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DETERMINATION OF PATIENT DOSAGE PROFICIENCY REGARDING PARACETAMOL-CONTAINING PRODUCTS AND RELATION TO SOCIO-DEMOGRAPHIC FACTORS IN THE TSHWANE DISTRICT, SOUTH AFRICA.

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ABSTRACT

Paracetamol is an active pharmaceutical ingredient used for the treatment of pain and fever. Consuming more than the recommended dose of paracetamol leads to hepatic- and renal toxicity. In South Africa paracetamol is easily available due to its assigned medicine scheduling status.The aim was to determine the dosage calculation proficiency of patients using paracetamol-containing products attending family medicine clinics in the Tshwane district, South Africa and to relate this to socio-demographic factors. This was a cross-sectional, descriptive observational study conducted in the Tshwane district at Pretoria West Hospital, Steve Biko Academic Hospital, Tshwane District Hospital and Kalafong Academic Hospital in Gauteng, South Africa. Semi-closed ended questionnaires were distributed to patients attending Family Medicine Outpatient departments (1 January 2016 to 31 May 2016).Only patientsconversantin the English language were included in the study.Descriptive statistics from the questionnaires were presented as frequency counts, percentages and cross tables.All exploratory testing was done at the 0.05 level of significance.Significant differences were observed between sex (p=0.029) and household income brackets (p=0.031). The participants alluded to using 50 unique paracetamol-containing products and 55% indicated the use of more than one such product in the recent past. Regarding proficiency in calculating the correct dose of paracetamol, 97% of the participants are at risk for possible overdose.It is proposed that the scheduling status of paracetamol-containing products be revisited.

1. Background

Paracetamol (also known as N-acetyl-*p*-aminophenol, APAP, Acetaminophen, or PARA) is the active pharmaceutical ingredient of products used in the treatment of pain and fever in both adults and children(Monthly Index of Medical Specialities, 2014). The maximum suggested dosage of paracetamol is 4 g/day in adults and 50-75 mg/kg/day in children (Mazaleuskaya et al., 2013). Consuming more than the recommended amount of paracetamol leads to toxic effects due to the highly active metabolite that is formed once metabolism has occurred(Lancaster et al., 2015). The active metabolite, known as N-acetyl-*p*-benzoquinone imine or NAPQI, is known to cause liver and kidney damage(Moyer et al., 2011).

Paracetamol is marketed in tablet, capsule, syrup, paediatric drops, suppositories or intravenous dosage formulations. Additionally it is available in various generic product formulations(Monthly Index of Medical Specialities, 2014). Brand name products and generic products are bioequivalent regarding the route of administration, dosage formulation, strength, safety, quality, efficacy and intended use(United States Food and Drug Administration, 2015). Brand name products are often substituted by its generic counterpart because of the associated lower costs and the benefit of the active pharmaceutical ingredients and chemical structures which are identical(United States Food and Drug Administration, 2015). Paracetamol is not always the only active compound present in medicine formulations. It is frequently combined with other active pharmaceutical ingredients to extend the indications, or enhance the synergism of such products. The combination of multiple active pharmaceutical ingredients enables the consumer to take one dosage formulation instead of numerous individual products, thereby ensuring patient compliance(Medicines and Related Substances Act, 2015).

Both intentional and accidental overdose of paracetamol is common. In addition, certain disease states and pathological conditions alter the pharmacokinetics and dynamics of a drug, thereby resulting in unforeseen

toxic effects leading to unintentional overdose. Hepatotoxicity due to paracetamol overdose may be exacerbated in patients who are predisposed to diminished glutathione stores, as this will result in an overproduction of NAPQI. This includes individuals who are malnourished, are in a fasting state, have chronic liver disease, are chronic alcohol consumers, or taking any medication which may induce hepatic CYP450 enzymes(Lancaster et al., 2015).

Paracetamol has been documented as the leading pharmaceutical product responsible for overdosing in the United Kingdom, the United States of America and in Australia(Lee, 2004; National Poisons Information Service UK, 2013; Wong et al., 2014).In America this equates to more than 100 000 cases of paracetamol overdose annually; of which 56 000 were emergency room visits, 2600 hospitalizations and 460 deaths(Joseph, 2014; Lee, 2004). Furthermore, 8000 Australians are treated for paracetamol overdose yearly, mostly taken to inflict self-harm(Kristen, 2014).

