently the subject of countless studies, as every day there are patients who are unable to adhere to the classic therapeutic plan. Although the triple combination has revolutionized antiviral efficacy, its drug composition has limitations in terms of tolerability, toxicity and drug interactions (CAHN et al., 2017). For this reason, research into dual antiretroviral therapy has gained prominence in recent years, as studies indicate that these regimens could reduce long-term toxicity, minimize drug interactions and improve the cost-effectiveness of treatment (VIZCARRA *et al*., 2019).

In view of this, the Ministry of Health (MS) approved in 2019 for patients who already adopt ART, but who have contraindications to the use of tenofovir, abacavir and zidovudine, the use of dual therapy with the following regimens: DTG + 3TC or darunavir with ritonavir booster (DRV/r) + 3TC (when there is a contraindication to DTG) (BRAZIL, 2019). However, to date, few Brazilian data on the use of dual therapy have been found. Furthermore, in order to be comprehensively implemented into medical routine, these schemes must be as effective and safe as the classic therapeutic plan. This work, therefore, will have as main objective to evaluate the effectiveness of using dual therapy in the antiretroviral treatment of patients with HIV/AIDS and the epidemiological profile of patients at the Infectious Diseases Outpatient

Clinic of Hospital Santa Casa de Misericórdia de Vitória (HSCMV), aiming to expand practical knowledge of dual therapy for HIV in Brazil.

METHOD

This is an observational, analytical and descriptive cohort study, with a retrospective and a prospective component, between August 2022 and August 2023. The retrospective component consisted of patients who started dual therapy in the recent past with DTG + 3TC; DRV/r + 3TC or DTG + DRV/r and are or have been using this regimen for at least 6 months. The prospective study consisted of patients who started this type of therapy during the study period.

The initial sample was selected from the analysis of the medical records of patients undergoing HIV treatment at the infectious disease outpatient clinic with selection of patients on dual therapy. HIV-positive patients aged 18 years or over who switched from a three-drug antiretroviral regimen to a double regimen for reasons of toxicity, failure due to poor adherence or for simplification were included. Exclusion criteria were: previous treatment failure with dolutegravir and/or *darunavir/r*; evidence of hepatitis B virus infection at screening (unless treated with entecavir); patients with documented resistance or mutations to drugs included in therapeutic plans and patients with incomplete medical records.

Information was collected from medical records and recorded on data collection forms and patients were followed for a minimum period of 6 months. Patients were identified by codes to protect the confidentiality of their data and authorized by them by signing the Informed Consent Form (TCLE). Patients in the retrospective component, when it was not possible to contact them, are guaranteed complete secrecy and confidentiality of the information obtained from the medical records in relation to their respective identities.

Information was collected such as: gender, age, current dual therapy and the reason for changing therapy. Efficacy was defined as the suppression of viral load (VL), that is, < 40 copies/ml, within a period of six months to one year after starting to use the medication, with no rebound (detectable VL in individuals who had achieved viral suppression under treatment). Therefore, patients who did not meet the aforementioned criteria were characterized as having virological failure. Poor adherence was considered when patients stopped taking medications at some point or used them irregularly. The variables analyzed are described in Appendices A and B.

Categorical variables were analyzed using frequencies and percentages, and numerical variables using data summary measures such as mean, median and standard deviation. The association between qualitative variables was performed using the chi-square test. Associations were considered significant if p-value < 0.05.

The data were tabulated in an EXCEL spreadsheet and analyzed in the program *IBM SPSS Statistics (Statistical Package for the Social Sciences)* version 29. The opinion number of the Research Ethics Committee (CEP) is 5,370,395.

RESULTS AND DISCUSSION

STUDY POPULATION

120 patients met the study inclusion criteria. Of those excluded, 8 patients had previously failed dolutegravir; 4 patients documented resistance or mutations to the drugs included in the therapeutic plans; another 4 had evidence of hepatitis B virus infection while using tenofovir; while 9 patients were excluded from the study due to incomplete medical records. Thus, the efficacy

and epidemiological profile of dual therapy were evaluated in 95 patients, 16 of whom belonged to the prospective group and 79 to the retrospective group. The average age of participants was 60.6 years.

