

## Alcohol Intake Improves Adherence of Pregabalin and Tramadol/Acetaminophen to RA and OA Patients

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### Abstract

Clinical managements of chronic pain in rheumatoid arthritis (RA) and osteoarthritis (OA) require deep understanding of patients. Since medication is mostly set under the guidelines of RA and OA to control of pain, but personal characteristics is not so much paid attention in terms of preferences. In the present study, alcohol preference was analyzed in the patients prescribed pregabalin and tramadol/acetaminophen in our hospital. All consecutive patients were requested to write up the medical questionnaire sheet before medical examination. The responses to this sheet are completely subjective. The close relation between habitual alcohol drinking and adherence of analgesics was observed in terms of adherence of pregabalin and tramadol/acetaminophen. That is, in OA patients, alcohol drinkers showed good adherence to pregabalin and also tramadol/acetaminophen. However, in RA patients, alcohol drinkers showed higher ratio to good adherence, but there was no significance between alcohol drinkers and non-alcohol drinkers. When total patients were analyzed, alcohol drinkers showed significantly higher adherence with pregabalin and also tramadol/acetaminophen. Therefore, it is recommended that precise personal preference had better to be taken in medical examination before prescription of pregabalin and tramadol/acetaminophen in RA and OA patients.

**Keywords:** Osteoarthritis; Rheumatoid arthritis; Alcohol drinking; Habits; Pregabalin; Tramadol/Acetaminophen

### Introduction

RA and OA are the major diseases in Japan and their estimated number of OA patients is 13,000,000, and RA, 700,000, which was calculated from the data of Comprehensive Survey of Living Conditions in Japan, Ministry of Health, Labor and Welfare [1]. This tendency has been also observed in The National Livelihood Survey, USA, describing that motor-organ pain in the form of low back pain, stiff shoulders, and arthralgia are the most common symptoms [2].

Such RA and OA patients have been commonly complaining pain, which is the single most important determinant of patient total assessment and lasts mostly rather long period in their life [3]. The number of chronic pain in USA counted 116 million people, more than the total affected by diabetes, heart disease, and cancer [4]. As pain is the initial and prevailing symptom of the diseases, leading to immobility, which in turn complications such as osteoporosis may be accompanied [5]. Therefore, management of pain in RA and OA patients is most important to maintain their higher quality of life (QOL).

In most of the countries, guidelines for arthritis-related pain are included [6], but sometimes do not fully address the nature of pain [7]. Management of chronic pain remains clinically challenging one for several reasons: the heterogeneity of the patient populations, the progressive nature of the disorders, the complex pain mechanisms involved, and the presence of comorbidities in predominantly elderly patients [8,9].

Recent analgesic agents carry a variety of risk, which has brought barriers in pain management, and many physicians may underestimate pain in an effort to level up patients' safety and minimize potential side effects [10,11].

Since NSAIDs are has been initially recommended in the patients care, we prescribe NSAIDs, but sometimes the effect of NSAIDs is limited or dissolves. Then, pregabalin [12] or tramadol/acetaminophen, which is compounding drug of tramadol and acetaminophen [1], has been prescribed. During the follow up of these patients with pregabalin or tramadol/acetaminophen, we feel that some patients with good adherence to pregabalin or tramadol/acetaminophen seem to be an alcohol drinker, and bad adherence, non-alcohol drinker. Therefore, we decided to perform the present study in order to clarify this relationship retrospectively.

### Methods

The medication used for analgesics after NSAIDs is pregabalin [12,13] or tramadol/acetaminophen [1].

We analyzed all the medical questionnaire sheet of patients prescribed analgesics retrospectively, and found that alcohol intake improve adherence of analgesics. This medical questionnaire sheet has been delivered to the patients for pre-clinic survey inquiring about physical conditions as well as clinical complaints. One of the questions is alcohol intake (alternative selection). Patients are requested to write up this sheet at the waiting room before medical examination. Thus, all the responses to this sheet are completely subjective.

