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Antipsychotics use in the community of Thessaloniki, Greece Primena antipsihotika na teritoriji Soluna, Grčka

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Abstract

Background/Aim. Under the current financial crisis in Greece, an effort has been made by the Greek health authorities to encourage generic prescribing, in order to lower medicinal cost. The purpose of this work was to study antipsychotics use, and to calculate utilization of generics in antipsychotics sales in a sample from the medicines market of Thessaloniki, the second largest city in Greece. Methods. A sample of antipsychotics registered sales was collected using the new Electronic Health Records that have been applied in pharmacies during the last years in Greece. The sample corresponded to a small amount of sales from the market of Thessaloniki during the period July 2014-June 2015, including only community and no hospital sales. All brand names (prototype and generics) of antipsychotics and their relative ratios in the sales were estimated, and the percentage of generics in the sale of each medicine was calculated. The amount of medicines was estimated in Defined Daily Doses (DDDs) of the

Apstrakt

Uvod/Cilj. Tokom ekonomske krize u Grčkoj, zdravstvene vlasti su, u cilju smanjenja troškova u zdravstvenoj delatnosti, stimulisali propisivanje i korišćenje generičkih oblika lekova. Cilj istraživanja je bio analiza potrošnje generičkih lekova 12 grupa antipsihotika na osnovu njihovog prometa u apotekama u Solunu, drugog po veličini grada u Grčkoj. Metode. Uzorak prodatih registrovanih antipsihotika formiran je na osnovu elektronskog zdravstvenog kartona, koji je u primeni tokom poslednjih nekoliko godina u apotekama Grčke. Uzorak se odnosio na vanbolničku potrošnju lekova na teritoriji Soluna tokom perioda jul 2014-jun 2015. godine, a ne i na primenu lekova u bolničkim uslovima. Analizirani su originalni i generički oblici antipsihotika koji su bili registrovani u Grčkoj. Izračunata je zastupljenost generičkih oblika lekova u primeni. Obim prometa lekova procenjivan je putem definisane dnevne doze (DDDs) referentnog oblika leka (originalni lekovi i njihovi generični oblici). Rezultati. Od

reference/prototype drug and its generics. Results. Olanzapine, quetiapine, haloperidol and risperidone sales corresponded to 77% of total antipsychotics sales with percentages of sales 25%, 19%, 19% and 14% respectively. The percentage of sales of other antipsychotics was 7% for amisulpride, 6% for aripiprazole, 4% for ziprasidone and 3% for clozapine. Generic use corresponded to 41% of total sales of antipsychotic drugs (10.884 DDDs out of 26.433 DDDs). Concerning second generation antipsychotics, generic use was high for amisulpride, olanzapine, risperidone and quetiapine. Conclusion. In the study sample, second generation antipsychotics corresponded to 78% of sales in the community of Thessaloniki. Haloperidol utilization was also notable. Considering Greek practices, the percentage of generics in antipsychotics sales was very high even for some of the newest antipsychotics.

Key words:

antipsychotic agents; drugs, generic; prescription drugs; economics, pharmaceutical; greece.

ukupnog prometa antipsihotika olanzapin je bio zastupljen sa 25%, kvetiapin sa 19%, haloperidol sa 19% i risperidon sa 14%. Procenat prodaje drugih antipsihotika iznosio je: amisulpirid - 7%, aripiprazol - 6%, ziprasidon - 4% i klozapin - 3%. Upotreba generičkih oblika lekova iznosila je 41% od ukupne prodaje antipsihotika (10,884 od 26,433 DDDs). Kada su u pitanju antipsihotici druge generacije, generički oblici lekova su korišćeni u visokom procentu u slučaju amisulpirida, olanzapina, risperidona i kvetiapina. **Zaključak.** Na ispitivanom uzorku, prodaja antipsihotika druge generacije iznosila je 78% od vanbolničke potorošnje antipsihotika na teritoriji Soluna. Potrošnja haloperidola je bila takođe značajna. Razmatrajući grčku praksu, procenat prodaje generičkih oblika lekova iz grupe antipsihotika je bio veoma veliki, čak i za neke novije antipsihotike.

Ključne reči:

trankvilizeri, veliki; lekovi, generički; lekovi, propisivanje; ekonomija, farmaceutska; grčka.

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Introduction

The use of generics in the Greek medicines market is generally lower than in other European countries ^{1, 2}, accounting for only 11.6% of total pharmaceutical expenditures in 2006. This can be attributed to a general lack of confidence in generics ^{3, 4}, a previous lack of national policy to encourage generic use ⁵ as well as to small difference in prices between generic and prototype medicines in Greece.