In South Africa medications with a scheduling status of schedule 0 to schedule 2 can be acquired without a prescription as an over-the-counter (OTC) product(Orsmon, 2014). These medications are indicated for slight illnesses or symptoms which can be easily recognized by patients. Schedule 0 medications can be obtained from general retail outlets, whereas schedule 1 and schedule 2 medications are limited to pharmacies and other licensed dispensaries(Orsmon, 2014). Products with a scheduling status of schedule 3 and higher are restricted to licensed dispensaries and requires a prescription to be obtained(Medicines and Related Substances Act, 2015). Consequently, single active ingredient medications containing 500 mg of paracetamol per unit can be acquired without a prescription in multitudinous instances. Additionally, many paracetamol-combination products are available on the market. As indicated in the Monthly Index of Medical Specialities (MIMS) and MIMS Over-The-Counter (OTC)there are 143 registered paracetamol-containing products available on the South African market alone(Monthly Index of Medical Specialities, 2014; Monthly Index of Medical Specialities OTC, 2012; The MIMS Desk Reference, 2015).

The aim was to determine the dosage calculation proficiency of patients using paracetamol-containing products attending family medicine clinics in the Tshwane district, South Africa and to relate this to socio-demographic factors

2. Materials and methods

This was a cross-sectional, descriptive observational study conducted in the Tshwane district at Pretoria West Hospital, Steve Biko Academic Hospital, Tshwane District Hospital and Kalafong Academic Hospital in Gauteng, South Africa.Ethical approval was obtained from the Faculty of Health Sciences Research Ethics Committee (FHSREC) of the University of Pretoria (project number 441/2015) to conduct the study. All the required consent forms and questionnaires were designed in accordance with the FHSREC regulations. Signed written approval was obtained from the hospital CEO's.

2.1 Questionnaire

Semi-closed ended questionnairesweredistributed topatients attending Family Medicine Outpatient departments over a five-month period (1 January 2016 to 31 May 2016).The questionnaire, participant information leaflets and consent forms were paper-based and only available in English.Participants were assured of their anonymity and had to sign informed consent. Only participants above the age of 18 years, and those conversant in the English language wereincluded in the study. The researcher was present during the completion of questionnaires and thoroughly explained all the questions to the participants. Demographical details of all participants were documented. Participants were allowed to complete the questionnaire in their own time while they were waiting in the designated queueing area of the clinic. The participantshad to complete the questionnaire individually and received no remuneration for taking part in the study.

In order to assess how many paracetamol-containing products the participants were using, they were given a list of commercially available products.A populated paracetamol-containing product list was constructed using the MIMS, MIMS-OTC and the MIMS Desk Reference (Monthly Index of Medical Specialities, 2014; Monthly Index of Medical Specialities OTC, 2012; The MIMS Desk Reference, 2015). This list contained 143 branded paracetamol products. Furthermore, the means of acquisition was assessed.

To establish a participant's ability to understand the concept regarding the recommended dosing and possible overdoses, a practical scenario was embedded in the questionnaire. The scenario was based on the usage of a 500 mg and a 200 mg paracetamol tablet (Figure 1). All the information was presented as it would have been in a standard package insert. Additionally, the maximum recommended dose of paracetamol in a 24-hour period was stated *de facto*. Five statements followed the scenario, where participants had to indicate which of the given options would be acceptable, based on the supplied information.These statements were designed to replicate real life situations to identify possible challenges patients are predisposed to when taking medication.

2.2 Statistical analysis

Descriptive statistics from the questionnaires were presented as frequency counts, percentages and cross tables. Discrete outcomes (sex, understanding package insert instructions, educational status, purchase behaviour, marital status and race) were reported with a 95% confidence interval. Age was the only continuous variable and data was summarized as the mean ± standard deviation. All exploratory testing was done at the 0.05 level of significance. Data analysis was carried out using Stata Release 13 and 14 statistical solutions software.

3. Results and discussion

3.1 Socio-demographic information

A total of 100 respondents completed the semi-closed ended questionnaire. Steve Biko Academic Hospital refers all family medicine outpatients to Tshwane District Hospital, which is in adjacent proximity to each other. In order to maintain the principle of equal probability, 50 participants were sourced from Tshwane District Hospital, and 25 each from Pretoria West – and Kalafong Academic Hospital. The male to female ratio was 1:1.1 (Table 1). Thirty-one percent of the respondents were low income pensioners above the age of 51 years. African participants represented 54% and Caucasian participants 37% of the study population. Nearly half (44%) of the study population indicated that they were married.

