Opioid Consumption Trends in Spain: The Case of the Island of La Gomera (2016-2019)

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Abstract

This study aimed to describe the consumption of opioid drugs in the island of La Gomera over a four-year period (2016–2019) at various levels (island, township and health areas). Data were extracted from the wholesaler in community pharmacies at a population level. Consumption patterns were expressed as number of Defined Daily Doses per 1000 inhabitant /day (DID) and by the number of sold units per 1000 inhabitants and year. A common classification system (ATC) and the two units of measurement proposed enabled comparisons at various levels. Major differences between island, township, and health areas are presented. Little is known about the reasons for these differences. The opioids belonging to the N02AJ groups and N02AX were the most consumed according to the “sold units” parameter, which accounted for 69.48% and 18.59%, respectively. The situation was similar in terms of DID, although with lower percentages, but a significative increase was observed in the use of fentanyl and buprenorphine, around 15% each. The balance between the uses of weak or strong opioids showed differences in La Gomera compared to those nationwide. In mainland Spain, almost 70% of the consumption came from weak opioids versus that of 58.67% in La Gomera. Fentanyl was the most frequently used strong opioid (16.10%) followed by tapentadol and buprenorphine, around 5% each, whereas in La Gomera buprenorphine was the most consumed (15.75%) followed by fentanyl (14.87%) and tapentadol (5.82%).

These differences in opioids consumption are most likely explained by different changes on the prescribing habits and sociodemographic characteristics.

Introduction

Drug utilization study (DUS) have great scientific and social interest, having formed a fundamental part of the discipline known as Pharmacoepidemiology. According to the World Health Organization (WHO, 2020), DUS includes the analysis of the commercialization, distribution, prescription and use of medicines in society, with special attention to the results of medical, social and economic consequences. DUS can be useful to know the pattern and use of the different medicines, their evolution over time and it can compare the data from one region to another and thus contribute to a more responsible use of them. It may also eventually serve to analyze the frequency and distribution of certain diseases, to identify possible areas of intervention, or to evaluate different measures, for example, Pharmacovigilance (Laporte and Tognoni 1993). DUS used the prescription data from a nationwide drug data bank as the main source of information (Hamunen et al. 2008; Jarlbaek 2019). Each country’s prescription database can be assessed on the internet to obtain more detailed information on the annual number of dispensed opioids (Jarlbaek 2019). Knowledge of the number of opioids prescribed at a determined geographic area (such as a township or an island) are not available in such database. However, in some DUS, information is obtained from the medical history or special records on the prescription of drugs (chronic administration). In some studies, it is essential to obtain basic information from an interview with the patient, with the prescribing doctor, or with other health professionals related to the use of medications (Ferrer et al. 2014).

WHO proposed an international technical unit for measuring the drug consumption called Defined Daily Dose (DDD), which is independent of variations in the price and weight content of the drug pharmaceutical preparation. This unit of measurement allows comparisons to be made between different geographical areas and between different times regardless of variations in the composition of units and the cost of pharmaceutical preparation. DDD of active ingredients are established by WHO and are published on the website of *WHO Collaborating Center for Drug Statistics Methodology* (WHO, 2018).

The treatment of chronic pain comprises both pharmacological and non-pharmacological strategies (Merskey and Bogduk 1994; Collins et al. 1997; Dale et al. 2005). Among the former are non-opioid pain relievers, opioids, and adjuvants (used to prevent or treat side effects of pain relievers or to enhance the pain relief itself).

Opioid drugs are a group of drugs characterized by having a selective affinity for central and peripheral opioid receptors, inhibiting the transmission of the nociceptive entry and the perception of pain (Dworkin 2002; McClean 2004; Dowell et al. 2016). They are widely accepted for the treatment of severe acute pain and chronic moderate to severe pain that does not respond to other medications. The use of these drugs is associated with the development of physical dependence and addiction, which has been a major health problem in developed countries due to the potential risk of abuse of these substances (Boudreau et al. 2009; Zhu et al. 2019; Bosetti et al. 2019). The use of opioids has increased the last decade in many developed countries (Hamunen et al. 2009; Hastie et al. 2014; Hider-Mlynarz et al. 2018; Alexander et al. 2018). For instance, the abuse of opioid prescription in the treatment of pain in the United States and its devastating consequences of such overdose are well known (Hamunen et al. 2009). The pattern of opioid use also varies considerably between countries, especially, in European countries, not only regarding total consumption but also the preference for different opioids (Bosetti et al. 2019). For example, fentanyl is the most frequently consumed opioid analgesic in many countries (García del Pozo et al. 2008; Hamunen et al. 2009; Hider-Mlynarz et al. 2018).

