

# TRENDS IN THE USE OF METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS OVER THE LAST THREE DECADES

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**Background:** Weekly low-dose MTX is now considered the anchor drug for the treatment of rheumatoid arthritis (RA) as improves both, short-term (disease activity) and long-term (radiographical progression, function and mortality rates) outcomes.

**Objectives:** To compare the probability of MTX utilization in patients with RA over three consecutive decades (80's, 90's y first decade of the 21st century) and to describe the variables associated with its use.

**Patients and Methods:** This was a retrospective analysis that included 1258 patients with RA (as per the 1987 ACR criteria) who were diagnosed between January 1980 and December 2009. The relationship between demographic (gender, age at first symptom and at diagnosis), clinical (date of diagnosis, diagnosis delay, presence of rheumatoid factor, sedimentation rate and joint erosions at diagnosis, extra-articular manifestations and follow-up time) and therapeutic (time to first time MTX) domains was examined. The cumulative rate of MTX utilization was estimated using the Kaplan-Meier method and the variables associated with its use analyzed with a Cox regression conditional model. Variables with a p value  $\leq 0.05$  were considered statistically significant.

**Results:** 1134 (91%) patients were ever treated with MTX and 680 (60%) reached doses  $\geq 15$  mg per week. Among those patients diagnosed during the 80' (N= 211), 197 (93%) used MTX, during the 90' (N= 426), 401 (94%) used MTX and during the first decade of this century (N= 610), 536 (88%) used MTX. The table below shows the cumulative rate of MTX utilization during the three decades (log rank test= 316.64;  $p < 0.001$ ).

Time from diagnosis to MTX use (months)	Decade		
	80 % (SE)	90 % (SE)	2000 % (SE)
0	6 (0.019)	40 (0.027)	60 (0.021)
3	7 (0.020)	43 (0.028)	64 (0.021)
6	9 (0.022)	45 (0.028)	70 (0.020)
12	10 (0.023)	50 (0.028)	75 (0.020)

In the multivariable analysis, age at diagnosis (HR= 1.01, CI95% 1.001-1.011;  $p= 0.020$ ) and the decade of diagnosis (HR= 2.15, CI95% 1.924-2.407;  $p < 0.001$ ) were associate the utilization of MTX.

**Conclusions:** In this study, the cumulative rate of MTX utilization has largely increased over the last three decades, placing in evidence an earlier indication of this drug when treating patients with RA. These findings are in accordance with local and international guidelines for the treatment of RA that denote the need of an early and effective treatment of patients with this disease, being this drug a standard and non-expensive therapeutic intervention.