Characteristic	N	%
Women	43	45,3
Male sex	52	54,7
Prior genotyping	6	6,3
Use of Dolutegravir + Darunavir/ ritonavir	63	66,3
Use of Dolutegravir + Lamivudine	26	27,4
Use of Darunavir + Lamivudine	6	6,3

Table 1: Profile of patients on dual therapy and clinical characteristics

Source: Prepared by the authors (2023).

Reason for exchange	N	%
Toxicity to the previous scheme	83	87,4
Poor adhesion	7	7,4
Simplification	3	3,2
Toxicity and simplification	2	2,1

Table 2: Reasons for introducing dual therapy

Source: Prepared by the authors (2023).

The results demonstrated no difference in effectiveness in relation to the data analyzed in the epidemiological profile; Similar results were found in male or female, adult or elderly patients. The utmost importance of epidemiological analysis is emphasized, since knowing patients who use dual therapy on a daily basis enables health professionals to identify prevalent groups, guiding the continuous improvement of therapy, personalizing treatment according to the individuality of patients, and this way, optimizing results in HIV treatment.

EFFICACY

Of the 95 patients included in the study, 87 (91.6%) achieved a sustained virological response after starting dual therapy, demonstrating that dual therapy was effective in virological suppression (p-value 0.000). The viral load was undetectable in 81 patients (85.3%) after 6 months (p-value 0.001), while at the end of 1 year of using the therapy, only 8 patients (10.1%) remained with the viral load detectable (p-value 0.000).

These findings corroborate previous studies that found promising results with the dual therapy approach, such as the "TANGO 2020" study in which an efficacy of 93.2% was verified at week 48 and 85.9% at week 144, in treatment with Dolutegravir + Lamivudine in fixed doses. In the "SALSA 2021" study, an efficacy of 94.3% was found in the treatment with Dolutegravir + Lamivudine and 92.7% in the gold standard treatment with triple therapy, both at week 48. While in the "DOLAM 2021" study, an efficacy of 93.1% in treatment with Dolutegravir + Lamivudine and 93.3% in the gold standard treatment with triple therapy, both at week 48 and in the "DUALIS 2020" study an efficacy of 86.3% was found in treatment with Dolutegravir + Darunavir.

In the total sample, only 8 patients reported non-adherence to dual therapy. Among the reasons were described: Depressive disorder (3.2%); Dementia syndrome (1.1%), and in 3 patients (3.2%) the reason for non-adherence was not clearly described in the patients' records.

It is worth noting that among the 7 patients who did not adequately adhere to dual therapy, 3 patients had a similar record of non-adherence to previous triple therapy. It is important to emphasize that the appropriate selection of antiretroviral agents used in dual therapy as well as the patient's commitment and adherence to treatment are essential to

guarantee effectiveness.

Logistic regression analysis showed a significant association between dual pre-therapy viral load and antiretroviral treatment efficacy ($p < 0.001$). Patients with a lower viral load (< 40 copies/ml) before the start of dual therapy were more likely to achieve virological suppression, which could result from the fact that previously adherent patients maintained the adherence profile after the start of dual therapy, while patients with poor prior adherence, by maintaining a poor adherence pattern, would end up compromising the effectiveness of dual therapy. Some clinical trials have demonstrated that dual therapy remains effective even in patients with high viral loads (100,000 to 500,000 copies/mL) (ZAMORA et al., 2019). Furthermore, studies have shown that a shorter period of viral suppression before switching can increase the risk of virological failure, and since there is no possibility of prior genotyping, dual therapy is recommended as a simplification after efficient virological suppression. (VASCONCELOS et al., 2022). There is no consensus on the initial viral load when choosing dual therapy as a therapeutic option. In Brazil, for the use of dual therapy containing lamivudine, an undetectable viral load (VL) is recommended in the last two exams, with the last VL being carried out less than 6 months ago (BRAZIL, 2021).

