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エイズ対策政策研究事業

HIV感染症診療の提供体制の評価及び改善に関する研究

(令和)3年度～5年度 総合研究報告書

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目 次

I. 総合研究報告		
HIV感染症診療の提供体制の評価及び改善に関する研究	-----	1
内藤 俊夫		
II. 研究成果の刊行に関する一覧表	-----	18

HIV 感染症診療の提供体制の評価及び改善に関する研究

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研究要旨

抗 HIV2 剤療法の使用状況と継続性について、詳細な解析は世界的にも発表されていない。我々は多施設コホート研究により 2 剤療法の対象患者と治療の継続期間を検討した。日本の 390 病院の 4,400 万名の患者データから、抗 HIV 薬を投与されていた 5,088 名の HIV 感染者を抽出し解析を行った。

当該 980 名の患者のうち、DTG/3TC に 122 名、BIC/FTC/TAF に 858 名が処方変更されていた。処方変更された患者の平均年齢は DTG/3TC 群で有意に高かった（DTG/3TC: 49 ± 12.5 歳、BIC/FTC/TAF: 45 ± 11.4 歳、 $P=0.005$ ）。性別には有意差を認めなかった。また、高血圧症（ $P=0.013$ ）、脂質異常症（ $P<0.001$ ）、糖尿病（ $P=0.02$ ）を有する患者で 2 剤療法が選択される傾向があった。AIDS 指標疾患の有無は 2 剤療法の選択率に影響していなかった。処方開始後 700 日の時点で、DTG/3TC 群と BIC/FTC/TAF 群で継続率の有意差はなかった（log-rank test $p=0.82$ ）。

高齢化し多疾患併存や多剤併用（ポリファーマシー）となっている HIV 感染者に対して、DTG/3TC による 2 剤療法が優先的に行われていることが明らかになった。2 剤療法の継続率は従来の 3 剤療法の継続率と有意差がなく、安全に継続できることが明らかになった。本研究から得られたデータは、特に多疾患併存の HIV 感染者を非専任医が診る状況等において、診療の重要な指針になると考えられた。

A. 研究目的

AIDS 指標疾患などの HIV に関連する病態の他に、加齢に伴う疾患も HIV 感染者の予後には多大な影響を及ぼす。本邦でも 2020 年より DTG/3TC による 2 剤療法が処方可能となり、安全性や薬剤負荷軽減を鑑み、多疾患併存や多剤併用（ポリファーマシー）の患者への使用が期待されている。

安全に持続可能な抗 HIV 薬を知ること

は大変重要である。しかしながら、日本の HIV 感染者の抗 HIV 薬 2 剤療法の処方割合、継続率についての報告はない。我々は本邦の HIV 感染者の多施設のレセプトを用い、データベース研究を行った。

B. 研究方法

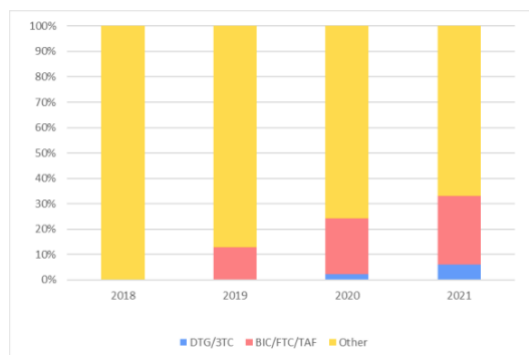
Medical Data Vision Co., Ltd. (MDV; Tokyo, Japan) に登録されているレセプトデータベースを用い、横断的後ろ向き観察

研究を行った。このデータベースには、2021 年 12 月時点で、日本の病院の 26% にあたる 390 病院の 4,400 万名の患者情報が含まれていた。この中で、2018 年 1 月 1 日から 2021 年 12 月 31 日までの期間に抗 HIV 薬を 2 回以上処方された HIV 感染者 5,088 名を対象として解析した。

HIV 感染症や合併症の有無は ICD-10 コードを元に決定した。最終の受診日を基準にして、年齢を 6 グループに分類した (18-29, 30-39, 40-49, 50-59, 60-69, ≥ 70)。患者の性別、合併症の数や種類、抗 HIV 薬とその他の内服薬、AIDS 指標疾患の有無について記述的に調査した。

C. 研究成果

対象患者のうち、該当期間中に DTG/3TC に 249 名、BIC/FTC/TAF に 1,280 名が処方変更されていた。処方割合の年次変化を図 1 に示す。



(図 1. DTG/3TC と BIC/FTC/TAF の処方割合)

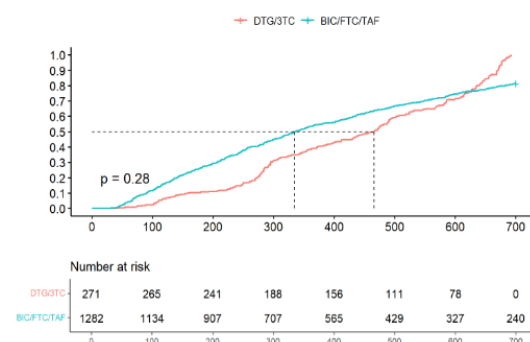
スイッチされた患者の平均年齢は、DTG/3TC 群 49 ± 12.5 歳、BIC/FTC/TAF 群 45 ± 11.4 歳であり、2 剤療法群で有意に高かった ($P=0.005$)。性別では有意差を認めなかった。

