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Tapering: Summary of Literature Review

With increasing opioid dependency among patients with chronic pain, clinicians and pain specialists suggest incorporating tapering is well-suited for reducing opioid dependency and chronic pain. However, defining a proper dosage of tapering for patients, speed of tapering, and effects of it are still. In general, tapering is unidirectional, and it is often part of treatment options for patients with chronic pain.

Finding an appropriate dosage for patients is one of challenges for clinicians but 10% of decrease from the original dose has become the accepted norm as a starting or lowest dose. American Association of Family Physician suggests is to decrease the dose 10-20% every 1-2 weeks, and adjust the rate based on patient response (AAFP, 2016). Centers for Disease Control and Prevention (CDC) recommends a decrease of 10% of the original dose per week for patients with chronic pain, whereas Partnership Health plan of California suggests that 10% of decrease is the most appropriate for many patients and 5% of decrease is for older and frail patients (CDC, 2016 & PHPC, 2016). All these suggestions indicate that a proper dose in tapering depends on patient's medical conditions and their physiological reactions to it.

According to CDC, tapering or discontinuation of opioid should occur when a patient requests dosage reductions, does not have clinically meaningful improvement in pain and function according to PEG scale, is on dosage less than 50 MME per a day without benefit, shows signs of substance use order, overdose risk and experiences overdose (CDC, 2016). In other words, tapering opioid should start with a lower dose, consultations with other specialists, and psychosocial support for patients and encouragements since the tapering process may be difficult and some patients may experience pain afterwards (CDC, 2016).

Partnership Health of California recommends that best candidates for taper are younger patients with motivation, declining function on opioids, hyperalgesia, complex polypharmacy, and high dose patients, who are on more than 120 MED opioids (Tapering Toolkit Provider Resource, 2016). The toolkit advises that patients should consider the tapering journal, where they track progression of pain and effects of medications (Tapering Toolkit Provider Resource, 2016). In other hand, the 2017 Canadian guidelines for Opioid use in chronic non-cancer pain advocates that once patients reach the 1/3 of the original dose, which is smaller dose reduction every 2-4 weeks, might be more successful taper (Ng & Renna, 2017). In Canada, the 90 mg/ day MED is the new upper dose limit, and any excess limit should be reassessed by clinicians and specialists (Ng & Renna, 2017).

Similarly, the U.S Department of Veteran Affairs suggests that an opioid tapering plan should include discussion with veteran, determination of a goal (dose reduction or complete discontinuation), and speed of tapering (U.S. Department of Veteran Affairs, 2016). The department suggests four different speed of tapers, which include lowest taper over years, reduction by 2 to 10% every 4 to weeks with pauses, slower tapering over months or years, reduced by 5 to 20% every four weeks with pauses, fastest taper reduction by 10-20% every week, and rapid taper, reduction by 20-50% of first dose and reduction by 10-20% every day (U.S. Department of Veteran Affairs, 2016). In addition, Washington state guideline for opioid discontinuation, which is rapid taper over a 2-3 weeks, is for patients with previous overdose or substance use disorder, and slow taper is patients with no acute pain (AMDG, 2015). These practices suggest that tapering speed is different based on patient's needs, willingness to change and their previous medical history.

But there is limited evidence to support one tapering strategy over. For instance, a fast or ultrafast tapering, 60 mg of extended-release, is more suitable for well-controlled randomized clinical trials and when a patient is under sedation, significant coexisting psychiatric, and

medical illness, such as unstable cardiac disease (Berma et al, 2015). Moreover, Kaiser Permanente recommends that rapid discontinuation is 15-33% per day over 3-7 days for patients whose behavior suggest possible misuses or diversion of medication, and who displays substance abuse concerns (Kaiser Permanente, 2016). Patients with opioid dependency or opioid misuse often have comorbid conditions such as concurrent use of benzodiazepines, psychological issues (depression, anxiety, or others), chronic obstructive pulmonary disease, congestive heart failure, and cognitive concerns (Kaiser Permanente, 2016).

These conditions add negative effects on opioid withdrawal symptoms such as nausea, insomnia, and hypertension (Berma et al, 2016). The typical time course for withdrawal are short acting opioids, which begins 8-12 hours after last use and peaks 48-72 hours after last use, and long acting opioids, which begins first 24-48 hours and peaks 3-5 days after last use (Kaiser Permanente, 2016). When patients experience intolerable withdrawal, the standard recommendations to decrease the dosage is by 5-10% of the original dose for everyone and four weeks for patients with long term opioid usage (Lembke et al, 2016).

In order to avoid such withdrawal and taper weaning, some recommend buprenorphine, lower level of dependency and comparatively higher levels of safety, as a helpful analgesic agent in patients with poorly controlled chronic pain. This strategy is for patients who discontinue opioid 8-12 hours prior, display significant pain dysfunction, and are on more than 100MMED opioid (Manhapra et al, 2017). Additionally, alternative method tapering may include methadone or buprenorphine/naloxone with gradual tapering when patients are at risk of overdose and have substance abuse (Murphy et al, 2018).