Although the consumption of opioid drugs has been studied in various countries (García del Pozo et al. 2008; Hamunen et al. 2009; Hastie et al. 2014 ; Hider-Mlynarz et al. 2018; Alexander et al. 2018; Zhu et al. 2019; Bosetti et al. 2019). However, few studies have focused on local zones such as an island, township or health area to establish a consumption pattern on opioid drugs. The aim of this work was to analyze the consumption pattern of opioids drugs in the island of La Gomera, Canary Islands, Spain, by means of a drug utilization study using the Anatomical Therapeutic Chemical classification (ATC) /DDD methodology to establish any trends on the consumption of opioids (WHO, 2019). Secondly, to detect if there were any deviations in the consumption of opioids at various levels (nationwide and local) and to analyze the possible changes in the opioids use during the period covered by this study. To accomplish this, the raw data obtained from wholesalers in community pharmacies on the population were used as database, which is a novelty.

Material And Methods

The evaluation of opioid use at the inpatient level was conducted using ATC/DDD methodology, which is internationally accepted for measuring medicine utilization within and across populations. The different opioid types were identified in the database by their ATC-code. Opioids indicated for analgesia all start with N02A. Few other opioids are also relevant as analgesics, like methadone and codeine. These drugs are not routinely included in the usual opioid use statistics, because they have other indications rather than analgesia (Jarlbaek 2019). The subgroups of the ATC classification studied have been N02AA (natural opium alkaloids), N02AB (phenylpiperidine derivatives), N02AE (oripavine derivatives), N02AJ (opioids combined with other pain relievers, except codeine with combinations) and N02AX (other opioids).

In this study, we used the raw data obtained from wholesalers in community pharmacies on the population level provided by the Pharmaceutical Cooperative located in the Canary Islands. Only data on opioids sale in the community pharmacies were included because this use could be linked to the prescription/dispensation through the health record and through the sale.

The data provided were: the sold units of the different pharmaceutical preparations according to the ATC classification, date of sale, national code and pharmaceutical preparation name (API dose, strength and units). The Postal Code (ZIP) was also included, given that this data provides information about the township where the community pharmacy is located, but not its identity, thus maintaining its anonymity in accordance with the current Data Protection Law in Spain.

We analyzed the data from the island of La Gomera during the 2016–2019 period. Population data used to calculate DID were obtained from the National Statistics Institute in Spain dated on January 1st of each year. For the data processing, the database and dynamic tables of the Microsoft Excel® program were used.

In our study, the consumption of opioids was measured in defined daily doses (DDDs) or in number of medications packages (boxes or sold units). In the first case, consumption of opioid drug was expressed as DDDs/ 1000 inhabitants/day (DID), where the number of DDDs was the total amount of the active ingredient consumed in a certain time period (in our case, day) divided by the DDD.

$$DID = \frac{DDDs \times 1000}{populations \times 365 \text{ days}}$$

where DDDs represents the total number of DDDs,

$$DDDs = \frac{UD \times N}{DDD}$$

where UD is unit dose in mg, N is the number of units per package, and DDD is the defined daily dose.

Results

Data analysis at the island level

Figure 1 shows the map of the island of La Gomera, with its six townships and health areas, being its capital San Sebastián de La Gomera (Grafcán, 2020).

Table 1
Demographic data and administrative distribution of the island of La Gomera (BOC, 2009).