Figure 1.The scenario based question used to assess the participants' calculation proficiency with regards to paracetamol use.

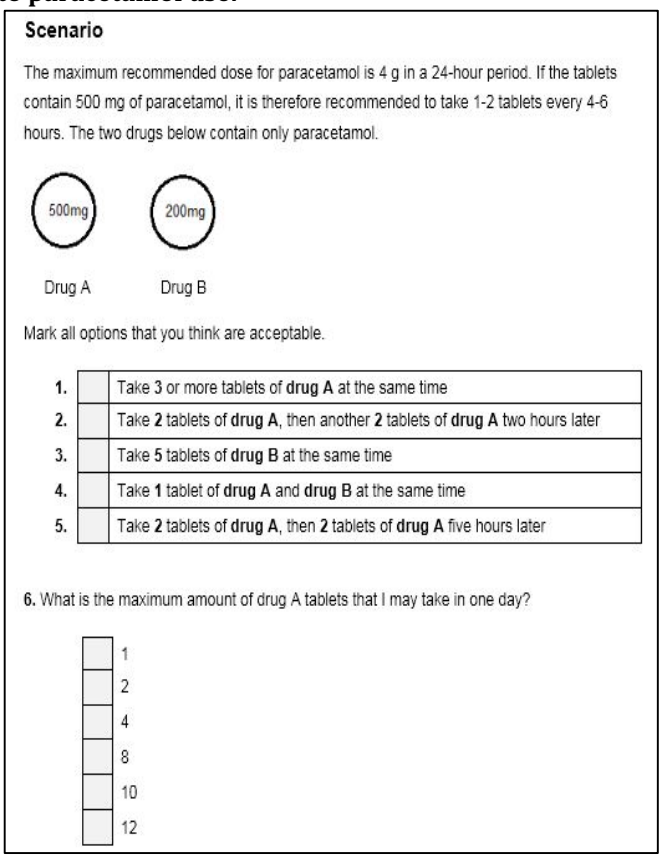

Table 1. Socio-demographic profile of patients attending family medicine clinics in the Tshwane district.

Socio-demographic information	Female [percentage, (n)]	Male [percentage, (n)]	Total [percentage, (n)]
Number of patients	100.00 (53)	100.00 (47)	100.00 (100)
Age			
21 - 30	20.75 (11)	34.04 (16)	27.00 (27)
31 - 40	24.53 (13)	29.79 (14)	27.00 (27)
41 - 50	18.87 (10)	10.64 (5)	15.00 (15)
> 50	35.85 (19)	25.53 (12)	31.00 (31)
Race			
African	52.83 (28)	55.32 (26)	54.00 (54)
Caucasian	41.51 (22)	31.91 (15)	37.00 (37)
Indian	1.89 (1)	0.0 (0)	1.00 (1)
Coloured	3.77 (2)	10.64 (5)	7.00 (7)
Other	0.0 (0)	2.13 (1)	1.00 (1)
Primary language			
Afrikaans	33.96 (18)	38.30 (18)	36.00 (36)
English	22.64 (12)	23.40 (11)	23.00 (23)
African language	43.40 (23)	38.30 (18)	41.00 (41)
Employment status			
Unemployed	54.72 (29)	48.94 (23)	52.00 (52)
Employed	54.28 (24)	51.06 (24)	48.00 (48)
Education level			
Low	18.87 (10)	19.15 (9)	19.00 (19)
Moderate	75.47 (40)	72.34 (34)	74.00 (74)
High	5.66 (3)	8.51 (4)	7.00 (7)
Annual income bracket			
< ZAR20 000	47.17 (25)	42.55 (20)	45.00 (45)
ZAR20 000 - ZAR50 000	24.53 (13)	34.04 (16)	29.00 (29)
ZAR50 000 - ZAR100 000	11.32 (6)	8.51 (4)	10.00 (10)
> ZAR100 000	16.98 (9)	14.90 (7)	16.00 (16)
Internet access			
No access	50.94 (27)	55.32 (26)	53.00 (53)
Access	49.06 (26)	44.68 (21)	47.00 (47)
Marital status			
Single	35.85 (19)	40.43 (19)	38.00 (38)
Married	39.62 (21)	48.94 (23)	44.00 (44)
Divorced	15.09 (8)	6.38 (3)	11.00 (11)
Widowed	9.43 (5)	4.26 (2)	7.00 (7)

Forty-one percent of the respondents preferred to speak an indigenous African language, while 36% were Afrikaans and 23% English. The level of education was grouped into three categories namely: low (no education and primary school), medium (Grade 12, college certificate or diploma) and high (bachelor's degree or postgraduate degree). Almost three quarters (74%) of the participants had a medium level of education, while those with low and high accounted for 19% and 7% of the study population, respectively (Table 1).

