A peer-reviewed version of this preprint was published in PeerJ on 28 July 2016.

View the peer-reviewed version (peerj.com/articles/2255), which is the preferred citable publication unless you specifically need to cite this preprint.

Castillo-Guzman S, González-Santiago O, Delgado-Leal IA, Lozano-Luévano GE, Reyes-Rodríguez MJ, Elizondo-Solis CV, Nava-Obregón TA, Palacios-Ríos D. 2016. Perception of the risk of adverse reactions to analgesics: differences between medical students and residents. PeerJ 4:e2255 https://doi.org/10.7717/peerj.2255

Perception of the risk of adverse reactions to analgesics: Differences between medical students and residents

Sandra Castillo-Guzman, Omar González-Santiago, Ismael A Delgado-Leal, Gerardo E Lozano-Luévano, Misael J Reyes-Rodríguez, Cesar V Elizondo-Solís, Teresa A Nava-Obregón, Dionicio Palacios-Ríos

Background. Medications are not exempt from adverse drug reactions (ADR) and how the physician perceives the risk of prescription drugs could influence their availability to report ADR and their prescription behavior. **Methods.** We assess the perception of risk and the occurrence of ADR associated with COX2-Inbitors, paracetamol, NSAIDs, and morphine in medical students and residents. **Results.** The analgesic with the highest risk perception was morphine, while the drug with the least risk perceived was paracetamol. Addiction was perceived as the most probable adverse effects developed by morphine. In the case of NSAIDs, the main adverse effect perceived was GI bleeding. **Discussion.** Our findings show that medical students give higher risk scores than residents toward risk due to analgesics. It is probable that both groups of students have morphinophobia, although more studies are necessary to confirm this. Continuing training and informing physicians about ADRs is necessary since the lack of training is known to induce inadequate use of drugs.

Perception of the risk of adverse reactions to analgesics: Differences between medical students and residents

Sandra Castillo-Guzmán[1], Omar González-Santiago[2], Ismael A Delgado-Leal[1], Gerardo E. Lozano-Luévano[1], Misael J Reyes-Rodríguez[1], Cesar V Elizondo-Solís[1], Teresa A Nava Obregón[1], Dionicio Palacios-Ríos[1]

1.- Clínica del Dolor y Cuidados Paliativos, Servicio de Anestesiología, Hospital Universitario Dr. José E. González

2.- Postgraduate division of the School of Chemical Science, Universidad Autonoma de Nuevo León

Corresponding author

Sandra Castillo-Guzman.

Av. Madero y Gonzálitos S/N, Mitras Centro, Monterrey, Nuevo León, 64460, México

Email address: castilloguzsan@yahoo.com.mx

Abstract

Background. Medications are not exempt from adverse drug reactions (ADR) and how the physician perceives the risk of prescription drugs could influence their availability to report ADR and their prescription behavior.

Methods. We assess the perception of risk and the occurrence of ADR associated with COX2-Inbitors, paracetamol, NSAIDs, and morphine in medical students and residents.

Results. The analgesic with the highest risk perception was morphine, while the drug with the least risk perceived was paracetamol. Addiction was perceived as the most probable adverse effects developed by morphine. In the case of NSAIDs, the main adverse effect perceived was GI bleeding.

Discussion. Our findings show that medical students give higher risk scores than residents toward risk due to analgesics. It is probable that both groups of students have morphinophobia, although more studies are necessary to confirm this. Continuing training and informing physicians about ADRs is necessary since the lack of training is known to induce inadequate use of drugs.