Similarly, the researchers randomized the 60 participants, assigning them to one of 6 months treatment protocols of buprenorphine and naloxone sublingual tablets: tapering doses for opioid weaning or detoxification, or steady doses for opioid replacement therapy (Blondell et al, 2010). They found that participants with chronic pain and coexistent opioid addiction were

more likely to adhere to an opioid replacement protocol than an opioid weaning protocol (Blondell et al, 2010). Additionally, the researchers combined pharmacotherapy for opioid discontinuation and behavioral counseling, which is a strategic treatment interruption that may contribute analgesic failure associated with the use of long term opioids (Blondell et al, 2010).

However, the effect of buprenorphine taper is unclear, and patients may experience harmful outcomes. According to the case study, the patient with opioid disorder, who was prescribed a rapid buprenorphine naloxone tapering in a medical facility and had a subsequent opioid overdose and death after the discharge (Chang et al, 2018). Overdose risk may increase with abstinence since physiological tolerance is reduced, rendering a previously tolerated dose potentially fatal. Most patients replace opioids agonist detoxification, which increases craving. Opioid-dependent individuals experience greater levels of craving and withdrawal before beginning opioid-agonist treatment, and experience significant symptoms during the tapering compared to patients with less opioid dependency (Northrup et al, 2015). More importantly, withdrawal drops from baseline to one week and decreases in craving are not observable until one week after, which suggests that intensity of withdrawal could be unclear after a long period of time (Northrup et al, 2015).

All these specific recommendations and guidelines propose that the effectiveness of tapering depends on patient's medical conditions and withdrawal reactions. But environmental factor and subpopulation may result different outcomes in tapering methods. For instance, the researchers examined the effects of tapering opioid prescriptions and reducing polypharmacy for inpatients with spinal cord injury at Rancho Los Amigos National Rehabilitation center (Atkins et al, 2014). The effective of tapering was dependent on the length of stay of the patients, the patient's willingness to change, different modalities of communications, and the provider's efforts (Atkins et al, 2014). Furthermore, the researchers found that the patients who were admitted to long-term residential opioid treatment were more likely to respond to tapering

positively than the patients who completed short term of residential treatments (Specka et al, 2017). In other words, the effects of tapering may derive from multiple factors such as supportive staff and patient's willingness to change.

Furthermore, long-term opioids use may not reduce pain sensitivity in chronic lower pain patients, and opioid tapering may induce brief hyperalgesia that can be normalized over a longer period (Wang et al, 2011). Similarly, the randomized trial of 12 patients shows that tapering may have moderate effects in improving sleeping, psychomotor functions, and opioid withdrawal symptoms but highly effective in stabilizing pain sensitivity over the time (Kurita et al, 2018). More importantly, the changes of pain sensitivity in patients with lower back pain under long-term opioid use and opioid tapering in longitudinal tapering may last less than six months (Wang et al, 2011). The dosage of opioid preparation was halved every 3 days until the patients became opioid clean under the supervisions (Wang et al, 2011).

In other hand, the patients among veteran population could be tapered to lower opioid doses, which the average percent reduction of opioid doses was 46% over a 12-month period (Harden et al, 2015). About the 70% of patients either experienced no charge in pain or had less pain when comparing baseline to 12 months (Harden et al, 2015). Additionally, the randomized clinical trial of 35 participants with 22 weeks or 18 weeks taper support programs illustrated that taper support might improve in pain interference, pain self-efficacy, and perceived opioid problems (Sullivan et al, 2017). Opioid tapering support intervention had an experienced pain medicine or psychiatry physician who evaluate a patient's condition, educate patients, adjust the dose, and provide coping skills when withdrawal symptoms display (Sullivan et al, 2017).

Patient's perspective of opioid tapering has more focuses on risks, barriers, facilitators, and benefits. Most patients describe opioid tapering difficult and often anxiety provoking process to initiate and sustain tapering but patients with social support and trusted health care provider may improve quality of life after tapering (Frank et al, 2016). In contrary, the focus group among

40 primary care providers reveal that emotional burden on providers, inadequate time, resources, and training in pain management and lack of trust in patient-provider relationship are challenges of implementing successful tapering (Kennedy et al, 2017). Successful tapering strategies include expressing empathy for patients, and incorporate discussion on opioid tapering planning into routine opioid monitoring (Kennedy et al, 2017).

All these studies suggest that interdisciplinary patient centered approach is a better fit for finding appropriate tapering for patients with comorbid conditions. Patients should feel to be heard and understand the process of tapering, and develop a sense of self-efficacy before tapering, which means healthcare team work as consultants (Wenger et al, 2018). While finding an appropriate dosage for patients is still a challenge, tapering could be successful if patients are well informed in tapering process and withdrawal symptoms, and providers have resource to implement tapering program with combination of other therapies. Tapering is a useful tool for reducing opioid dependency among patients with chronic pain.

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