Fifty-two percent of the participants were unemployed, which is higher than, the current average nationalSouth African statistics of 26.7%(Statistics South Africa, 2016). Sixteen percent of the participants had an annual income of more than ZAR100,000.00 which is in accordance with national statistics(Statistics South Africa, 2011). Those participants earning a yearly family income of less than ZAR20,000.00consisted of 45% of the study population (Table 1). The high percentage of unemployed and low income participants could be attributed to public hospitals being their only option to access healthcare, whereas high-income participants tend to make use of the private healthcare system. Provided that the majority were unemployed and earning a low income, more than half (53%) of the interviewed participants had no internet access.

3.2 Paracetamol-containing product usage

The 100 respondents indicated the use of one or a combination of 50 unique indexed items from the list of 143 paracetamol-containing products. Between one and six paracetamol-containing products were indicated as being used byeach of the participants.Although the median number of products used was 2.0 with interquartile (IQR) range of 1.0 to 3.0, more than half (55%) of the participants alluded to using more than one paracetamol-containing product within two weeks prior to questioning. No literature could be found to directly compare the number of paracetamol products used by participants attending outpatient clinics. However, recent data from an acute liver failure study group in North America revealed that the median number of paracetamol-containing products used by this cohort was 4.0 (IQR, 2.0 to 6.0)(Serper et al., 2016). Although this was higher than the current study, the North American data represented patients admitted for paracetamol overdose, and not patients attending outpatient clinics.

Graudins (2015)reported that 29% of adult admissions for paracetamol overdose, were the result of the simultaneous paracetamol-combination product ingestion of the selected 50 paracetamol-containing products, it was determined that the five most commonly usedproducts werePanado® tablets, Grand-pa® powders, Myprodol® capsules, Sinucon® tablets and Sinumax® tablets(Table 2). The majority of respondents (78%) indicated using Panado® tablets (500 mg paracetamol per tablet). The use of this branded product was triple that of Grand-pa® powders (324 mg paracetamol per 842.4 mg sachet), and nearly eight times (7.8) greater than Myprodol® capsules (250 mg per capsule), Sinucon®

tablets (200 mg paracetamol per tablet) and Sinumax® tablets (500 mg paracetamol per tablet). The majority (60%) of respondents admitted using paracetamol-containing products at least once a week, 18% expressed regular daily use whereas only 10% proclaimed to virtually never use paracetamol-containing products.

Table 2. Paracetamol usage patterns as pertaining to sex.

Paracetamol-containing product usage information	Female [percentage (n)]	Male [percentage (n)]	Total [percentage (n)]
Score obtained for questionnaire scenario			
1 (17%)	1.89 (1)	12.77 (6)	7.00 (7)
2 (33%)	11.32 (6)	27.66 (13)	19.00 (19)
3 (50%)	56.60 (30)	31.91 (15)	45.00 (45)
4 (67%)	20.75 (11)	17.02 (8)	19.00 (19)
5 (83%)	5.66 (3)	8.51 (4)	7.00 (7)
6 (100%)	3.77 (2)	2.13 (1)	3.00 (3)
Frequency of paracetamol-containing product use			
Everyday	16.98 (9)	19.15 (9)	18.00 (18)
Once a week	43.40 (23)	40.43 (19)	42.00 (42)
Once a month	26.42 (14)	34.04 (16)	30.00 (30)
Almost never	13.21 (7)	6.38 (3)	10.00 (10)
Offering medication to other people			
No	32.08 (17)	46.81 (22)	39.00 (39)
Yes	67.92 (36)	53.19 (25)	61.00 (61)
Top five paracetamol brands used			
Panado® tablets	31.97 (39)	36.79 (39)	34.21 (78)
Grand-pa® powders	6.56 (8)	16.98 (18)	11.40 (26)
Myprodol® capsules	6.56 (8)	1.89 (2)	4.39 (10)
Sinucon® tablets	6.56 (8)	1.89 (2)	4.39 (10)
Sinumax® tablets	4.92 (6)	3.77 (4)	4.39 (10)
Other drugs	43.44 (53)	38.68 (41)	41.23 (94)
Paracetamol-containing products obtained from			
Hospital	23.77 (29)	16.98 (18)	20.61 (47)
Doctor	0.00 (0)	0.94 (1)	0.44 (1)
Retail outlets	24.59 (30)	41.51 (44)	32.46 (74)
Pharmacy	45.08 (55)	33.02 (35)	39.47 (90)
Combinations of the above	6.56 (8)	7.54 (8)	7.01 (16)