Introduction

Analgesics are the cornerstone of pain management and their availability is critical for the alleviation of unnecessary chronic and acute pain, especially in developing countries (Lohman, schleifer and Amon 2010). However, these medications are not exempt from adverse reactions (ADR). The use of opioids is associated with a variety of ADRs ranging from nausea and vomiting to urinary retention and respiratory depression. Paracetamol is relatively safe when taken in a therapeutic dose (≤ 4 g/day for adults). However, overdosage leads to hepatotoxicity and also nephrototoxicity.(Chun et al 2009; Waring et al 2010; Hodgman and Garrard 2012) Non-Steroidal Anti-inflammatory-drugs (NSAIDs) can result in gastrointestinal (GI) complications, ranging from dyspepsia to peptic ulcer and GI bleeding (Castellsague et al 2012). On the other hand, COX2 inhibitors could create an ulcerogenic dual-COX inhibitor when administered with low-dose aspirin. Moreover, by inhibiting COX2, they could delay ulcer healing. Similar to traditional NSAIDs, COX2 inhibitors compromise the glomerular filtration rate in patients at increased risk, and also may cause peripheral oedema and hypertension. In combination with an oral anticoagulant they increase the international normalized ratio (Mattia and Coluzzi 2005).

On the other hand, how the physician perceives the risk of prescription drugs could influence their availability to report ADR and their prescription behavior. In the case of opioids, an apprehensive attitude when using morphine as an analgesic could lead to resistance to administer morphine to patients suffering from severe pain. Such reluctance can have a negative impact on pain management as well as quality of life (Joranson et al 200; Bandieri et al 2009).

With this in mind the aims of this study was 1) to investigate the risk perception of medical students and residents towards opioid and non-opioid analgesics, 2) to evaluate the perception of common ADR caused by these analgesics.

Methods

This study was conducted in the Faculty of Medicine of the Autonomous University of Nuevo León (UANL) and the Dr José E. Gonzalez University Hospital located in the Metropolitan area of Monterrey, Mexico. The sample of medical students was conformed only by those who had already taken a pharmacology course while resident from all specialties were included.

Instrument. A visual analogue scale was used to assess the perception of risk and the occurrence of ADR associated with COX2-Inbitors, paracetamol, NSAIDs, and morphine. ADRs were assessed by measuring the distance between the left side of the scale (equal to zero) and the mark made by the participant. Since each scale measured 10 cm, the perceived risk of ADRs could be considered as a quantitative score ranging from 0 to 10. The following ADRs were assessed to each class of analgesic: gastrointestinal (GI) bleeding, kidney damage, liver damage, sedation, bronchospasm and addiction

Statistical analysis. Mean and 25^{th} -75^{th} centiles were calculated. The Mann-Whitney U-test was used for comparison of the two groups of students. The statistical package SPSS V20 was used for all analyses.

Ethical approval and consent. This study was approved by the Ethical committee of the Faculty of Medicine of the Autonomous University of Nuevo León. The reference number is AN15-011. The questionnaire was completed after obtaining written consent.

Results

Five hundred and five students were interviewed. Women and men represented 39.7% and 60.3%, respectively. Medical students on the other hand, represented 58.9% and residents 41.1%. Overall, the analgesic with the highest risk perception was morphine, while the drug with the least risk perceived was paracetamol (Figure 1). This pattern was observed in both genders. According to the level of study, undergraduate students had a greater perception of risk than residents (Table 1). This difference was significant for all individuals only in the case of morphine and NSAIDs. In the case of men and women, this difference was significant in the four drugs studied (Table 1).

Addiction and GI bleeding were perceived as the most and least probable adverse effects developed by morphine. This pattern was similar in undergraduates, residents, and both genders. However, undergraduates perceived a major risk more often than residents independent of gender and type of adverse effect (Table 2). In the case of NSAIDs, the main adverse effect perceived by undergraduates and residents was GI bleeding (7.20 and 6.60, respectively), while the least adverse effect was addiction (3.23) and sedation (2.02) for undergraduates and residents, respectively. The main adverse effect perceived by undergraduates and resident men was GI bleeding (7.12 and 6.35 respectively). The less adverse effect perceived by NSAIDS was addiction (3.09) for undergraduates and sedation (1.79) for residents, respectively. In the case of females, the main adverse effect perceived by undergrads and residents was GI bleeding (7.31 and 7.03 respectively) and the least adverse effect was addiction (3.44 and 2.16, respectively).