The patients included in this study is a consecutive patient (Jan 1, 2013-June 30, 2013) at the outpatient clinic, Orthopedics, Sakai

Hospital, Kinki University Faculty of Medicine, and counted 200 (OA (121 cases) and RA (79 cases)).

## Results

### Case of good adherence

55 y/o male of 177 cm and 95 kg was suffered from painful knee throughout the year and diagnosed with osteoarthritis of the knee at advanced stage. He has been of diabetes and high cholesterol, otherwise healthy. NSAID (etodolac 400 mg/day) was prescribed as typical medications. Further, diclofenac (75 mg/day) was prescribed for joint pain, but chronic pain (VAS: 84, pain DETECT (10) score: 18 point) was still continued. Then, pregabalin (300 mg/day) capsules were administered further. After this prescription, his complaints gradually decreased without any side effects. After 2 months, his chronic pain was significantly decreased (VAS: 36, pain DETECT score: 11 point). We found that he is alcohol preference after examining his medical questionnaire sheet.

### Case of bad adherence

66 y/o male of 168 cm and 70 kg with RA (stage 4, class 2) of 22 years history. He has been also suffered from hypertension and diabetes mellitus. He is administered as RA treatment by eternercept 50 mg and methotrexate 8 mg weekly. However, his chronic pain has persisted further, diclofenac 75 mg/day was prescribed, but chronic pain (VAS: 76, pain DETECT score: 24 point still continued. Finally, pregabalin (150 mg/day) was prescribed. Upon pregabalin treatment, stagger and dizziness appeared immediately, then low dose pregabalin 75 mg was prescribed with anti-dizziness agent of travelmin. However, such prescription was discontinued due to further side effects. Finally,

iv administration of infliximab 400 mg/6 week and methotrexate 12 mg/week were proceeded for 4 months, chronic pain is improved, which is confirmed with pain scores (VAS: 34, pain DETECT score: 11 point). Look at his medical questionnaire sheet, we found he has never taken alcohol beverage.

Based on these typical cases, we analyzed all the medical questionnaire sheet of OA and RA patients prescribed analgesics retrospectively (Jan 1, 2013-June 30, 2013). This sheet has been used for pre-clinic survey asking about physical conditions as well as clinical complaints. One of the questions is alcohol intake (alternative selection). After describing the medical questionnaire, doctors examine the patients, and adherence of pregabalin and tramadol/acetaminophen was carefully evaluated after close examination of the patients.

As summarize in Table 1, the close relation between habitual alcohol drinking and adherence was observed in terms of adherence of pregabalin and tramadol/acetaminophen. That is, in OA, alcohol drinker showed good adherence to pregabalin (80% vs 50%,  $p=0.015$ ) and also tramadol/acetaminophen (79% vs 47%,  $p<0.01$ ). However, in RA, alcohol drinker showed higher ratio to good adherence of pregabalin (81% vs 61%,  $p<0.05$ ) and tramadol/acetaminophen (88% vs 65%,  $p<0.01$ ), but there was no significance between alcohol drinkers and non-alcohol drinkers. When total patients were analyzed, alcohol drinker showed significantly higher adherence with pregabalin (80% vs 55%,  $p<0.01$ ) and also tramadol/acetaminophen (83% vs 55%,  $p<0.01$ ).

Therefore, alcohol drinkers showed significantly higher adherence with pregabalin and also tramadol/acetaminophen, and non-alcohol drinkers diminish adherence of analgesics such as pregabalin and tramadol/acetaminophen.

	RA 79 cases	OA 121 cases	Total 200 cases
Pregabalin	39 cases	60 cases	99 cases
Good adherence	27 cases (69%)	39cases (65%)	66 cases (67%)
Good adherence/Alcohol Yes	13 cases/16 cases (81%)	24 cases/30 cases (80%)*	37 cases /46 cases (80%)**
Good adherence/Alcohol No	14 cases/23 cases (61%)	15 cases/30 cases (50%)*	29 cases /53 cases (55%)**
Analgesic effect Yes	74%	65%	69%
Tramadol/Acetaminophen	40 cases	61 cases	101 cases
Good adherence	30 cases (75%)	38 cases (62%)	68 cases (67%)
Good adherence/Alcohol Yes	15 cases/17 cases (88%)	23 cases/29 cases (79%)**	38 cases /46 cases (83%)**
Good adherence/Alcohol No	15 cases/23 cases (65%)	15 cases/32 cases (47%)**	30 cases /55 cases (55%)**
Analgesic effect Yes	76%	67%	70%

\* $p<0.05$ , \*\* $p<0.01$  between Alcohol Yes vs Alcohol No.

