Cannabis for Symptom Management in Patients with CKD: A Review

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Background: Symptom burden in patients with chronic kidney disease (CKD) is significantly debilitating, yet it is often inadequately treated. Legalization of cannabis may attract increasing interest for its use for managing refractory symptoms, but efficacy and long-term adverse health impacts are poorly established. This creates a challenge for clinicians to support its use. In this review, we summarize key clinical studies of non-synthetic cannabinoids for the treatment of symptoms encountered in patients with advanced CKD, including chronic pain, nausea and vomiting, anorexia, pruritus, and insomnia.

Methods: A search was conducted in MEDLINE and EMBASE (inception to March 1st, 2018) on cannabis and CKD symptoms of interest, complemented with a manual review of bibliographies. Studies that examined synthetic cannabinoids that are manufactured to mimic the effects of Δ^9-tetrahydrocannabinol such as dronabinol, levonantradol, nabilone, and ajulemic acid were excluded. We focused on studies with high level of evidence based on the Oxford Centre for Evidence-based Medicine Levels of Evidence (2b and above).

Results: Based on studies conducted in patients without renal impairment, those treated with non-synthetic cannabinoids were 43 to 300% more likely to report a ≥ 30% reduction in chronic neuropathic pain compared to placebo. There is currently insufficient evidence to recommend non-synthetic cannabinoids for other medical indications, although preliminary investigation into topical endocannabinoids for uremia-induced pruritus in end-stage renal disease is promising. Lastly, any benefits of cannabis may be offset by potential harms in the form of cognitive impairment, increased risk of mortality post-myocardial infarction, orthostatic hypotension, respiratory irritation and malignancies (with smoked cannabis).

Limitations: Non-synthetic cannabinoid preparations were highly variable between studies, sample sizes were small and study durations were short. Due to an absence of studies conducted in CKD, recommendations were extrapolated from the general population when appropriate.

Conclusion: Evidence for using non-synthetic cannabinoids for symptom management is currently limited to the treatment of chronic neuropathic pain, with promising potential for topical treatment of uremic pruritus. Non-synthetic cannabinoids, particularly smoked cannabis, may pose significant health risks which must be weighed against its limited substantiated therapeutic benefits.

Summary of Evidence of Non-synthetic Cannabinoids for Symptom Management in CKD

Indication	Level of Evidence[1]	Conclusion
Chronic Pain	1a	Based on extrapolated evidence from patients without renal impairment, non-synthetic cannabinoids have a moderate effect on the reduction of chronic neuropathic pain – at least a 30% pain reduction.
Nausea	-	Non-synthetic cannabinoids have not been studied for the treatment of uremia-induced nausea and vomiting.
	2b	Based on limited evidence extrapolated from patients without renal impairment, non-synthetic cannabinoids may be effective in the treatment of chemotherapy-induced nausea and vomiting secondary to low to moderate emetogenic chemotherapy regimens.
	1a[2,3]	Based on evidence extrapolated from patients without renal impairment and receiving moderate to highly emetogenic chemotherapy regimens, synthetic cannabinoids, nabilone and dronabinol, have comparable efficacy to prochlorperazine and metoclopramide for the treatment of chemotherapy-induced nausea and vomiting, but with higher incidences of adverse effects.
Anorexia	-	Non-synthetic cannabinoids have not been studied as an appetite stimulant for uremia-induced anorexia and cachexia.
	2b	Based on evidence extrapolated data from patients without renal impairment with HIV associated wasting syndrome, there is limited evidence that non-synthetic cannabinoids are effective in increasing caloric intake and body weight in the short term.
	1b	Based on evidence extrapolated from patients without renal impairment, non-synthetic cannabinoids are ineffective for increasing appetite or improving quality of life in cancer-related anorexia-cachexia syndrome
Uremic Pruritus	2b	Topical endocannabinoids may be effective for uremic pruritus in patients receiving hemodialysis based on limited evidence from a small observational study (n=21).
Insomnia	-	Non-synthetic cannabinoids have not been studied for the treatment of primary insomnia.

[1] Graded based on the Oxford Centre for Evidence-based Medicine Levels of Evidence (1a to 5).
[2].Synthetic cannabinoids were excluded from this review but their role in chemotherapy-induced nausea and vomiting is well-studied.
[3]*Cochrane Database Syst Rev* 2015; 11: CD009464.