Discussion

Previous studies have investigated the risk perception of health professionals, students and patients toward drugs (Durrieu et al 2007; Durrie et al 2010; Cullen et al 2006; Bongard et al 2002); however, differences between medical students of different levels has been poorly studied. In this study, we searched for differences in the risk perception due to drugs between medical students and residents. Our findings show that medical students give higher risk scores than residents toward risk due to analgesics. This was independent of the class of analgesic and gender. We speculate that this difference could be explained by the recent courses of pharmacology taken by medical students (Durrieu et al 2007; Durrieu et al 2010). As has been previously demonstrated the pharmacology course increases global perception of risk. Others factors, such as the persuasive methods of pharmaceutical representatives, could affect these perceptions especially in residents who are more in touch with them than medical students.

In both groups of students, the decreased order of risk perceived was as follows: morphine, NSAIDS, COX2 inhibitors and finally, paracetamol. The low risk perceived for paracetamol could have serious implications. Clearly, they underestimated its risk in spite of being the single most important cause of acute fulminant hepatic failure. Until now, there are no studies that report the risk perception due to paracetamol using the measurement instrument of this study. The score assigned to NSAIDS is similar to that of other studies with mean values of 6.2 (4 – 7.6) (Cullen et al 2006; Bongard et al 2002).

Although it is not possible to demonstrate with our results, it is probable that both groups of students have morphinophobia, this due to the highest risk score assigned to morphine. The term morphibophobia can be defined as either a number of beliefs based on the side effects of morphine prescribed for pain management, or an inadequate management of chronic pain due to lack of knowledge on how to use morphine (Ferreira et al 2013). More studies in this respect are

necessary in Mexicans physicians. With regard to specific ADRs due to NSAIDs, GI bleeding was identified as the most common. In the case of morphine, addiction was perceived as more frequent. As with paracetamol, there are no studies, similar to this that allow us to compare the magnitude of GI bleeding and addiction. Continuing training and informing physicians about ADRs is necessary since the lack of training is known to induce inadequate use of drugs (McDowell et al 2009). In addition, poor training could complicate the transmission of information to their patients regarding ADRs. Studies suggest that the increase of information to patients will lead to a reduction in ADR and therefore hospital admissions and associated morbidty and cost.

Conclusions

There is a difference in the risk perception toward analgesics between medical students and residents. The former have a major risk perception toward analgesics than latest. In both groups of students, the decreasing level of risk was as follows: morphine, NSAIDs and paracetamol. GI bleeding and addiction were the more frequent ADR perceived to NSAIDs and morphine respectively by both groups of students.

We should encourage the rational use of analgesics by physicians to decrease opiophobia, over-prescription and self-prescription of NSAIDs. A good strategy will be the impartation of pain and palliative care curses in the curricula of physicians.

Acknowledgement

We thank Sergio Lozano-Rodriguez, M.D. for his help in editing the manuscript.

References

Bandieri E, Chirarolanza A, Luppi M, Magrini N, Marata AM, Ripamonti C. 2009. Prescription of opioids in Italy: everything but the morphine. Annals of Oncology 20:961–962.

Bongard V, Ménard-Taché S, Bagheri H, Kabiri K, Lapeyre-Mestre M, Montastruc JL. 2002. Perception of the risk of adverse drug reactions: differences between health professionals and non health professionals. British Journal of Clinical Pharmacology, 54, 433–436.

Castellsague J, Riera-Guardia N, Calingaert B, Varas-Lorenzo C, Fourrier-Reglat A, Nicotra F, Sturkenboom M, Perez-Gutthann S, and Safety of Non-Steroidal Anti-Inflammatory Drugs (SOS) Project Individual NSAIDs and upper gastrointestinal complications: a systematic review and metaanalysis of observational studies (the SOS project). Drug Safety 2012; 35: 1127– 1146.

Cullen G, Kelly E, Murray FE. 2006. Patients' knowledge of adverse reactions to current medications. British Journal of Clinical Pharmacology 62:2 232–236 232

Chun LJ, Tong MJ, Busuttil RW, Hiatt JR. 2009. Acetaminophen hepatotoxicity and acute liver failure. Journal of Clinical Gastroenterology. 43: 342–349.

Durrieu G, Hurault C, Bongard V, Damase-Michel C, Montastruc JL. 2007. Perception of risk of adverse drug reactions by medical students: influence of a 1 year pharmacological course. British Journal of Clinical Pharmacology 64:2 233–236 233.