Township	2016	2017	2018	2019	Health area
Agulo	1074	1066	1067	1096	G02
Alajeró	1971	1983	2006	2017	G06
Hermigua	1924	1808	1805	1822	G02
San Sebastián	8707	8760	8945	9093	G01
Valle Gran Rey	4285	4371	4484	4564	G04
Vallehermoso	2979	2988	2829	2901	G03, G05
Total inhabitants	20940	20976	21136	21493	6

Table 2 shows the number of sold units by therapeutic subgroup / active pharmaceutical ingredient (API) and year. The tramadol-acetaminophen combination was the number one option under the tablet pharmaceutical form and presentation at low-dose and low-unit per packages (37.5mg / 325mg; 20 tablets) accounted for 74.13% of the total versus 13.25% for presentation with 60 units in 2016. However, this tendency changed at the end of the mentioned period due to the increase of the sales on the generic equivalent forms from 20–25%. Consumption for presentations with high-dose and high-unit per packages (75mg/650mg; 60 tablets) was 12.6% of the total, but this tendency decreased down to 7.13% in 2019. Note that the tramadol- dexketoprofen combination presented a continuous increase since its appearance on the market in 2017, representing about 6.5% of the total, and only available under the commercial tradename (75mg /25mg, 20 tablets).

Table 2
Variation (expressed as percentage of observed mean value during the analyzed period) for both indicators by API in La Gomera and in Spain.

	La Gomera		Spain
Subgroup / API	% packs	% DID	% DID
N02AA01-Morphine	2.22	1.83	1.58
N02AA03-Hydromorphone	0.09	0.12	0.29
N02AA05-Oxycodone	0.40	0.24	0.67
N02AA55-Oxycodone_Naloxone	1.58	2.71	3.49
N02AB02-Pethidine	0.02	< 0.001	0.02
N02AB03-Fentanyl	6.29	14.87	16.10
N02AE01-Buprenorphine	1.33	15.75	4.62
N02AJ13_Tramadol_Acetaminophen	63.35	34.73	49.43
N02AJ14_Tramadol_Dexketoprofen	6.12	3.98	1.27
N02AX02-Tramadol	13.80	19.96	17.58
N02AX06-Tapentadol	4.79	5.82	4.95

On the other hand, the consumption of buprenorphine is characterized by high-dose and long-acting preparations (transdermal patches, 70µg/h, 5 units), and low-doses and short-acting formulations (tablets, 0.2 mg, 20 units) accounted for 25% and 35% of the total N02AE consumption. The relationship between these two pharmaceutical forms has evolved over the years, from a 40/60 ratio in favor of the patches in 2016 until reaching a balance in 2019.

A change in tendency was also observed in morphine consumption, from 20.7 packs in 2016 to 13.9 in 2019, this represents a decrease of 29.6 %. The high-dose formulation (10 mg / 12 tablets) was the most consumed. Regarding oxycodone, a dramatic reduction in consumption was observed, with a decrease of 96% of the total of sold units in 2019 in comparison to the data observed in 2016. However, within the N02AA subgroup, oxycodone-naloxone consumption was rather stable, around 1.58% on average, being the high-dose and low-units per packages (10 mg/ 5mg and 20mg / 10mg with 28 tablets) the most demanded presentations. The presence of hydromorphone and pethidine were testimonial.

In the case of the fentanyl, the most frequently consumed pharmaceutical form throughout the study period were tablets (400 mg / 30 tablets) and patches (12mg and 25mg/ 5 units). The presence of fentanyl in the form of nasal spray was very low, 1.31% in 2019m its lower value against that of 8.5% in 2017.

Regarding the consumption of tramadol, the long-acting and high-dose (100 mg) tablets, under the presentation of 20 or 60 units and its generic equivalent represents, approximately, 13.8% of the total. However, the formulation at 50 mg dose of both products accounted for, around 15% in the first two years, passing to just over 30% in 2019, doubling its demand. In addition, it should be noted that the oral solution pharmaceutical form had a demand close to 13.3 % in the last two years, after reaching its peak in 2017 with 22.6% of the total. The tapentadol derivatives, under the presentation of 60 tablets and dose of 25/50/100 mg were the most consumed, in a 30%/40%/25% ratio, whereas the greater doses were below 5%. Finally, the combination of tramadol and dexketoprofen is remarkable for its increase in 2019, it almost doubled its consumption compared to 2017, the year of its introduction in the market, from 5.62% in 2017 to 10.29% in 2019.

Figure 3 shows the variation in overall DID in the island of La Gomera. This has varied from 13.83 DID in 2016 to 14.69 DID in 2019, which represented an increase of 6.2%, although remained rather steady throughout the last three years. However, the population only increased 2.64% (see Table 1) in the same period.