Under the current financial crisis, an effort has been made by the Greek health authorities to encourage generic prescribing in order to lower medicinal $\cos t^{6-9}$.

Published data on generic use in Greece are generally limited and Greece has not participated in large European studies on drug utilization, probably due to, until recently, lack of detailed Electronic Health Records. The purpose of this work was to study antipsychotics use, and to calculate utilization of generics in the community of Thessaloniki – the second largest city in Greece – after the adoption of measures to contain medicinal cost.

Methods

A sample of antipsychotics registered sales was collected using the new Electronic Health Records that have been applied in pharmacies during the last years in Greece ^{7–9}. The sample corresponded to a small amount of sales from the market of Thessaloniki during the period July 2014 – June 2015, including only community and no hospital sales from the areas of central and Eastern Thessaloniki city and the suburban municipalities of Kalamaria and Panorama. The majority of medicines were obtained after prescribing by a physician, with a negligible percentage (less than 1%) of over the counter sales.

All brand names (prototype and generics) of antipsychotics and their relative ratios in the sales were estimated and the percentage of generics in the sale of each medicine was calculated. The amount of medicines was estimated in daily defined doses (DDDs) of the reference drug and its generics, according to the World Health Organization (WHO) Drug Statistics Methodology, as described in the 2015 Guidelines for Anatomic Therapeutic Chemical (ATC) classification and DDD assignment⁹.

Statistical analysis was performed by means of the statistical package SPSS 17.0 (SPSS Inc, Chicago, IL).

Results

In our study sample, all medication products were single-ingredient products. A total of 26,433 DDDs of antipsychotic drugs was sold during the study period in the pharmacies that participated in the study.

Olanzapine, quetiapine, haloperidol and risperidone sales corresponded to 77% of total antipsychotics sales with percentages of sales 25%, 19%, 19% and 14%, respectively. The percentage of sales of other antipsychotics was 7% for amisulpride, 6% for aripiprazole, 4% for ziprasidone and 3% for clozapine. Detailed results on antipsychotics sales can be seen in Table 1 and Figure 1.

Although second generation antipsychotics shared the 78% of the sales in the study sample, haloperidol utilization was also considerable (19%, see Table 1 and Figure 1).

Generic use corresponded to 41% of total sales of antipsychotic drugs (10.884 DDDs out of 26.433 DDDs). The percentage of generics in second generation antipsychotics sales was high for olanzapine (66%), quetiapine (41%), risperidone (59%) and amisulpride (100%). Results on generic use of other antipsycotics can be seen in Table 1 and Figure 1.

The use of prototypes (reference drugs) was high for some of the newest second generation antipsychotics as well as for all first generation antipsychotics that were consumed in our study sample (see Table 1 and Figure 1).

The relative use of reference drugs and generics is presented in Figure 1.



Antipsychotics	sales in the mark	et of Thessaloniki	Table 1 Greece
Active Substance			nsumption
	Reference drug	DDDs 1.512	Percentage (%) 41
Risperidone	Generic	2.192	59
	Total	3.704	100
Quetiapine	Reference drug Generic	2.936	59
	Total	2.076	41
		5.012	100
Olanzapine	Reference drug	2.254	34
	Generic	4.326	66
	Total	6.580	100
Aripiprazole	Reference drug	1.549	100
	Generic	0	0
	Total	1.549	100
Clozapine	Reference drug	817	100
	Generic	0	0
	Total	817	100
Ziprasidone	Reference drug	1.078	100
	Generic	0	0
	Total	1.078	100
Amisulpride	Reference drug	0	0
	Generic	1.890	100
	Total	1.890	100
Paliperidone	Reference drug	28	100
	Generic	0	0
	Total	28	100
Haloperidol	Reference drug	4.919	100
	Generic	0	0
	Total	4.919	100
Chlorpromazine	Reference drug	0	0
	Generic	400	100
	Total	400	100
Levomepromazine	Reference drug	69	100
	Generic	0	0
	Total	69	100
Zuclopenthixol	Reference drug	387	100
	Generic	0	0
	Total	387	100
	Reference drug		59
Total	-	15.549	
	Generic	10.884	41
	Total	26.433	100

DDDs - Defined Daily Doses.