185 Durrieu G, Huraulta C, Damase-Michela C, Montastruc JL. Perception of risk of adverse drug
186 reactions: a 3-year follow-up of a cohort of medical students. 2010. Fundamental & Clinical
187 Pharmacology 24; 423–427
188
189 Ferreira M, Verloo H, Margarida, Vieira MMS, Marques-Vidal P. 2013. Attitudes towards
190 morphine use among nurses and physicians working in French-speaking. Nursing: Research and
191 Reviews. 3 141–153.
192
193 Hodgman MJ, Garrard AR. 2012. A review of acetaminophen poisoning. Critical Care Clinics.
194 28: 499–516.
195
196 Joranson DE, Ryan KM, Gilson AM, Dahl Jl. 2000. Trends in medical use and abuse of opioid
197 analgesics. JAMA.;13:1710–1714.
198
199 Kane-Gill SL, Rubin EC, Smithburger PL, Buckley MS, Dasta JF. 2014. The cost of opioid-
200 related adverse drug events. Journal of Pain and Palliative Care Pharmacotherapy 28(3):282-93.
201 doi: 10.3109/15360288.2014.938889
202
203 Lohman D, Schleifer R, Amon JJ. 2010. Access to pain treatment as a human right. BMC
204 Medicine. 8:8
205
206 Mattia C., Coluzzi F. 2005. COX-2 inhibitors: pharmacological data and adverse effects.
207 Minerva Anestesiologica 71:461-70

McDowell SE, Ferner, HS, Ferner RE. 2009. The pathophysiology of medication errors: how and where they arise. British Journal of Clinical Pharmacology. 67(6), 605–613. http://doi.org/10.1111/j.1365-2125.2009.03416.x

Waring WS, Jamie H, Leggett GE. 2010. Delayed onset of acute renal failure after significant paracetamol overdose: a case series. Human and Experimental Toxicology. 29: 63–68.

1

Risk perception toward different analgesic between medical students and residents