Figure 4 shows the evolution of the DID per quarter and year. The consumption per quarter presents fluctuations over the four-year period. The peak was reached in the third quarter of 2016, followed by a sharp decrease, and later DID increased in the following three quarters again. Nevertheless, from that time until the beginning of 2019, there is a continuous and slow decrease in DID, except in the second quarter of 2018 where a slight increase was observed, later returning to values close to 2016. The reason for this change in the tendency could be related with the introduction of the co-payment of medicines from pensioners, the age group most affected by pathologies related to pain; 21.4% of the population of La Gomera is over 65 years old, which represents more than 5 points compared to the average of the Canary Islands, 15.6% (Istac, 2020). In addition, the slight rebound in consumption observed during the second and subsequent quarters of 2019 could be related to the withdrawal of the co-payment mentioned above.

During this period, the most consumed subgroup was N02AJ, with tramadol in combination with acetaminophen with an average of 34.73% of total consumption (see Table 2). The following subgroup was the tramadol in monotherapy with 19.96%, followed by derivatives of the buprenorphine and the phenylpiperidine, with 15.75% and 14.87%, respectively. In the fifth position, we find tapentadol with 5.82%, followed by tramadol in combination with dexketoprofen, with just over 4% of the total. Among the natural opium alkaloids, the consumption of oxycodone-naloxone remained steady throughout the period, 2.71% on average, whereas there were fluctuations in the consumption of morphine, around 2%. The consumption of hydromorphone and oxycodone represented less than 0.4% of total consumption.

Data analysis at the township and health areas level

Data on consumption by therapeutic subgroup and API and year show that the combination of tramadol-acetaminophen is the number one choice, in all them, followed by the tramadol, fentanyl and tapentadol, whereas the consumption of API from N02AA subgroup was very low, less 4% of the total. A curious

observation, the consumption of oxycodone barely represents a dozen units, as occurred in the Alajeró, Hermigua or Vallehermoso townships. Tramadol in combination with dexketoprofen represented 10% of total consumption within N02AJ subgroup and very similar to those data observed for fentanyl, ranking fourth. However, tapentadol represents 25% of the total consumption within subgroup N02AX, being tramadol the most consumed. The presence of hydromorphone and pethidine is more than a testimonial.

Table 3 shows the obtained DID per township and year during the 2016–2019 period. The data shows the huge variability among all the townships. Alajeró and Hermigua, two of the smallest townships, approximately 2000 inhabitants each, show DID values above the annual DID at the island level. For example, Alajeró has an average DID of 5 points above that observed at the island level (Table 3). In contrast, the township of Valle Gran Rey, with half the population of the capital, and Vallehermoso, with just under 3,000 inhabitants, have lower DID. In 2019, the difference was almost 9 points (14.69 vs 5.90). A more detailed analysis shows that the main city constitutes 45% of the wholesales with 42% of the island's population. Alajeró together with Hermigua represent 14% of the island's population with a similar percentage of sales, around 9% each. Valle Gran Rey presents a slightly higher consumption in comparison with the total population, 20.9% vs 20.4%. An exceptional case is Vallehermoso Township where there has been a significant decrease in the sold units, from 113.4 packs in 2016 to 43.9 in 2019; this represents a decrease of 65.5%, while the population has also decreased, but a lesser degree, only 2.62%. The reason for this change in the tendency could be related with sociodemographic factors.

Table 3
Variation of DID by townships and year in the island of La Gomera during the 2016–2019 period.

Township	2016	2017	2018	2019
Agulo	12.76	13.95	16.56	14.67
Alajeró	18.28	18.15	17.55	18.75
Hermigua	15.62	15.50	19.97	20.61
San Sebastián	12.55	12.84	14.78	15.15
Valle Gran Rey	12.00	10.40	10.02	10.86
Vallehermoso	10.83	12.51	7.87	5.90
Island DID	13.83	14.59	14.45	14.69