Discussion

In our study, the most widely used antipsychotics were olanzapine, quetiapine, haloperidol and risperidone (in 77% of cases), followed by amisulpride, aripiprazole, ziprasidone and clozapine. These results are in accordance with the National Institute for Health and Care Excellance (NICE) Guidelines 10 and reflect prescribing patterns similar to those observed in other countries $^{11-15}$.

As expected, second generation antipsychotics replaced older antipsychotics and represented the majority of sales in the study (78% of total sales), with olanzapine, quetiapine and risperidone sharing the 58% of sales. Among first generation antipsychotics, haloperidol shared a considerable perThe percentage of generics in antipsychotic use was unexpectedly high for Greek standards ^{2, 8} (41%), being much higher than the percentage of generics in antidepressant use (26%), as observed in a recent study in Greece ^{7, 16}. This is contrary to the fact that psychiatrists are more likely to choose generic antidepressant than generic antipsychotics ⁴. Nevertheless, it is consistent with worsening of depressive symptomatology in cases that antidepressants were switched from original to generics ¹⁷. On the contrary, in the case of antipsychotics, concerns about the interchangeability from original to generics seem to have a realistic basis mainly for clozapine ¹⁷. This is in accordance with our finding that only original clozapine was consumed in our study in Thessaloniki.

The use of generics was generally higher in second generation antipsychotics, with 66% for olanzapine, 59% for risperidone, 41% for quetiapine and 100% for amisulpride. On the contrary, among first generation of antipsychotics, only reference drugs were used. This can be explained by the low price of first generation antipsychotics, which makes the use of generics financially indifferent. On the other hand, the price of second generation antipsychotics is much higher, and this makes generic use financially favorable.

In spite of the general lack of confidence on generic use in antipsychotic therapy ^{3, 4}, the use of generics seems inevitable in order to lower medicinal cost. Nevertheless, in the past there was no difference in price of generics and reference drugs in Greece; there was no motivation for psychiatrists to prescribe generics. In a recent study on utilization of antipsychotics in Greece, the use of generics in 2009 was only 4% ¹⁸. After the financial crisis that hit Greece since early 2010 onwards, a series of measures were implemented to contain public medicines expenditure, including price cuts, changes in reimbursement rates, delisting, internal reference price, international nonproprietary name (INN) prescribing ^{6, 17}. Although prices of generics were cut by only 10% (before being equal to reference drug prices) ¹⁹, the implemented measures encouraged generic prescribing ²⁰. Due to the high cost of second generation antipsychotics, even this small percentage in the reduction of prices represents a

- 1. Tsiantou V, Zavras D, Kousoulakou H, Geitona M, Kyriopoulos J. Generic medicines: Greek physicians' perceptions and prescribing policies. J Clin Pharm Ther 2009; 34(5): 547-54.
- Godman B, Shrank W, Wettermark B, Andersen M, Bishop I, Burkhardt T, et al. Use of Generics: A Critical Cost Containment Measure for All Healthcare Professionals in Europe? Pharmaceuticals (Basel) 2010; 3(8): 2470-94.
- 3. *Dunne SS, Dunne CP.* What do people really think of generic medicines?, A systematic review and critical appraisal of literature on stakeholder perceptions of generic drugs. BMC Med 2015; 13: 173.

large component of public savings on medicines expenditure. Thus, it seems, that the measures adopted to face the financial crisis really work towards reducing the burden of medical costs.

A limitation of our study is the small sample of sales used. Nevertheless, Thessaloniki is a representative commercial center, and probably the most vivid market, in Greece. In spite of this limitation, our study appears to reflect the real situation in prescribing and consumption of antipsychotics in the community of Thessaloniki²⁰.

Another limitation of this study is that our sample does not correspond to a specific area or district of the town and the size of population corresponding to consumed antipsychotics in the studied period cannot be estimated; thus, the utilization of antipsychotics cannot be calculated in standard units DDDs/1000 inhabitants/day, and is roughly calculated in DDDs. Nevertheless, our study is one of the few studies on drug utilization in Greece expressing consumption in DDDs and not in cost ^{18, 20–22} and our results on specific antipsychotics preference seem to be comparable to those observed in other countries ^{12–15}.

Moreover, since there are no major studies on drug utilization in Greece, our study appears to be useful in presenting data on antipsychotics utilization in Greece.

Conclusion

In our study sample, second generation antipsychotics predominated in antipsychotics use in the community of Thessaloniki. Haloperidol utilization was also considerable. The percentage of generics in antipsychotics sales was high (considering Greek practices) even for some of the newest antipsychotics. These results reflect the impact of measures for decreasing medical costs in the years of financial crisis in Greece, and show that psychiatrists try to contain the medical cost within health expenses.