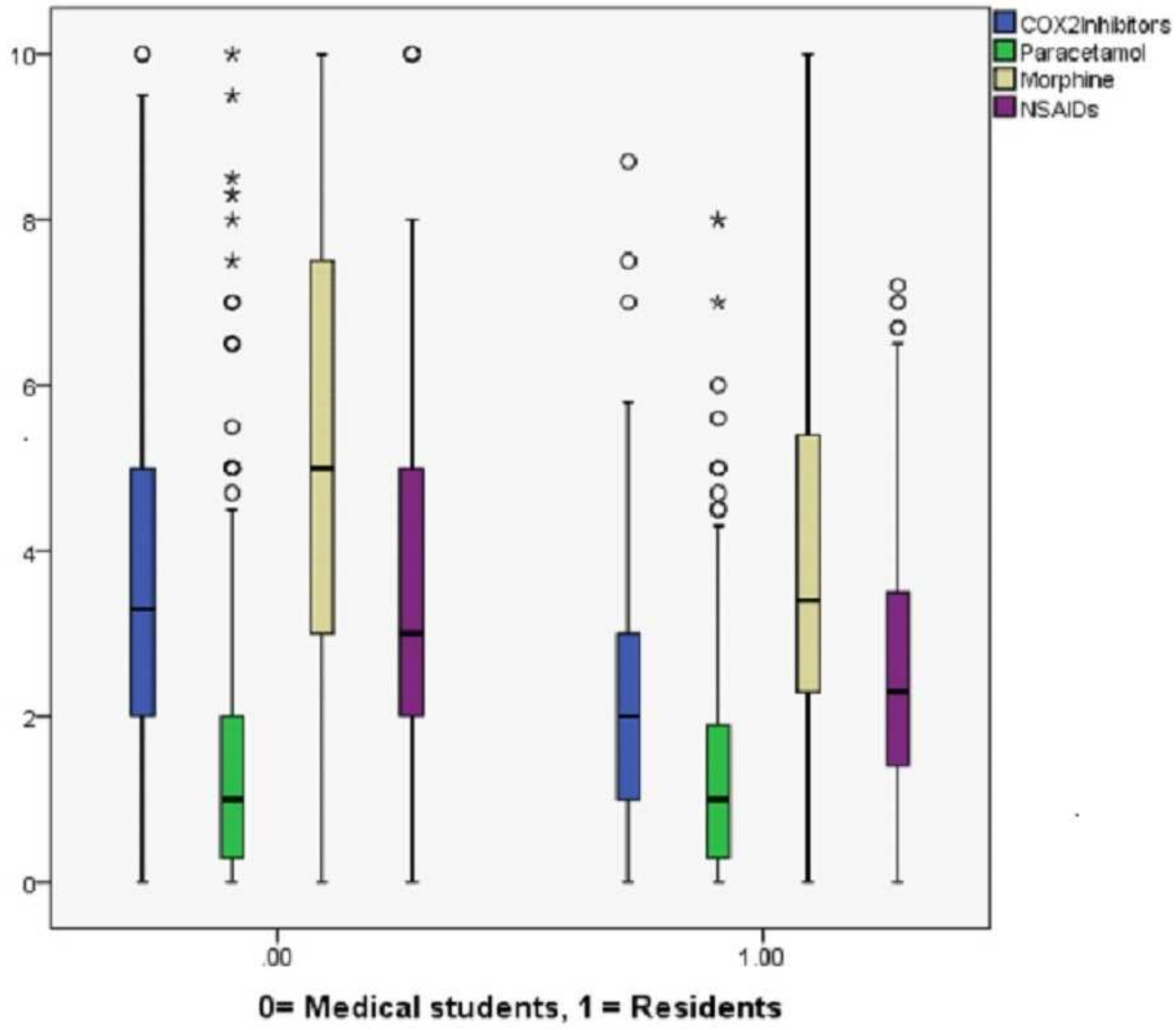

Figure 1. Risk perception toward different analgesics between medical students and residents

Table 1 (on next page)

Risk perception toward the analgesics according the gender between medical students and residents

MS = medical students, R = residents, P = <0.05, S = significant, NS = Non significant

Table 1.- Risk perception toward the Analgesics according the gender between medical students and residents

	COX2 Inhibitors			Paracetamol			Morphine			NSAIDs		
	M S	R	P	MS	R	P	MS	R	P	MS	R	P
Total	3.7	2.41	S	1.58	1.36	NS	5.27	3.92	S	3.35	2.55	S
Male	3.88	2.21	S	1.74	1.43	S	5.26	3.95	S	3.49	2.60	S
Female	3.46	2.02	S	1.36	1.24	S	5.28	3.86	S	3.16	2.48	S

MS = Medical student, R = Resident, P = <0.05, S = Significative

Table 2(on next page)

Risk perception toward different ADR

MS = medical students, R = residents, P = <0.05, S = significant, NS = non significant

Table 2.- Risk perception toward different ADR

	GI Bleeding			Kidney Damage			Liver Damage			Sedation			Bronchospasm			Addiction		
Drugs	MS	R	P	MS	R	P	MS	R	P	MS	R	P	MS	R	P	MS	R	P
Morphine																		
Total	4.50	2.72	S	4.78	3.38	S	5.24	3.87	S	7.35	5.92	S	5.44	3.98	S	7.72	5.89	S
Male	4.23	2.78	S	4.60	3.15	S	5.22	3.78	S	7.14	5.96	S	5.44	4.00	S	7.61	5.92	S
Female	4.88	2.62	S	5.03	3.78	S	5.27	4.03	S	7.64	5.85	S	5.44	3.94	S	7.88	5.84	S
NSAIDs																		
Total	7.20	6.60	S	6.34	6.14	NS	6.09	4.11	S	3.82	2.02	S	3.55	2.30	S	3.23	2.23	S
Male	7.12	6.35	S	6.18	6.26	NS	6.10	3.90	S	3.83	1.79	S	3.43	2.20	S	3.09	2.27	S
Female	7.31	7.03	NS	6.57	5.93	NS	6.08	4.48	S	3.81	2.41	S	3.72	2.48	S	3.44	2.16	S

MS = Medical students, R = Residents, P = <0.05, S = Significative