Statistical analysis using the chi-square test revealed no statistical significance in the relationship between the initial CD4 cell level and the efficacy of dual therapy ($p > 0.05$). This indicates that the distribution of patients among the dual therapy efficacy categories was not affected by the initial CD4 cell level in our study, possibly indicating that the initial immunological impact may not play as crucial a role in the success of dual therapy.

However, it is worth highlighting that a meta-analysis published in the journal Clinical Microbiology and Infection in 2021 presented divergent results. In this study, an increased frequency of therapeutic failure was observed in patients with low initial CD4 cell counts (< 200 cells/ml), which suggests that, in these cases, triple therapy can still be considered as the gold standard for viral suppression. (PISATURO et al., 2021). This highlights the importance of additional studies on the interaction between immune level and dual therapy.

			Efficacy			
			Failure	Suppression	Total	p-value
initial CD4	< 200	Score	0	6	6	0,443
		%	0,0	100	100	
	> 200	Score	8	81	89	
		%	9,0	91,0	100,0	

Table 3: Relationship between baseline CD4 values and efficacy

Source: Prepared by the authors (2023).

CONCLUSION

It is possible to verify the high efficacy of dual therapy in suppressing viral load, which makes it an appropriate alternative for patients with contraindications or intolerant to the triple regimen, who represent the main population identified in the study.

REFERENCES

CAHN, Pedro et al. Dolutegravir-lamivudine as initial therapy in HIV-1 infected, ARV-naive patients, 48-week results of the PADDLE (Pilot Antiretroviral Design with Dolutegravir LamivudinE) study. **Journal of the International AIDS Society**, v. 20, n. 1, p. 21678, 2017. Disponível em: https://doi.org/10.7448/ias.20.01.21678. Acesso em: 2 jun. 2022.

LLIBRE, Josep M. *et al.* Efficacy and Safety of Switching to the 2-Drug Regimen Dolutegravir/Lamivudine Versus Continuing a 3- or 4-Drug Regimen for Maintaining Virologic Suppression in Adults Living With HIV-1: Week 48 Results From the Phase 3, Non-inferiority SALSA Randomized Trial. **Clinical Infectious Diseases**, 2 mar. 2022. Disponível em: https://doi.org/10.1093/cid/ciac130. Acesso em: 26 ago. 2023.

MINISTÉRIO DA SAÚDE. **Nota informativa No 007/017-DDAHV/.DCCI/SVS/MS.** Departamento de Vigilância, Prevenção e Controle das IST, do HIV/AIDS e das Hepatites Virais. 007/2017. Brasília/DF: Secretaria de Vigilância em Saúde, 2017.

MINISTÉRIO DA SAÚDE. **Nota informativa No 28/2021-CGAHV/.DCCI/SVS/MS.** Departamento de Doenças de Condições Crônicas e Infecções Sexualmente Transmissíveis. 28/2021. Brasília/DF: Coordenação-Geral de Vigilância do HIV/AIDS e das Hepatites Virais, 2021.

MINISTÉRIO DA SAÚDE. **OFÍCIO CIRCULAR No 48/2019/CGAHV/.DCCI/SVS/MS.** Departamento de Doenças de Condições Crônicas e Infecções Sexualmente Transmissíveis. 48/2019. Brasília/DF: Coordenação-Geral de Vigilância do HIV/AIDS e das Hepatites Virais - CGAHV, 2019.

PISATURO, Mariantonietta *et al.*Risk of failure in dual therapy versus triple therapy in naïve HIV patients: a systematic review and meta-analysis. Clinical Microbiology and Infection, v. 27, n. 1, p. 28-35, jan. 2021. Disponível em: https://doi.org/10.1016/j.cmi.2020.09.048. Acesso em: 30 ago. 2023.

