

Concentrated Alpha-2 Macroglobulin Rich Autologous Plasma Injections for Chronic Pain and Reduction in Opioid Use

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Editorial

The US Opioid Epidemic has been a serious continuous threat to Americans since the early 2000s. "More than 932,000 people have died since 1999 from a drug overdose. Nearly 75% of drug overdose deaths in 2020 involved an opioid" (CDC, 2022). Prescription opioids are highly addictive and are commonly prescribed to treat moderate, severe, or chronic pain. Chronic pain is a multidimensional experience that encompasses both sensory and emotional elements in patients who suffer from it. Opioids are highly effective in treating these symptoms, however chronic opioid use causes many unwanted side effects. Thus, the challenge of providing effective pain treatment while minimizing these unwanted side effects is an ongoing issue with significant clinical and societal impact. Researchers also see that in many situations, medical care providers are more willing to prescribe opioid drugs for chronic pain in clinical settings [1].

Opioid prescriptions in patients with chronic pain are often misused and can lead to the use of illegal drugs such as heroin [2].

Many different conditions can cause someone to experience chronic pain including osteoarthritis (OA), joint injuries, and neuropathy. OA is a degenerative joint disease that causes cartilage to

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slowly erode. One of the major symptoms of OA is chronic joint pain. Treatments for OA are limited and include surgery, medication (Opioids/NSAIDs), and physical therapy [3,4].

However, many alternative medical care treatments are becoming available for this population. Alpha-2-macroglobulin (A2M) is a naturally occurring plasma protein that can potentially halt the progression of this disease. To date, there is limited research on the effectiveness of A2M in clinical settings [5].

Individuals suffering from chronic pain are often faced with functional limitations during their day-to-day lives. The inability to perform daily tasks can harm the livelihood of these individuals. It is common to be faced with socio-economic burdens, a decrease in quality of life, and progression of other health problems. In research by Garrison, et al.,[6] it is shown that there is a significant correlation between low health-related quality of life and prescription opioid use in OA patients. The demonstration of significant negative health impacts of opioids in this population is critical to assessing clinical outcomes and drug development decisions. Studies also show that chronic pain can cause a variety of negative health outcomes such as obesity, depression, and sexual dysfunction. When long-term chronic pain is left untreated patients are faced with physical and psychological consequences. As chronic pain progresses over time, it also becomes more pathologically complex. This can potentially cause neuroplastic changes that will increase pain. These neurological effects may become refractory to treatment [5].

Osteoarthritis (OA) is progressed by the overproduction of certain proteases and cytokines in the joint. These biological proteins become trapped in the joint due to their large size and the joint's avascular nature. While trapped in the joint they slowly erode the cartilage which in turn causes chronic pain. To reverse the progression of this disease, the proteases and inflammatory cytokines found trapped in the joint must be inhibited [7]. "A2M is a broad-spectrum proteinase inhibitor detected in both serum and synovial fluid, which is capable of blocking almost all kinds of proteinases. Proteinases that induce chronic inflammation can be captured by A2M" [2]. In theory, concentrated A2M rich autologous plasma can be considered a powerful treatment for OA. However, few studies exist showing the effectiveness of concentrated A2M rich autologous plasma therapy in clinical settings. A recent study on the effectiveness of A2M on OA of the knee concluded that concentrated A2M rich autologous plasma therapy injections showed a significant decrease in arthritic symptoms and knee pain caused by OA [8].

The conceptual framework for understanding opioid abuse among OA patients is influenced by individual behavior, social factors, medical care, and biological factors. Individual behavior that can influence the progression of opioid abuse during pain management treatment includes perception of risk, trauma and stress, emotional capacity, and education. Social factors include socio-economic status, cultural norms, occupation, and income. Medical care quality and access play a major role in this framework. OA treatment options, prescription monitoring, abuse identification and management, and availability of drug counseling all influence drug abuse and misuse in OA patients. Possible outcomes of these determinants of health are increased opioid related hospitalizations and adverse health outcomes from chronic misuse of opioids. Opioid abuse among

OA patients is highly dependent on the individual, however, prescription mismanagement is likely the root cause of progression to substance abuse. By increasing the availability to alternative forms of pain management treatments amongst OA patients there could be a serious reduction in opioid abuse in this population of users.