No literature could be found regarding the percentage of patients using 500 mg paracetamol tablets for comparative purposes. However in Ireland, of all the paracetamol-containing products dispensed, 31% contained 500 mg paracetamol(Usher et al., 2005). This data excludes the proportion of paracetamol-containing products sold at retail outlets in Ireland.

More than half (54.82%) of the paracetamol-containing products were listed in schedule 0, and 30.7% in schedule 2. The products classified in schedule 1 (2.63%), schedule 3 (8.33%) and schedule 5 (3.51%) totalled 14.48%. It is thus evident that nearly 55% of all the paracetamol-containing products (schedule 0) are obtained without any limit being set on the quantity. Moderate limits on the quantity being supplied (33.3%) for schedule 1 and schedule 2 is set, but participants can however circumvent this by purchasing products from different pharmacies. Only 11.8% of paracetamol-containing products require a prescription (schedule 3 and schedule 5) and can therefore be controlled.

The means by which participants acquired the 50 identified paracetamol-containing products included licensed dispensaries (hospital, pharmacy and doctor or dentist) and general retail outlets (supermarket, café, gas station, street vendor and family or friends). Pharmacies were the main source for obtaining paracetamol-containing products (39.47%), which was followed by retail outlets (32.46%) and hospitals (20.61%). Only one product (0.44%) was obtained from a dispensing doctor and approximately 7% of these products were gathered from multiple access points (Table 2). Of the latter, 4.81% included licensed dispensaries and 2.19% retail outlets. It was evident that licensed dispensaries accounted for the distribution of 64.9% of all paracetamol-containing products, while non-licensed access points amounted to approximately 40%. With no significant differences between sex, age and race, 61% of the participants indicated that they offer some of their medication to either family or friends (Table 2). Of these participants, 94% indicated to do so without permission from a healthcare professional. Although females alluded to offer their medication more frequently compared to males, the difference in frequency did not reach significance ($p=0.096$).

3.3 Dosage calculation proficiency

With regards to participant's proficiencyof calculating the correct dose of paracetamol intake, the scenario set in Figure 1 is applicable.Question 5 was the only question to be answered correctly by more than a third of the participants. For question 4, 32% of the respondents were able to indicate the correct option, followed by question 2 (28%), question 6 (21%), question 3 (19%) and question 1 (13%). A score of five points and higher was deemed as proficient with regards to dosing calculations. Individuals with more than one incorrect answer were considered prone to supra-therapeutic ingestion as two and more incorrect answers are indicative of overdosing in the questionnaire scenario.Only 3% of the participants were able to answer all the questions correctly, with 10% being regarded as calculation proficient and are therefore at a lower risk of supra-therapeutic ingestion of paracetamol.

Twenty-one percent of participants were able to correctly calculate the maximum recommended daily dose, whereas 72% indicated a lower maximum dosage within 24 hours. In a study conducted by Shone and co-workers (2011)it was shown that 53% of young adolescents between the age of 16 and 23 were able to correctly identify the maximum daily dose, with 23% indicating a dose lower than the recommended daily maximum. A higher proportion correctly identified the maximum daily dose when compared to the current study, which may be ascribed to participants being older. It was clear that the participants had difficulty in converting mg to g (1000 mg = 1 g), which was one of the key concepts required to answer the questions correctly. Furthermore, the statement "take 1-2 tablets every 4-6 hours" led to confusion among the participants and resulted in poor scores. Participants relied on the tablet quantity and hourly guidelines, which led to misinterpretation of two tablets every four hours or one tablet every six hours. Furthermore, is it possible that some participants with primary education (19% of the study population) are not cognisant of the fact that "one day" resembles 24 hours.Hence "24 hours" should rather be referred to instead of "one day" to prevent further confusion.

It was anticipated that the level of education would correlate with the dosage calculating proficiencyof

paracetamol (questionnaire score).No statistical significant difference (p=0.713) in scores was obtained, which is contradictory to what has been postulated in non-related studies(van der Heide et al., 2013). Notwithstanding the fact that 7% of the participants were regarded as having a high educational level, literature supports that participants in general have a limited health literacy, predisposing them to medication and dosing errors(King et al., 2011; Shone et al., 2011).