Despite the differences in population and sold units between townships, differences in DID persist among the health areas (AEMPS, 2020), similar to what was individually observed for the townships. G01 area presents a 15.15 DID in 2019, while for the G04 area was 10.86 DID. Both areas have a similar “sold units / population” ratio and, therefore DID should be similar. However, this relationship is not enough to explain this difference. The explanation for it could found in the increase in consumption of those pharmaceutical preparations and presentations with higher DDD. For example, in 2019, the contribution to the total DID from formulations containing tramadol or in combination with acetaminophen and dexketoprofen was similar for both areas (8.08 vs 8.63). The number of sold units accounted for 83.04%

for G01 area compared to 91.25% for G04 one (582.1 vs 523.7 packs). Nonetheless, the contribution of the formulations that contain buprenorphine and fentanyl was 5.78 DID versus 1.54 DHD in G04 area. These two API have DDD very low (1.2 mg) in comparison with tramadol-acetaminophen (3 g). In sold units it represented 10.20% of the total for G01 area (71.5 packs), while for the G04 one was 4.43% (25.2 packs). This situation was repeated throughout the analyzed period with minor variations.

Comparative analysis with the nationwide data

The Spanish Agency for Medicines and Medical Devices (AEMPS) published in June 2019 its report on the "*Use of opioid drugs in Spain during the 2010–2019 period*" (AEMPS 2020a). According to this report, opioid consumption in Spain has increased from 10.03 DID in 2010 to 19.83 DID in 2019, doubling the value in a decade (AEMPS, 2020a), although in the last four years (2016 to 2019) the increase has been lower, 22.3%. This report includes all the subgroups listed in the N02A- category according to the ATC classification. In our study, we excluded the codeine combined with other analgesics since these drugs could be used in other pathologies (Jarlbaek 2019). Therefore, and for comparative purposes, the data of the nationwide report were re-analyzed to consider this fact (Fig. 3).

The recalculated DID varied from 14.75 in 2016 to 18.04 in 2019, values that are above the overall DID at an island level (see Fig. 2). During this period, the observed increase in La Gomera was 6.22%, three times lower than the nationwide, whereas the average increase of population was 2.64%. The nationwide data seems to suggest a greater consumption of opioids drugs but the increase of population does not justify enough this consumption.

The nationwide data indicates that tramadol with acetaminophen was the most consumed subgroup in Spain, around 50%, followed at a great distance by tramadol with 17.58% and fentanyl with 16.10%. The rest of the subgroup and API present percentages lower than 4%, with the exception of buprenorphine and tapentadol with 4.62 and 4.95%, respectively. (Table 2). This situation is very similar to those observed at the island, township and pharmaceutical areas level, tramadol with acetaminophen being the most consumed, while the order of the remaining groups is different depending on the analyzed geographic area. Therefore, there are no differences in terms of the more consumed groups. However, data analysis shows differences between geographic areas in function of DID. At the island level, the main group, tramadol-acetaminophen, contributes an average of 34.73% compared to 49.43% nationwide, (see Table 2), followed by the tramadol, which contributes with 19.96%, two and half points above the nationwide value. The contribution of the fentanyl was around 15% versus 16.10 nationwide, but with a positive tendency, an increase from 1.95 DID to 2.27 DID, during these four years was observed in La Gomera. The contribution of buprenorphine was three and a half times greater than in the rest of Spain (15.75 vs 4.62). It is important to notice the strong increase in the consumption of tramadol in combination with dexketoprofen, was three times greater in La Gomera than it was nationwide. The contribution of tapentadol was closer to 6%, against 4.95% in the rest of the country. Finally, the observed values for morphine and oxycodone in combination with naloxone presented percentages of 1.83 and 2.71% of the total.

Discussion

The obtained data with the two used parameters in this DUS seems to show different results and conclusions, so that both the classification by importance of consumption (expressed as packs/1000/year) and the percentage of each subgroup based on DID varied considerably (Table 2). This is because the two used parameters have different purposes. The use of the “sold units” indicator provides information on the guidelines for the use of a specific therapeutic subgroup within a defined geographical area, in our case, the island of La Gomera and its townships. For example, the tramadol-acetaminophen combination from N02AJ subgroup is the number one option throughout the island and townships, while hydromorphone and oxycodone are the least consumed, barely representing 0.5% of the total. The second option is the N02AX subgroup (tramadol) followed by fentanyl and / or buprenorphine, this order varies in some townships. All they show an increase in the consumption of tramadol in combination with dextetoprofen, displacing the natural opium derivatives. This difference in behavior is due to variations in the number of sold units that do not have to reflect a real variation in consumption.

