# A study on risk factors eliciting opioid adverse reactions in elderly males

Jiyoung Kim[1], Soo Jin Song[1],Youn-joo Jung[1], Hyokeun Jeong [1]
Joo Hee Kim[2], Jeong Yee[2], Hye Sun Gwak[2]
[1] Department of Pharmacy, Veterans Health Service Medical Center, Seoul, Korea
[2]College of Pharmacy & Division of Life and Pharmaceutical Sciences, Ewha Womans University, Seoul, Korea

## Background and Purpose

Opioid administration for pain control and relevant reports of adverse reactions have rapidly increased in the last several decades. In particular, elderly patients with various underlying disorders are administered with multiple drugs and prone to drug-drug interactions, and special attention is necessary in prescribing opioids. This study attempts to verify the incidence rates of opioid adverse reactions, the sympotomatic manifestations, and examine causative factors in elderly male patients.

## METHOD

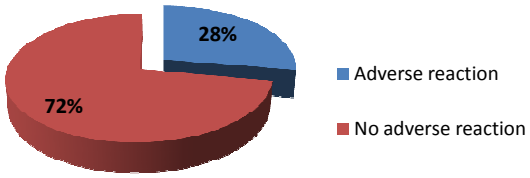
This retrospective study, conducted via electronic medical records, included a total of 320 male patients, 65 years old or older, who had been prescribed with oral opioids in this hospital from January 1 to December 31, 2012. These subjects were divided into two groups: Group one for paitents with adverse reaction manifestations(ARM) and another group for patients with no ARM. The correlations with age, body mass index, alcohol drinking and smoking, underlying diseases, previous opioid usage and concurrently-administered drugs were analyzed.

## RESULT

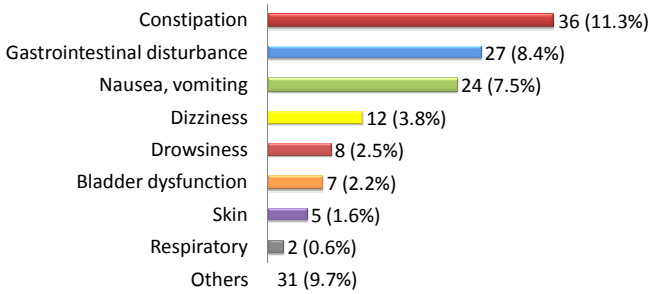
### Result 1 ) Baseline characteristics (total n=320)

| Characteristics | | Mean±SD/No(%) |
|---|---|---|
| Age (years) | | 70.9±5.7(65.0-88.0) |
| Height (cm) | | 164.9±5.6(136.0-179.3) |
| Weight (kg) | | 65.7±10.8(40.4-97.0) |
| BMI (kg/m$^2$) | | 24.2±3.6(15.2-37.5) |
| Alcohol | Yes | 97 (32.6) |
| | No (past) | 201 (67.4) |
| Smoking | Yes | 73 (24.2) |
| | No (past) | 229 (75.8) |
| Underlying disease | Gastrointestinal disease | 286 (89.4) |
| | Cardiovascular disease | 247 (77.2) |
| | Cancer | 136 (42.5) |
| | Endocrine disease | 135 (42.2) |
| | Hepatic disease | 38 (11.9) |
| | Renal disease | 30 (9.4) |
| Indication | Cancer pain | 81 (25.3) |
| | Dyspnea | 61 (19.1) |
| | Back pain | 52 (16.3) |
| | Neuralgia | 52 (16.3) |
| | Operation pain | 6 (1.9) |
| | Traumatic pain | 5 (1.6) |
| | Chest pain | 1 (0.3) |
| | Others | 61 (19.1) |
| Duration | < 90days | 198 (61.9) |
| | ≥ 90days | 122 (38.1) |
| Previous opioid | Yes | 196 (61.3) |
| | No | 124 (38.8) |
| Opioid type | Codein | 94 (29.4) |
| | Codein+fentanyl | 4 (1.3) |
| | Codein+oxycodone | 8 (2.5) |
| | Fentanyl | 4 (1.3) |
| | Fentanyl+oxycodone | 10 (3.1) |
| | Morphine | 78 (24.4) |
| | Morphine+oxycodone | 10 (3.1) |
| | Oxycodone | 111 (34.7) |
| Combination | Opioid | 33 (10.3) |
| | Tramadol, fentanyl patch | 145 (45.3) |
| | GABA analogue (gabapentin, pregabalin) | 161 (50.3) |
| | NSAIDs | 145 (45.3) |
| | TCA (amitriptyline) | 85 (26.8) |
| | Benzodiazepine | 93 (29.1) |

### Result 2-1 ) Percentage of patients developed adverse reactions




### Result 2 -2) Type of adverse reactions




### Result 3-1 ) Multivariate analysis of factors affecting adverse drug reactions- Model Ⅰ

| Characteristics | Unadjusted OR (95%CI) | Model Ⅰ Adjusted OR (95%CI) |
|---|---|---|
| Age (≥70) | 0.983 (0.599-1.614) | |
| Cancer | 0.312 (0.179-0.542) | 0.305 (0.145-0.642) |
| Endocrine disease | 1.938 (1.182-3.177) | |
| Duration (≥90days) | 2.328 (1.413-3.834) | 2.127 (1.137-3.980) |
| Previous opioid | 1.549 (0.923-2.601) | |
| TCA | 1.675 (0.980-2.862) | |
| GABA analogue | 4.439 (2.565-7.682) | |
| Benzodiazepine | 1.933 (1.151-3.248) | |
| Codeine | 1 | 1 |
| Morphine | 13.755 (5.030-37.608) | 7.520 (2.547-22.208) |
| Oxycodone | 8.197 (3.059-21.968) | 7.259 (2.545-20.701) |

### Result 3 -2) Multivariate analysis of factors affecting adverse drug reactions- Model Ⅱ

| Characteristics | Unadjusted OR (95%CI) | Model Ⅱ Adjusted OR (95%CI) |
|---|---|---|
| Age (≥70) | 0.983 (0.599-1.614) | |
| Cancer | 0.312 (0.179-0.542) | 0.323 (0.169-0.617) |
| Endocrine disease | 1.938 (1.182-3.177) | |
| Duration (≥90days) | 2.328 (1.413-3.834) | 2.054 (1.149-3.673) |
| Previous opioid | 1.549 (0.923-2.601) | |
| TCA | 1.675 (0.980-2.862) | |
| GABA analogue | 4.439 (2.565-7.682) | 3.259 (1.777-5.977) |
| Benzodiazepine | 1.933 (1.151-3.248) | |
| Combination | 2.399 (1.151-5.000) | 2.793 (1.089-7.163) |

## CONCLUSIONS

In elderly male patients with opioid administration, factors that relatively lower development of adverse reactions were malignancy and codeine. Administrations of long-term opioid, concurrent GABA analogue and multiple opioids increase adverse reactions. Further investigation is necessary to overcome the limitation of this retrospective study and to include factors that had not been fully scrutinized yet.

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Corresponding author : jIiyoung Kim. Department of pharmacy, Veterans Health Service Medical Center, 53, Jinhwangdo-ro 61-gil , 05368, Gangdong-gu, Seoul, Korea
E-mail : jy8099@bohun.or.kr

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