ROJAS, Jhon *et al.* Efficacy and safety of switching to dolutegravir plus lamivudine versus continuing triple antiretroviral therapy in virologically suppressed adults with HIV at 48 weeks (DOLAM): a randomised non-inferiority trial. **The Lancet HIV**, v. 8, n. 8, p. e463-e473, ago. 2021. Disponível em: https://doi.org/10.1016/s2352-3018(21)00100-4. Acesso em: 26 ago. 2023.

SPINNER, Christoph D. *et al.* Efficacy and Safety of Switching to Dolutegravir With Boosted Darunavir in Virologically Suppressed Adults With HIV-1: A Randomized, Open-Label, Multicenter, Phase 3, Noninferiority Trial: The DUALIS Study. **Open Forum Infectious Diseases**, v. 7, n. 9, 13 ago. 2020. Disponível em: https://doi.org/10.1093/ofid/ofaa356. Acesso em: 26 ago. 2023.

VAN WYK, Jean *et al.* Efficacy and Safety of Switching to Dolutegravir/Lamivudine Fixed-Dose 2-Drug Regimen vs Continuing a Tenofovir Alafenamide–Based 3- or 4-Drug Regimen for Maintenance of Virologic Suppression in Adults Living With Human Immunodeficiency Virus Type 1: Phase 3, Randomized, Noninferiority TANGO Study. **Clinical Infectious Diseases**, v. 71, n. 8, p. 1920-1929, 6 jan. 2020. Disponível em: https://doi.org/10.1093/cid/ciz1243. Acesso em: 26 ago. 2023.

VASCONCELOS, Melina Maria Loiola Melo et al.Simplificação terapêutica com lamivudina e dolutegravir em pacientes vivendo com HIV no Ceará (Estudo LAMDO). Research, Society and Development, v. 11, n. 9, p. e59711932251, 20 jul. 2022. Disponível em: https://doi.org/10.33448/rsd-v11i9.32251. Acesso em: 30 ago. 2023.

VIZCARRA, Pilar *et al.* Efficacy and safety of dolutegravir plus boosted-darunavir dual therapy among highly treatment-experienced patients. **Antiviral Therapy**, v. 24, n. 6, p. 467-471, 2019. Disponível em: https://doi.org/10.3851/imp3319. Acesso em: 2 jun. 2022.

ZAMORA, Francis J. et al. Dolutegravir And Lamivudine Combination For The Treatment Of HIV-1 Infection. **HIV**/AIDS - Research and Palliative Care, Volume 11, p. 255-263, out. 2019. Disponível em: https://doi.org/10.2147/hiv.s216067. Acesso em: 30 ago. 2023.

APPENDICES

A – DATA COLLECTION FORM: PROFILE OF PATIENTS IN DUAL THERAPY

- Initials:_____ - Sex: () M () F
- Medical record number:_____ - Age:_____
- Initial A.R.T.:_____
- Current dual therapy: () DTG+DRV/r () DTG + 3TC () DRV + 3 TC
() Start () Exchange in (____/____/_____)
- Reason: () Toxicity: _____ () Simplification () Poor adhesion
- Previous genotyping: () Yes () Not

B – DATA COLLECTION FORM: ADHERENCE AND EFFICACY

- **Accession**: () Yes () No - Reason:_____
- **Efficacy**:

Viral charge	Pre - double T.	After 6 months	After 1 year
Value (copies/mL) (log)	V: _____ log: _____	V: _____ log: _____	V: _____ log: _____

- Double pre-therapy viral load: () < 40 copies () ≥ 40 copies () ≥
- 1000 copies
- CD4 pre-dual therapy: () < 200 () ≥ 200

Virological outcome with dual therapy

- After 6 months: () viral suppression () virological failure
- After 1 year: () viral suppression () virological failure