At the island level, the tramadol-acetaminophen combination represents 63.35% of the total sold units, while in DID it represents 34.73%. Tramadol ranks second in both the number of sold units and its contribution to DID. Natural opium derivatives (subgroup N02AA) represent 4.30% of total consumption (and fourth place in order of consumption), being 5.19% in DID, thus ranking last. Buprenorphine represents only 1.33% of the sold unit's total, lower than morphine and oxycodone-naloxone, but it ranks third in its contribution to DID with 15.75%. For fentanyl, we have a percentage of 6.29% in the number of sold units, around 10% with respect to tramadol-acetaminophen, in comparison with 14.87% in DID, occupying the fourth position for DID.

Although data expressed in DID provides more accurate information on opioid consumption than simply using the number of sold units, the unexpected findings invite us to analyze the problem from other point of view, for example, by analyzing data on strong or weak opioids separately. Opioids are classified in two groups-the weak (tramadol in monotherapy and combinations) and the strong opioids (the remainders). The data analysis based on this classification shows that the weak opioids are the most consumed, especially, those presentations with lower-dose and lower number of units per package. So, tramadol in combination with acetaminophen for a dose of 37.5/325mg and 20 tablets, covered 74.13% of the total, compared to 13.25% for the presentation of 60 tablets. The remaining correspond to the great dose (75/650mg), although its percentage is decreasing. The most frequent dose and presentation for tramadol was 50 mg and 20 tablets, about 30%, in comparison with 15% of the 100 mg dose and 20 tablets. The oral solution pharmaceutical form also has a relevant and not insignificant role, an average of 13.3%.

In the case of strong opioids, the low-dose and low-unit for package is not always the most consumed form. In the case of fentanyl, the formulations with 400µg dose, 30 tablets, and the patches, especially, 12µg/h and 25µg/h doses and five units are the most frequent. Fentanyl under the form of nasal spray is minority due to its addiction problems (AEMPS, 2020b). A similar situation was observed with

buprenorphine, the patches and tablets being the pharmaceutical preparations the most consumed, representing 55% of the total. At present, the consumption of both pharmaceutical forms is very similar.

In the case of natural opium derivatives, we find that the first choice for morphine is tablets with 10mg doses and 12 or 60 units per packages; the oxycodone-naloxone combination predominate the high doses (10mg/5mg and 20mg/10mg) with 28 units per package. Hydromorphone consumed, around 80%, as tablets, 30 units and high-dose (8mg). In all cases, the high-dose was the first option.

The consumption of weak opioids (as DID) in Spain represents 68.28% of the total; tramadol in combination with acetaminophen was the most consumed, indicated in the treatment of moderate to severe intensity pain, whereas tramadol in monotherapy was the second option in severe pain. This tendency in consumption of tramadol is not an isolated event. The use of tramadol has increased worldwide during the last decades. For example, in Denmark, it increased twice its use from 2011 to 2013, (Muller et al. 2019), although a decline in tramadol use was observed from 2014 to 2019 (Sorensen et al. 2021).

In contrast, strong opioids represent 31.72% of the total, being fentanyl with 16.10% of the total, the most outstanding, followed by tapentadol (4.95%), buprenorphine (4.62%), oxycodone combined with naloxone (3.49%) and morphine (1.58%). All of them are prescript for the treatment of pain with very precise indications. Fentanyl is indicated for cancer patients with breakthrough pain or buprenorphine is indicated for the treatment of moderate to severe cancer pain and severe pain that does not respond to non-opioid analgesics (Dowell et al. 2016). A recent study reports a relevant use of fentanyl in noncancer patients (González-Bermejo et al. 2021). The easy administration of transdermal and transmucosal formulations could explain the increase in fentanyl consumption, particularly in Western and Northern European countries and also in Spain (Bosetti et al. 2019; González-Bermejo et al. 2021). Oxycodone-naloxone is indicated for the treatment of severe pain that can only be adequately treated with analgesics opioid, which explains its consumption.

