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

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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.

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19 Abstract

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

Analgesics are the cornerstone of pain management and their availability is critical for the 45 alleviation of unnecessary chronic and acute pain, especially in developing countries (Lohman, 46 schleifer and Amon 2010). However, these medications are not exempt from adverse reactions 47 (ADR). The use of opioids is associated with a variety of ADRs ranging from nausea and 48 49 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 50 and also nephrototoxicity.(Chun et al 2009; Waring et al 2010; Hodgman and Garrard 2012) 51 52 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). 53 On the other hand, COX2 inhibitors could create an ulcerogenic dual-COX inhibitor when 54 administered with low-dose aspirin. Moreover, by inhibiting COX2, they could delay ulcer 55 healing. Similar to traditional NSAIDs, COX2 inhibitors compromise the glomerular filtration 56 rate in patients at increased risk, and also may cause peripheral oedema and hypertension. In 57 combination with an oral anticoagulant they increase the international normalized ratio (Mattia 58 and Coluzzi 2005). 59

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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.
- 69

70 Methods

71 This study was conducted in the Faculty of Medicine of the Autonomous University of Nuevo

72 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

⁷⁴ already taken a pharmacology course while resident from all specialties were included.

75 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

ronsidered as a quantitative score ranging from 0 to 10. The following ADRs were assessed to

80 each class of analgesic: gastrointestinal (GI) bleeding, kidney damage, liver damage, sedation,

81 bronchospasm and addiction

Statistical analysis. Mean and 25th -75th 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.

89 **Results**

Five hundred and five students were interviewed. Women and men represented 39.7% and 90 60.3%, respectively. Medical students on the other hand, represented 58.9% and residents 41.1%. 91 Overall, the analgesic with the highest risk perception was morphine, while the drug with the 92 least risk perceived was paracetamol (Figure 1). This pattern was observed in both genders. 93 According to the level of study, undergraduate students had a greater perception of risk than 94 residents (Table 1). This difference was significant for all individuals only in the case of 95 morphine and NSAIDs. In the case of men and women, this difference was significant in the four 96 drugs studied (Table 1). 97 Addiction and GI bleeding were perceived as the most and least probable adverse effects 98 developed by morphine. This pattern was similar in undergraduates, residents, and both genders. 99 However, undergraduates perceived a major risk more often than residents independent of 100 gender and type of adverse effect (Table 2). In the case of NSAIDs, the main adverse effect 101 perceived by undergraduates and residents was GI bleeding (7.20 and 6.60, respectively), while 102 the least adverse effect was addiction (3.23) and sedation (2.02) for undergraduates and 103 residents, respectively. The main adverse effect perceived by undergraduates and resident men 104 was GI bleeding (7.12 and 6.35 respectively). The less adverse effect perceived by NSAIDS was 105 addiction (3.09) for undergraduates and sedation (1.79) for residents, respectively. In the case of 106 females, the main adverse effect perceived by undergrads and residents was GI bleeding (7.31 107 108 and 7.03 respectively) and the least adverse effect was addiction (3.44 and 2.16, respectively). 109

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111 Discussion

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Previous studies have investigated the risk perception of health professionals, students and 112 patients toward drugs (Durrieu et al 2007; Durrie et al 2010; Cullen et al 2006; Bongard et al 113 2002); however, differences between medical students of different levels has been poorly 114 studied. In this study, we searched for differences in the risk perception due to drugs between 115 medical students and residents. Our findings show that medical students give higher risk scores 116 117 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 118 pharmacology taken by medical students (Durrieu et al 2007; Durrieu et al 2010). As has been 119 previously demonstrated the pharmacology course increases global perception of risk. Others 120 factors, such as the persuasive methods of pharmaceutical representatives, could affect these 121 perceptions especially in residents who are more in touch with them than medical students. 122 In both groups of students, the decreased order of risk perceived was as follows: morphine, 123 NSAIDS, COX2 inhibitors and finally, paracetamol. The low risk perceived for paracetamol 124 125 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 126 report the risk perception due to paracetamol using the measurement instrument of this study. 127 128 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). 129

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 135 was identified as the most common. In the case of morphine, addiction was perceived as more 136 frequent. As with paracetamol, there are no studies, similar to this that allow us to compare the 137 magnitude of GI bleeding and addiction. Continuing training and informing physicians about 138 ADRs is necessary since the lack of training is known to induce inadequate use of drugs 139 140 (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 141 patients will lead to a reduction in ADR and therefore hospital admissions and associated 142 morbidty and cost. 143

144

145 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, overprescription and self-prescription of NSAIDs. A good strategy will be the impartation of pain

and palliative care curses in the curricula of physicians.

156

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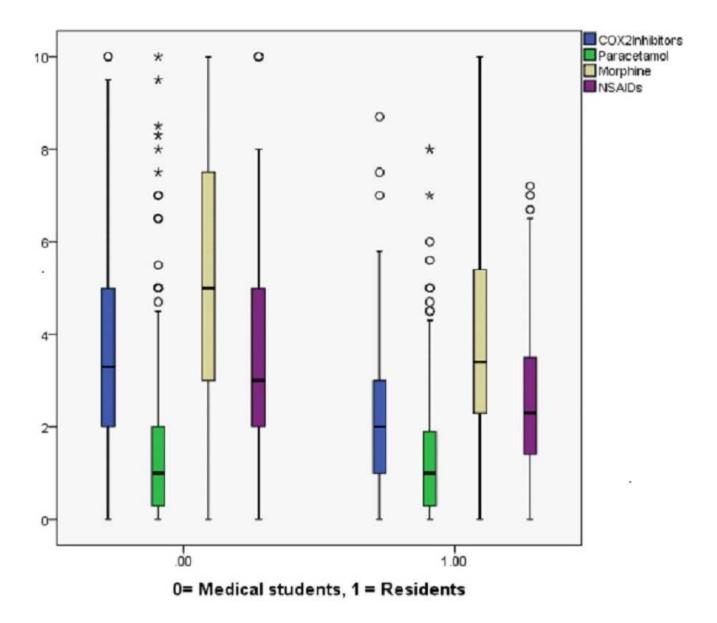
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Risk perception toward different analgesic between medical students and residents



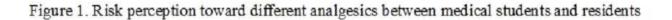


Table 1(on next page)

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

	COX	2 Inhib	itors	Paracetamol			Мо	Morphine			NSAIDs	
	ΜS	R	Р	MS	R	Р	MS	R	Ρ	MS	R	Ρ
				1.5	1.3	Ν	5.2	3.9		3.3	2.5	
Total	3.7	2.41	S	8	6	S	7	2	S	5	5	S
				1.7	1.4		5.2	3.9		3.4	2.6	
Male	3.88	2.21	S	4	3	S	6	5	S	9	0	S
				1.3	1.2		5.2	3.8		3.1	2.4	
Female	3.46	2.02	S	6	4	S	8	6	S	6	8	S

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

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 I	Damage	Sec	Sedation		Bronchospasm		Addiction	
Drugs	MS	R	Р	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