Opioid abuse and misuse are a dramatically increasing public health issue in the United States." Opioid overdoses accounted for more than 42,000 deaths in 2016, more than any previous year on record. An estimated 40% of opioid overdose deaths involved a prescription opioid" (Assistant Secretary of Public Affairs) [9]. Researchers see that in many situations, medical care providers are more willing to prescribe opioid drugs for chronic pain in clinical settings. "There are various driving factors relating to prescribing medication, including the availability of the compound and cost, which may, at times, be the main driving factor" [7]. Prescription pain relievers are very effective drugs and have a significant purpose in clinical treatment, however, when they are not used as intended, they are destructive. Opioid abuse and misuse negatively affect physical, mental, social, and environmental aspects of daily life. Public health concern regarding opioid abuse and misuse has been steadily increasing for the last 20 years. There have been efforts to reduce these issues by federal, state, and local governments. Policy reform and interventional programs have shown to be effective, but they have not been able to reverse the growth of the epidemic. The utilization of public health strategy and framework is key to keeping people healthy and increasing their quality of life.

Alternative care treatments such as concentrated A2M rich autologous plasma are not easily accessible because they are not covered through standard health insurance companies. These procedures can be expensive and must be paid out-of-pocket. Many people are not able to pay for these treatments and are forced to undergo surgery. The downside to surgery is that it requires a prolonged healing period and opioids are often prescribed as a form of pain management. This is where opioid prescription mismanagement leads to abuse or misuse of these drugs. It is a cycle that happens more often than it should and reform must become a priority.

Analysis of current public health concepts against best balanced goals for individual and societal health opens room for new ideas and conversations in the medical community. This could increase the application of concentrated A2M rich autologous plasma in clinical settings, as well as the number of patients who could benefit from treatment. New perspectives on concentrated plasma protein research could potentially inspire researchers to focus more on addressing public health concerns with alternative care rather than conventional medicine.

References

1. Cahill CM, Taylor AM. Neuroinflammation-A Co-Occurring Phenomenon Linking Chronic Pain and Opioid Dependence. *Curr Opin Behav Sci.* 2017;13:171-177. [PubMed](#) | [CrossRef](#)
2. de Castro J. Alpha-2-Macroglobulin: The New Weapon of Neuropathic Pains. *J Clin Res Anes.* 2018;4(1). [CrossRef](#)
3. <https://www.cdc.gov/opioids/data/index.html>
4. Faber J, Fonseca LM. How Sample Size Influences Research Outcomes. *Dental Press J Orthod.* 2014;19(4):27-9. [PubMed](#) | [CrossRef](#)

5. Fine PG. Long-Term Consequences of Chronic Pain: Mounting Evidence for Pain as a Neurological Disease and Parallels with Other Chronic Disease States. *Pain Med.* 2011;12(7):996-1004. [PubMed](#) | [CrossRef](#)
6. Garrison LP, Schepman P, Bushmakina AG, Robinson RL, Tive L, Hall J, et al. Concern about Addiction is Associated with Lower Quality of Life in Patients with Osteoarthritis: An Exploratory, Real-World Data Analysis. *Qual Life Res.* 2022;31(1):185-191. [PubMed](#) | [CrossRef](#)
7. Pergolizzi J, Böger RH, Budd K, Dahan A, Erdine S, Hans G, et al. Opioids and the Management of Chronic Severe Pain in the Elderly: Consensus Statement of an International Expert Panel with Focus on the Six Clinically Most Often Used World Health Organization Step III Opioids (Buprenorphine, Fentanyl, Hydromorphone, Methadone, Morphine, Oxycodone). *Pain Pract.* 2008;8(4):287-313. [PubMed](#) | [CrossRef](#)
8. Thompson K, Klein D, Campbell K, Gonzalez-Lomas G, Alaia M, Strauss E, et al. The Effectiveness of Alpha-2-Macroglobulin Injections for Osteoarthritis of the Knee. *Arthroscopy.* 2021;37(1):e80. [CrossRef](#)
9. Assistant Secretary of Public Affairs (ASPA). 2021. About the epidemic. HHS.Gov.