If we compare these data with those obtained in the island of La Gomera we find a different consumption pattern. The weak opioids (as DID) represent 58.67% of the total, tramadol with acetaminophen being the most frequent, with 34.73%, approximately 10 points lower than in Spain whereas the percentage of tramadol in monotherapy is slightly higher in La Gomera (19.96 vs 17.58). The remainder corresponds to tramadol-dexketoprofen, which is three times higher in La Gomera than the nationwide level. However, the percentage of strong opioids represent 41.33%, higher than those observed at the nationwide, 31.72%. In this case, fentanyl and buprenorphine are the most consumed, approximately, an average of 15% of the total each. Between the natural opium derivatives have the morphine (1.83%) and oxycodone-naloxone (2.71%), although their percentages vary slightly, but their net contribution is the same, around 5%. The consumption of oxycodone, hydromorphone and pethidine barely represent 0.36% of the total, while in Spain reached values close to 1%.

This difference in consumption pattern could be related with sociodemographic characteristics and health-related factors among others. Approximately, the half of the population in La Gomera is located in

the main city with a high economic level with great access to all essential services, whereas the population in the smallest townships is very dispersed, far-away to essential service and oldest people. The proportions of 65 + aged people are 21.4% of the population of La Gomera, the second oldest in the Canary Islands after the island of El Hierro with 22.3% (Istac, 2020). The older people report more pain conditions, especially musculoskeletal pain, and more likely to be prescribed with opioids than younger population (Zin et al. 2014). This creates a dilemma for clinicians, they should prescribe the less potent opioids but with a few adverse effects. However, poorly controlled pain is a public health issue and the personal, familiar and societal cost cannot be measured, especially, at the older age group. All these factors should consider in the therapeutic strategy and if this fails to yield the desired results and/or the quality of patient life is additionally burdened, the overall strategy must be reviewed (O'Brien et al. 2017).

The use of health areas as criteria does not provide any relevant or additional information to those obtained when we refer to the townships for both indicators. This fact has been also observed on the island of El Hierro and the island of Fuerteventura, Canary Island (data not shown).

Conclusions

This work shows that the information provided by the wholesales in community pharmacies is valuable. To have access to reliable and detailed statistics on drug sales could be used in drug utilization research as an alternative database to those based on prescribing patterns among other criteria.

The data analysis shows different results depending on the used parameter: packs/1000/year or the DID. The N02AJ subgroup is the most consumed by the number of sold units as well as its contribution to overall DID with 34.73%, although lower than those observed nationwide are. The N02AX subgroup with tramadol is situated in the second place followed by the N02AE and N02AB subgroups with buprenorphine and fentanyl at the head.

The N02AA subgroup is the least consumed and with the lowest weight in the DID, just 4.90%.

This overall picture of opioid consumption appeared rather steady at the island, township and health areas level, although with small variations. Within the weak opioids, tramadol as monotherapy or in combination with acetaminophen and dexketoprofen, are the most consumed, always in presentations of low-doses and low number of units per package. Within the strong opioids, presentations with high-doses and the number of units per presentations are consumed, as in the case of buprenorphine and fentanyl. Both active ingredients are consumed almost equally either the form of patches and tablets.

The balance between uses of weak or strong opioids showed remarkable changes in La Gomera in comparison with the rest of Spain. Consumption of weak opioids was 58.67% versus 68.28 % in Spain, while consumption of strong opioids is superior to the average nationwide (41.33% vs 31.72%). This change could be associated with a change in prescribing patterns characterized by an increased prescription of high-dose and long-acting preparations and a decrease in the low-dose and short-acting formulations. Differences in the proportion of 65 + aged people in the populations could also play a role

in changing patterns of opioid use. A data, 21.4% of the population of La Gomera is over 65 years old, the second oldest in the Canary Islands, whereas the sociodemographic characteristics could explain the distribution of this age group between the different townships.

Declarations

Ethical Approval Not applicable

Consent to Participate Not applicable

Consent to Publish Not applicable

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Availability of data and materials

The data that support the findings of this study are available from COFARTE and COFARES, but restrictions apply to the availability of these data, which were used under licence for the current study, and so are not publicly available. Data are however available from the corresponding author upon reasonable request and with permission of COFARTE and COFARES.

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Figures

Figure 1

La Gomera Island with its six townships Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

Figure 2

Variation of the number of packs per 1000 inhabitants and year in the island of La Gomera over a four-year period (2016-2019)

Figure 3

Evolution of the DID at La Gomera and nationwide during the analyzed period.

Figure 4

Evolution of the DID per quarter and year in the island of La Gomera.