1521-0103/389/S3/supplement: ASPET 2024 Annual Meeting Abstract
The Journal of Pharmacology and Experimental Therapeutics

dx.doi.org/10.1124/jpet.500.924370
J Pharmacol Exp Ther 389: June 2024

Morphine-Induced Antinociception and Fecal Motility in Rats Eating a High Fat/High Carbohydrate or Ketogenic Diet

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Abstract ID 92437 **Poster Board 500**

Opioid drugs (e.g., morphine) are used medicinally for pain-relief but can also produce adverse effects such as constipation. Further, patients diagnosed with obesity often experience pain-related conditions and are prescribed opioids for pain management. Eating a diet that is high in fat and carbohydrates can lead to obesity; however, it is not known if the therapeutic or adverse effects of morphine are impacted by dietary manipulation. To explore this, the effects of acute morphine administration were assessed in male and female Sprague-Dawley rats (n = 8/dietary group) eating a standard (low fat) laboratory chow (17% kcal from fat), a high fat/high carbohydrate chow (60% kcal from fat), or a ketogenic (high fat/low carbohydrate) chow (90.5% kcal from fat). Morphine-induced antinociception was assessed using the warm water tail withdrawal procedure (0.32 – 17.8 mg/kg IP) in both sexes. Additionally, fecal motility was assessed by counting and weighing fecal output hourly, following an injection of saline or morphine (1, 3.2, or 10 mg/kg IP) for male rats eating wet homogenized chows (n = 2-3/dietary group). It was hypothesized that rats eating high fat chow would be more sensitive to the antinociceptive effects of morphine as compared to rats eating standard or ketogenic chow. It was further hypothesized that rats eating high fat chow would be more sensitive to the impact of morphine on gastrointestinal transit than rats eating other diets. Warm water tail withdrawal latencies were converted to a % of the maximum possible effect and were averaged by each dietary group. Mixed model ANOVAs revealed that there were no diet- or sex-related differences in morphine-induced antinociception. While fecal output was generally greater for rats eating standard chow as compared to rats eating other diets, morphine consistently decreased fecal output for rats in all dietary conditions. However, this effect was only significant following the largest dose of morphine (10 mg/kg) for rats eating standard chow, whereas all doses of morphine significantly decreased fecal output for rats eating the high fat/high carbohydrate chow or the ketogenic chow. These results suggest that while the therapeutic effects of morphine are consistent regardless of dietary intake in both sexes, dietary intake might impact individual susceptibility to the effects of morphine on gastrointestinal transit. Future studies are under way to assess the impact of diet on morphine-induced changes to fecal output in female rats, along with other effects of morphine including the rewarding effects, tolerance, and withdrawal.

K.M.S., was supported by the NIDA of the NIH under award R25DA033613, and by a NIDA RCMI supplement under award 3U54MD007592-29S4, and experiments were funded through NIGMS of the NIH under award R16 GM149426-01.