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REFERENCES

- 4. Hamann J, Mendel R, Kissling W, Leucht S. Psychiatrists' decision making between branded and generic drugs. Eur Neuropsychopharmacol 2013; 23(7): 686–90.
- 5. Karampli E, Souliotis K, Polyzos N, Kyriopoulos J, Chatzaki E. Pharmaceutical innovation: Impact on expenditure and outcomes and subsequent challenges for pharmaceutical policy, with a special reference to Greece. Hippokratia 2014; 18(2): 100-6.
- Leopold C, Mantel-Teeuwisse AK, Vogler S, Valkova S, de Joncheere K, Leufkens HG, et al. Effect of the economic recession on pharmaceutical policy and medicine sales in eight European countries. Bull World Health Organ 2014; 92(9): 630-640D.

- 7. *Papaioannidou P, Ntaralas A*. Attitudes in Antidepressants Use in Greece. Pharmacoepidemiol Drug Saf 2014; 23(S1): 115-6.
- Papaioannidou P, Ntaralas A. Generic Use In Statin Sales In The Community of Thessaloniki, Greece. Clin Ther 2015; 37(8S): e148-9.
- 9. World Health Organization. Guidelines for ATC classification and DDD assignment. 2015. [cited 2015 Sep 8]. Available from: http://www.whocc.no/atc ddd publications/guidelines/
- NICE CG 178. Psychosis and schizophrenia in adults: Treatment and management. 2014. [cited 2015 Sep 8]. Available from: https://www.nice.org.uk/guidance/cg178/ resources/guidance-psychosis-and-schizophrenia-in-adultstreatment-and-management-pdf
- 11. Leiderman EA, Lorenzo L. Prescription patterns in the treatment of schizophrenia. Vertex 2015; 26(119): 11–6. (Spanish)
- 12. Leopold C, Zhang F, Mantel-Teeuwisse AK, Vogler S, Valkova S, Ross-Degnan D, et al. Impact of pharmaceutical policy interventions on utilization of antipsychotic medicines in Finland and Portugal in times of economic recession: Interrupted time series analyses. Int J Equity Health 2014; 13: 53.
- Jarema M, Meder J, Araszkiewicz A, Tyszkowska M. Antipsychotics in clinical practice. Treatment of the first schizophrenic episode. Psychiatr Pol 2008; 42: 841–58. (Polish)
- 14. Meder J, Tyszkowska M, Jarema M, Araszkiewicz A, Szafrański T. Antipsychotics in clinical practice. The refractory schizophrenic patients treatment. Psychiatr Pol 2008; 42(6): 859-73. (Polish)
- 15. Apiquian R, Fresán A, de la Fuente-Sandoval C, Ulloa RE, Nicolini H. Survey on schizophrenia treatment in Mexico:

Perception and antipsychotic prescription patterns. BMC Psychiatry 2004; 4: 12.

- 16. *Papaioannidou P, Ntaralas A*. Generic use in antidepressant sales in Greece. J Bas Clin Pharmacol Toxicol 2014; 115(S1): 70.
- 17. Desmarais JE, Beauclair L, Margolese HC. Switching from brand-name to generic psychotropic medications: a literature review. CNS Neurosci Ther 2011; 17(6): 750-60.
- Papaioannidou P, Kasviki P, Moschopoulos NP, Nimatoudis I. Antipsychotic Prescribing in a Tertiary Hospital Under the Financial Crisis in Greece. Pharmacoepidemiol Drug Saf 2016; 25(S3): 668.
- 19. Vogler S, Zimmermann N, Leopold C, de Joncheere K. Pharmaceutical policies in European countries in response to the global financial crisis. South Med Rev 2011; 4(2): 69–79.
- 20. *Papaioannidou P, Kasviki P.* Utilization of Antipsychotics in Eastern Thessaloniki and Kalamaria. Rev Clin Pharmacol Pharmacikinetics 2015; 29: 119-23.
- 21. Papaioannidou P, Michailidou M, Ntaralas A. Attitudes in statins use in Greece. Pharmacoepidemiol Drug Saf 2015; 24(S1): 144.
- 22. Papaioannidou P, Michailidou M, Ntaralas A, Michailidou S. Use of Antidepressants Under the Financial Crisis in Greece. Pharmacoepidemiol Drug Saf 2016; 25(S3): 665-6.

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