**Table 1:** Relation between alcohol drinking habit and adherence of pregabalin and tramadol/acetaminophen

## Discussion

The present study is the first report, where the close relation between habitual alcohol drinking and adherence of pregabalin and tramadol/acetaminophen was observed. Though the design is based on

the patients' subjective enrollment and its size is small, the results obtained showed the statistically significant (Table 1). But, we could not analyze further the relation between the alcohol consumption volume and adherence.

Rheumatoid arthritis (RA) and osteoarthritis (OA) are one of major diseases which cause chronic pain affect big populations to lower the qualities of life (QOL). Chronic pain derived from RA and OA is most serious to suppress physical activities as well as mental activities. In severe cases, patients may become depressed and/or bedridden person with extremely worse QOL [14]. Thus, the control of pain seems to be most serious and essential for the treatment of RA and OA patients as well as their families.

According to the guidelines for RA and OA at orthopedic surgery, the first pain killer is recommended to prescribe NSAIDs [8], but sometimes enough analgesic effect is not obtained. In such cases, pregabalin [12,13] or tramadol/acetaminophen [1] is then prescribed. This rather new analgesic agents exhibit occasionally side effect of nausea/vomiting, poor physical health, headache, itching, staggering/falling or lethargy, which may bring discontinuation of medications such as pregabalin or tramadol/acetaminophen.

In the present study, we analyzed the alcohol drinking habits [15] of outpatient clinic in our hospital. Initial idea comes from our impression that alcohol drinkers well tolerate from side effect of pregabalin or tramadol/acetaminophen. Then, we investigate whether this impression is correct by analyzing precisely the medical questionnaire sheet signed up patients themselves before medical examination.

The results obtained show clear relationship between adherence of pregabalin or tramadol/acetaminophen and alcohol intake (Table 1). That is, alcohol drinkers in both RA and OA show good adherence, which does not complain severe side effect and physicians, keep prescription of pregabalin or tramadol/acetaminophen without interruption to control the chronic pain.

In order to achieve good adherence, side effect of pregabalin and tramadol/acetaminophen must first be considered [1], with adding the personal preference of patients. The present study reveals that habitual alcohol intake shows big influence to adherence of pregabalin and tramadol/acetaminophen.

With these results, we recommend the following issues to control chronic pain in RA and OA: pregabalin and tramadol/acetaminophen are prescribed to the patients with RA and OA when NSAIDs do not rescue their chronic pain. Then, physician had better to inquire habitual alcohol intake of these patients, which improves adherence of pregabalin and tramadol/acetaminophen. Otherwise, for non-alcohol drinker, low dose of pregabalin and tramadol/acetaminophen is initially recommended to improve adherence. Thus, good adherence to pregabalin and tramadol/acetaminophen brings good control of chronic pain, and therefore patients' QOL may be boosted.

In summary, [12] though clinical managements of chronic pain in rheumatoid arthritis (RA) and osteoarthritis (OA) are proceeded according to the guideline, personal preference may decide adherence of analgesics. That is, the close relation between habitual alcohol drinking and adherence of analgesics was observed. In OA patients, alcohol drinkers showed good adherence to pregabalin and tramadol/acetaminophen, though in RA patients, there was no significance

between alcohol drinkers and non-alcohol drinkers. When total patients were analyzed, alcohol drinker showed significantly higher adherence to pregabalin and tramadol/acetaminophen. Therefore, it is recommended that personal preference had better to be taken in medical examination before prescription of pregabalin and tramadol/acetaminophen in RA and OA patients.

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