併存症については、高血圧症 ($P=0.013$)、脂質異常症 ($P<0.001$)、糖尿病 ($P=0.02$) を有する患者で有意に BIC/FTC/TAF よりも DTG/3TC にスイッチされていた。AIDS 指標疾患の有無では 2 剤療法の選択率に有意差は認めなかった。

スイッチ後の薬剤継続率 Kaplan-Meier 解析を図 2 で示す。処方開始後 700 日の時点で、DTG/3TC 群と BIC/FTC/TAF 群で継続率の有意差を認めなかった。

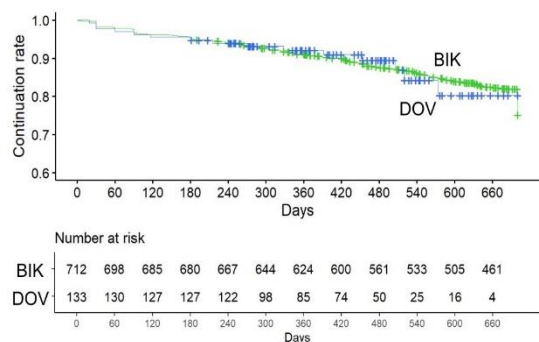
併存症については、脂質異常症 ($P=0.002$) または糖尿病 ($P=0.011$) を有する患者で、有意に BIC/FTC/TAF よりも DTG/3TC にスイッチされていた。AIDS 指標疾患の有無では 2 剤療法の選択率に有意差は認めなかった。

日本で薬剤が使用可能になってから処方されるまでの期間については、両群間で差を認めなかった ($p=0.28$)。



(図 2. 発売開始からの処方数)

スイッチ後の薬剤継続率 Kaplan-Meier 解析を図 3 で示す。処方開始後 700 日の時点で、DTG/3TC 群と BIC/FTC/TAF 群で継続率の有意差を認めなかった。



(図 3. 3 剤療法と 2 剤療法の継続率比較)

D. 考察

我々は現在までに「高年齢化する HIV 感染者の診療において、糖尿病、高血圧、脂質異常症などの生活習慣病が重要であること」を示している(Ruzicka DJ, *J Infect Open*, 2018. Ruzicka DJ, *J Infect Chemother*, 2019. Naito T, *HIV Medicine*, 2022)。HIV 診療医はこれらの生活習慣病の診療に関する正しい知識を持つとともに、この状況下でも継続可能な抗 HIV 薬について理解する必要がある。

また、16,069 名を対象としたビッグデータ解析により、インテグラーゼ阻害剤が抗 HIV 薬のキードラックの中で、最も長い期間変更されにくいことを報告している(Naito T, *Scientific Reports*, 2022)。さらには、BIC/FTC/TAF に代表される Single-tablet regimens (STR) が従前の Multi-tablet regimens (MTR) より継続率が優れていることも示した (Wang X, *J Infect Chemother*, 2022)。これらの研究成果に加え、今回の解析から 2 剤療法の処方状況、継続率が明らかとなったのは大変有意義である。

本邦では 2020 年より DTG/3TC による 2 剤療法が使用可能となり、安全性や経済性の意味から注目されている。今回の研究により、同年から使用が増加しているものの、2019 年に適応となった 3 剤療法の BIC/FTC/TAF に比較すると少数の患者にのみ処方されていることが示された。2 剤のみの内服による安全性のメリットが重視されたためか、高年齢の患者、高血圧症や糖尿病を有する患者、に優先的に投与されていることも明らかになった。本邦で「2 剤療法がどのような対象に処方されているか」の報告はなく、今後の薬剤選択のための貴重な基盤データとなりうる。

2 剤療法による治療の失敗・中断が危惧されていたが、本データベース研究では治療開始後 700 日においても、従来の 3 剤療法の継続率と差を認めなかった。これらの結果から、2 剤療法は薬剤負荷を減らしつつも、安全に継続できる薬剤であることが推測できる。

本データベースには CD4 陽性細胞数や HIV-RNA 量等の検査データを含まないため、2 剤療法にスイッチ後の免疫学的/ウイルス学的影響を評価することは困難である。このため、スイッチした後に入院した患者の情報を詳細に解析したが、2 群ともに明らかな薬剤変更による AIDS 発症や副作用による入院を認めなかった。

E. 結論

今回の全国レセプトデータベース研究結果から、2 剤療法が高年齢患者や生活習慣病を有する患者に積極的に用いられていることが明らかになった。HIV 感染者数の増加や高齢化により併存症が増えることによ

り、今後日本では HIV 診療専門医だけでなく総合診療/プライマリ・ケア医が処方する機会が増えることが予想される。本研究成果は、総合診療/プライマリ・ケア医が利用しやすい抗 HIV 薬についての有用なビッグデータ解析の情報である。

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