Fujii T, Orita S, et al. Progressive change in joint degeneration in patients with knee or hip osteoarthritis treated with fentanyl in a randomized trial. Yonsei Med J 2014;55(5):1379-1385.

Design: randomized clinical trial

Purpose of study: to investigate the possibility that in the setting of knee or hip osteoarthritis, opioids lead to progressive OA changes more than do NSAIDS

Reasons not to cite as evidence:

- The study randomized 70 patients to loxoprofen, a nonselective NSAID not marketed in the United States, 65 patients to tramadol/acetaminophen, and 65 patients to transdermal fentanyl
- The main outcomes were pain and Kellgren-Lawrence (KL) grade of OA after 12 weeks of treatment
- The average pain scores at the end of 12 weeks were lower (VAS=2.0) than in the loxoprofen group (VAS=3.3)
- The average joint space after 12 weeks of treatment was statistically the same with loxoprofen (6.65 mm) and with fentanyl (6.35 mm)
- However there was an apparent progressive change of OA, meaning a 50% reduction in joint space after 12 weeks, in 3 fentanyl patients but in no loxoprofen or tramadol/acetaminophen patients
- The problem with the study is that the films were done with the patients supine rather than standing, and this is not the generally recommended way to assess joint space narrowing according to the American College of Radiology, which recommends that the patient be standing rather than supine
- In addition, the statistical significance of the progressive change of OA is not as great as reported in Table 4, where the p value is reported as 0.02
- Rather, the data ought to be analyzed with Fisher's exact test, with the treatments treated as categorical variables, due to the fact that the "expected" counts for three of the six cells in a cross-tabulation are less than 5, for which Fisher's is a preferred test

If this is done, the p value is 0.067 rather than 0.02 as computed with SPSS:

rx * progression Crosstabulation

Count

		progression		
		0	1	Total
rx	FENTANYL	62	3	65
	NSAID	70	0	70
	TRAMADOL	65	0	65

Total	197	3	200

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)
Pearson Chi-Square	6.326[a]	2	.042	.067
Likelihood Ratio	6.839	2	.033	.067
Fisher's Exact Test	4.262			.067
N of Valid Cases	200			

a. 3 cells (50.0%) have expected count less than 5. The minimum expected count is .98.

- The conclusion that fentanyl leads to increased joint space narrowing cannot be sustained for these reasons
- In addition, it is not a practical management strategy to prescribe transdermal fentanyl long term in patients with a chronic condition like osteoarthritis, and if the disease has progressed to the point where this is being considered as an option, the patient is likely to be a candidate for joint replacement

Reference:

American College of Radiology, ACR Appropriateness Criteria®, Nontraumatic Knee Pain, 1995