Employment status did not have any significant differences (p=0.429) on the scores obtained. However, when comparing the annual household income, a compelling difference (p=0.031) was observed. A possible explanation could be that participants with higher incomes are able to gain access to more information with regards to medication. This phenomenon needs to be further investigated, since there was no difference (p=0.563) between participants who had internet access and those who did not. Nonetheless, participants with internet access were deemed 13.04% calculation proficient, compared to 7.55% for those without a regular internet connection.

Classifying participants as being 'calculation proficient' regarding paracetamol dosingbased on product intake frequency also proved to be non-significant (p=0.56). Twenty percent of respondents using paracetamol once a month were regarded as being calculation proficient, whereas daily use, once a week and almost never constituted16.67%, 7.38% and 0% of those considered calculation proficient. It is postulated that the participants who indicated the use of paracetamol-containing products only once a month, were more cautious and cognisant of the risks associated with medication.

As to age, participants older than 50 years appeared more calculation proficient with regards to paracetamol dosing (25.81%) compared to their younger counterparts. A possible explanation could be that older people are more acquainted with the use of paracetamol-containing products. However, the different scores obtained between the age groups alluded to be non-significant (p=0.806).Significant differences (p=0.029) were observed between males and females with a score ofthree or more being obtained by 86.79% of females compared to 40.43% for males. Married participants tended to use more paracetamol-containing products compared to single, divorced and widowed participants (p=0.06). The finding of woman obtaining higher general scores than men could be the result of females fulfilling a caregiver role and mostly being responsible for administering medication to their families, i.e. using such medications more frequently.Two independent studies, based in America, evaluated 169 and 565 high school students respectively with regards to their proficiency of paracetamol dosages and warnings by means of a questionnaire. No significant differences with regards to sex or age were found (Gilbertson et al., 1996; Myers et al., 1992).

3.4 Paracetamol-containing products in South Africa

The 143 identified paracetamol-containing productsconsisted of 11 different pharmaceutical dosage formulations. The most prolific delivery system constituted tablet formulations (44.75%), followed by capsules (21.64%) and syrups (18.89%). Caplets, drops, effervescent tablets, intravenous infusions, liquids, powders, suppositories and suspensions made up the remaining 16.08% of the dosage formulations.The majority (84.62%) of the identified products were combination preparations, of which 63.64%were categorized as schedule 2. Combination paracetamol preparations listed in schedule 1 only accounted for 2.09% of the total identified brands.

Oral dosage formulations (95.8%) are the preferred administration vehicle, since it can be executed effortlessly. Patients experiencing difficulty in swallowing tablets or capsules may use syrups and liquids as a suitable alternative, thereby explaining the high representative quantities of oral dosage formulations. More complex dosage formulations such as intravenous infusions, are usually administered by healthcare professionals rather than consumers themselves. Likewise, suppositories are mostly reserved for children or debilitated adults which explain the low representative numbers for these formulations.

Schedule 0 paracetamol-containing substances (16.8%) are the principle reason for concern as a result of their unrestricted accessibility and ease of acquisition through non-regulated retail outlets(O'Rourke et al., 2002). When including products from schedule 1 (2.1%) and schedule 2 (55.2%), which is partly controlled by pharmacy regulations, an additional 57.3% of products is readily obtainable by consumers. This implies that 74.1% of all paracetamol-containing products registered in South Africa are available in "unlimited" quantities without requiring a prescription. Limited data is available with regards to the paracetamol overdose incidence in South Africa. The lack of reported data can be ascribed to incomplete and missing patient record data (Wegner and Rhoda, 2013). However, Laubscher and co-workers (2007) reported that during 2005, 20.4% of all overdose cases presented at the Paarl Hospital in South Africa were due to paracetamol ingestion.Currently there are ongoing pilot studies conducted to determine preliminary data for overdoses in South Africa related to paracetamol intake.During 2012 researchers based in Iceland reported similar findings, revealing that 18% of all overdose cases were linked to paracetamol (Kjartansdottir et al., 2012).

The Irish Medicines Board allows for products containing 500 mg paracetamol to be distributed from general retail outlets provided that each primary pack does not contain more than 6 g (12 tablets) of paracetamol(Irish Medicines Board Act No 29 of 1995, 2016; Laffoy, 2000). If the same product is sold in a pharmacy under supervision, the maximum quantity may not exceed 12 g (24 tablets) of paracetamol per pack. Prescriptions are required when quantities exceeding 25 g (50 tablets) need to be dispensed(Irish Medicines Board Act No 29 of 1995, 2016; Laffoy, 2000). Compared to Ireland, South African regulations allow for more than double (12.5 g compared to 6 g) the amount of paracetamol per primary pack sold from retail outlets. Schedule 0 paracetamol-containing products in South Africa are therefore regulated as pharmacy only products in Ireland.

Since 2011 the United States FDA has implemented a regulation instructing pharmaceutical manufacturers to refrain from producing combination analgesics containing more than 325 mg paracetamol per dosage unit, regardless of the dosage formulation(United States Food and Drug Administration, 2014b). This regulation was introduced due to the high incidence of acute liver failure

resulting from paracetamol ingestion in the US(Lee, 2004; United States Food and Drug Administration, 2014a). The aim was to remove all non-compliant products from the US market by January 2014. Consequently the FDA has advised healthcare professionals to stop dispensing these combination products(United States Food and Drug Administration, 2014a; United States Food and Drug Administration, 2014b). When a pharmacist is presented with a prescription listing a product containing more than 325 mg paracetamol, they are obliged to contact the prescriber and discuss a more suitable medicinal product(United States Food and Drug Administration, 2014a). If South Africa had to comply with the US FDA regulations, approximately 31% of the currently available paracetamol-containing products would have to be reformulated.

3.5 Study limitations

The study population included limitedamounts of patients from ethnic groups other than African or Caucasian. Only patients conversant in English were included in this study. Furthermore, the study was conducted in a public health setting, therefore favoring participants with a lower level of income.

4. Conclusions

No significant differences were observed in the level of dosage calculation proficiency of paracetamol intake between the age groups, marital status, the level of education, employment status and access to internet facilities. The participants alluded to using 50 unique paracetamol-containing products and 55% indicated using more than one paracetamol-containing product in the recent past. Regarding dosage calculation proficiency of paracetamol intake, 97% of the participants were at risk for possible overdose.

Recommendations

It is proposed that the scheduling status of paracetamol-containing products be revisited. Stricter regulations governing paracetamol aresuggested as these products are easily accessible to a population who is not always proficient in calculating the correct dosage. In so doing the possibility of overdosing on paracetamol via incorrect usage may be reduced.

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CONFLICT OF INTEREST

The authors declare no competing interests.

REFERENCES

1. Gilbertson, R. J., Harris, E., Pandey, S. K., Kelly, P., Myers, W., 1996. Paracetamol use, availability, and knowledge of toxicity among British and American adolescents. Arch Dis Child. 75**,** 194-198.
2. Graudins, A., 2015. Paracetamol poisoning in adolescents in an Australian setting: Not quite adults. Emerg Med Australas. 27**,** 139-144.
3. Irish Medicines Board Act No 29 of 1995. Medicinal Products (Control of Paracetamol) Regulations, 2001. S.I. No. 150/2001. Ireland, 2016.
4. Joseph, M., FDA Finally Changes Prescription Recommendations for High-Dose Acetaminophen. Available from: http://articles.mercola.com/sites/articles/archive/2014/03/26/acetaminophen-overdose.aspx[accessed 4 May 2015].
5. King, J. P., Davis, T. C., Bailey, S. C., Jacobson, K. L., Hedlund, L. A., Di Francesco, L., et al., 2011. Developing consumer-centered, nonprescription drug labeling a study in acetaminophen. Am J Prev Med. 40**,** 593-8.
6. Kjartansdottir, I., Bergmann, O. M., Arnadottir, R. S., Björnsson, E. S., 2012. Paracetamol intoxications: a retrospective population-based study in Iceland. Scand J Gastroenterol. 47**,** 1344-1352.
7. Kristen, A., Paracetamol 'poisons hundreds of Australians every week'. Available from: http://coach.ninemsn.com.au/2015/02/16/17/11/paracetamol-poisons-hundreds-of-australians-every-week[accessed 4 May 2015].
8. Laffoy, M. S., E. Byrne, G., Paracetamol availability and overdose in Ireland. Eastern Regional Health Authority, Dr. Steeven's Hospital, Ireland, 2000, 1-7.
9. Lancaster, E. M., Hiatt, J. R., Zarrinpar, A., 2015. Acetaminophen hepatotoxicity: an updated review. Arch Toxicol. 89**,** 193-9.
10. Laubscher, C., Van Rooyen, E. E., 2007. The profile of the overdose patient presenting to Paarl Hospital Emergency Department. S Afr Fam Pract. 49**,** 16.
11. Lee, W. M., 2004. Acetaminophen and the U.S. Acute Liver Failure Study Group: lowering the risks of hepatic failure. Hepatology. 40**,** 6-9.
12. Mazaleuskaya, L., Sangkuhl, K., Thorn, C., FitzGerald, G., Altman, R., Klein, T., Acetaminophen Pathway (therapeutic doses), Pharmacokinetics. Available from: https://www.pharmgkb.org/pathway/PA165986279 [accessed 22 March 2015].
13. Medicines and Related Substances Act. Schedules. Act 101 of 1965. South Africa, 2015
14. Monthly Index of Medical Specialities. Vol. 53(11), South Africa, 2014.
15. Monthly Index of Medical Specialities OTC. Vol. 18(1), South Africa, 2012.
16. Moyer, A. M., Fridley, B. L., Jenkins, G. D., Batzler, A. J., Pelleymounter, L. L., Kalari, K. R., et al., 2011. Acetaminophen-NAPQI Hepatotoxicity: A Cell Line Model System Genome-Wide Association Study. Toxicol Sci. 120**,** 33-41.
17. Myers, W. C., Otto, T. A., Harris, E., Diaco, D., Moreno, A., 1992. Acetaminophen overdose as a suicidal gesture: a survey of adolescents' knowledge of its potential for toxicity. J Am Acad Child Adolesc Psychiatry. 31**,** 686-690.
18. National Poisons Information Service UK, Annual Report. In: Health, D. o., (Ed.). Public Health England, England, 2013, 15-16.
19. O'Rourke, M., Garland, M. R., McCormick, P. A., 2002. Ease of access is a principal factor in the frequency of paracetamol overdose. Ir J Med Sci. 171**,** 148-150.
20. Orsmon, L., 2014. Understanding the medicine schedules. S Afr Pharm Assist. 14**,** 2-6.
21. Serper, M., Wolf, M. S., Parikh, N. A., Tillman, H., Lee, W. M., Ganger, D. R., 2016. Risk Factors, Clinical Presentation, and Outcomes in Overdose With Acetaminophen Alone or With Combination Products: Results From the Acute Liver Failure Study Group. J Clin Gastroenterol. 50**,** 85-91.
22. Shone, L. P., King, J. P., Doane, C., Wilson, K. M., Wolf, M. S., 2011. Misunderstanding and potential unintended

misuse of acetaminophen among adolescents and young adults. J Health Commun. 16 Suppl 3**,** 256-67.
23. Statistics South Africa, Income and Expenditure of Households 2010/2011. South Africa, 2011, 9.
24. Statistics South Africa, Quarterly Labour Force Survey - Quarter 1, 2016. South Africa, 2016, xiv.
25. The MIMS Desk Reference. Vol. 49(1), South Africa, 2015.
26. United States Food and Drug Administration, Acetaminophen Prescription Combination Drug Products with more than 325 mg: FDA Statement - Recommendation to Discontinue Prescribing and Dispensing. Available from: http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm381650.htm [accessed 5 May 2016].
27. United States Food and Drug Administration, All manufacturers of prescription combination drug products with more than 325 mg of acetaminophen have discontinued marketing. Available from: http://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm390509.htm [accessed 18 March 2015].
28. United States Food and Drug Administration, 2016. What Are Generic Drugs? Available from: http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/ucm144456.htm [accessed 10 July 2016].
29. Usher, C., Teeling, M., Bennett, K., McGowan, B., Feely, J., 2005. Usage of paracetamol-containing combination analgesics remains high in primary care. Br J Clin Pharmacol. 60**,** 648-652.
30. van der Heide, I., Wang, J., Droomers, M., Spreeuwenberg, P., Rademakers, J., Uiters, E., 2013. The relationship between health, education, and health literacy: results from the Dutch Adult Literacy and Life Skills Survey. J Health Commun. 18 Suppl 1**,** 172-84.
31. Wegner, L., Rhoda, A., 2013. Missing medical records: An obstacle to archival survey-research in a rural community in South Africa. S Afr J Physiother. 69**,** 15-19.
32. Wong, A., Graudins, A., Kerr, F., Greene, S. L., 2014. Paracetamol toxicity: What would be the implications of a change in Australian treatment guidelines? Emerg Med Australas. 26**,** 183-187.