

## Prescribing patterns of tramadol in hemodialysis patients

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### ABSTRACT

**Background:** Pain is the most common complaint in hemodialysis patients. Tramadol had become analgesic of choice in these patients, and its prescription is increasing day by day. With this background, we evaluated the prescribing trends of tramadol in patients undergoing maintenance hemodialysis.

**Methods:** A total of 70 prescriptions were audited to assess the prescribing trends of tramadol (usually prescribed as a combination of 37.5 mg tramadol and 325 mg of paracetamol two times a day). Included prescriptions were from both male and female patients above 18 years of age undergoing maintenance hemodialysis. Demographic, clinical and medication use were recorded from the patients.

**Results:** The mean age of patients was 48±11.7 years, duration of dialysis 2.2±1.4 years. Tramadol consumptions were observed in 40/70 (56%) of patients. Majority of tramadol consumption was found in 30/40 (75%) males, 23/40 (59%) between 40-59 years and 28/40 (70%) undergoing two dialyses per week and 13/40 (32.5) were diabetics. During our exploratory analysis, we found that 15/40 (38%) of tramadol users, were concurrently prescribed with clonidine as add on antihypertensive. We noticed that the tramadol pill count during the preceding week was 81 in patients concurrently using clonidine and 139 in the patients who were not using clonidine (p>0.05).

**Conclusions:** In our study, tramadol consumptions were observed in 56% of patients. We also noticed analgesic interaction between clonidine and tramadol.

**Keywords:** Clonidine, Interaction, Potentiation, Analgesic, Hemodialysis, Tramadol

### INTRODUCTION

Pain is common among patients on dialysis. Among dialysis patients, the prevalence of pain ranges from 8–82%.<sup>1</sup> The high prevalence of pain in the dialysis patients has been linked to depression, and diminished quality of life and poor QOL scores were associated with increased hospitalisation and death.<sup>2-4</sup> The sources of pain arise predominantly (62%) from the musculoskeletal system, followed by other organ systems.<sup>5</sup>

Under treatment of pain in patients on hemodialysis (HD) might be due to analgesic-induced renal-related complications and other drug-accumulation-related complications due to reduced renal clearance.<sup>6,7</sup> Nonsteroidal anti-inflammatory drugs in dialysis patients because of well-known gastrointestinal, renal toxicities and hypertensive effect.<sup>8</sup>

Paracetamol, a non-narcotic analgesic and tramadol, a centrally acting narcotic analgesic are generally preferred for moderate pain in CKD patients. Paracetamol, at low

doses, is least nephrotoxic and tramadol is not-nephrotoxic.

Additionally, tramadol appears to produce less constipation and dependence than equianalgesic doses of potent opioids. Combination of paracetamol and tramadol has become analgesic of choice to nephrologists.

With this background, we evaluated the prescribing trends of a combination of tramadol and paracetamol in patients undergoing maintenance hemodialysis.

## METHODS

This retrospective data review study was conducted at Narayana Medical College Nellore, during January 2019 to June 2019. Institutional ethics committee approved the study proposal. A total of 70 prescriptions were audited to assess the prescribing trends of tramadol (usually prescribed as a combination of 37.5 mg tramadol and 325 mg of paracetamol two times a day). Included prescriptions were from both male and female patients above 18 years of age undergoing maintenance hemodialysis. Demographic, clinical and medication use were recorded from the patients.

## Statistical analysis

Data was recorded in predesigned case record forms. Results were tabulated as mean and standard deviation for continuous variables and actual numbers and percentages for categorical variables. Chi-square test was an inferential test for categorical variables. A p value of less than 0.05 was considered statistically significant. The data was analyzed by using statistical software IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.

## RESULTS

The mean age of patients was  $48 \pm 11.7$  years, duration of dialysis  $2.2 \pm 1.4$  years. Demographic, clinical and tramadol use can be observed from Table 1 and 2. Tramadol consumptions were observed in 40/70 (56%) of patients. Majority of Tramadol consumption was found in 30/40 (75%) males, 23/40 (59%) between 40-59 years and 28/40 (70%) undergoing two dialyses per week and 13/40 (32.5) were diabetics.

**Table 1: Age and gender distribution of tramadol consumers among hemodialysis patients.**

Age (years)	Female		Male		Total		P value
	N	%	N	%	N	%	
	(15/40)	(25.0)	(30/40)	(75.0)	(40/70)	(57)	
20-39	2	20	6	20	8	20	>0.05
40-59	6	60	17	57	23	59	
60-79	2	20	7	23	9	21	

**Table 2: The pattern of tramadol prescription across frequency of dialysis.**

Tramadol prescription	N	%	P value
Two dialysis/week	28/40	70.0	>0.05
Three dialysis/week	12/40	30.0	

**Table 3: Tramadol consumption in hemodialysis patients concomitantly with antihypertensive medications.**

Tramadol consumption with antihypertensive medications	N	%
<b>Tramadol + Acetaminophen*</b>	40	57
<b>Anti HTN drugs</b>		
One drug	7	18
Two drugs	23	58
>= Three drugs	10	26
Clonidine	15	38
Calcium channel blockers	28	70
Beta-blockers	30	75
Angiotensin-converting enzyme inhibitors	3	8
Angiotensin receptor blockers	1	3
Diuretics	4	10
Reserpine	3	8

\*40 out of 70.

During our exploratory analysis, we found that 15/40 (38%) of tramadol users, were concurrently prescribed with clonidine as add on antihypertensive (Table 3). We also found that the tramadol pill count during the preceding week was 81 in patients' concurrently using clonidine and 139 in the patients who were not prescribed clonidine. This difference appears to be apparent and is not statistically significant ( $p>0.05$ ) (Table 4).

**Table 4: Total number of tramadol pills consumed by the hemodialysis patients receiving concurrent clonidine as add no antihypertensive drug.**

Pill count	No clonidine		Clonidine		P value
N	N	%	N	%	
4	3	7	2	8	>0.05
5	10	22	8	32	
6	7	16	2	8	
7	5	11	3	12	
<b>Total</b>	139 per last week		81 per last week		

## DISCUSSION

Pain is one of the common problem in patients with end-stage renal disease (ESRD).<sup>9</sup> Managing pain in these patients is always challenging. Tramadol has dual action of pain relief, removed by dialysis, directly non-nephrotoxic and having less abuse potential.<sup>10,11</sup> Thus, immediate-release tramadol would be the choice of analgesia for hemodialysis patients with mild to moderate pain.<sup>12</sup>

In our study, we found that the Tramadol consumptions were in 40/70 (56%) of patients. It was prescribed in combination with paracetamol as a fixed-dose combination in the strength of 37.5 mg tramadol/ 325 mg paracetamol. During our exploratory analysis, we found that 15/40 (38%) of tramadol users, were concurrently prescribed with clonidine. The pain relief mechanisms of tramadol are by acting as a central opiate agonist and by inhibiting CNS reuptake of norepinephrine and serotonin.<sup>10</sup> The literature says that concurrent clonidine use potentiates the analgesic activity of tramadol by locking sympathetic release through the  $\alpha_2$ -adrenergic system.

To assess this potentiation activity, we counted the number of tramadol pills consumed in the last week and found that the pill count was 81 in patients concurrently using clonidine and 139 in those patients who were not prescribed clonidine. This difference appears to be apparent and is not statistically significant ( $p>0.05$ ).

We also assessed the effect of frequency of hemodialysis on the consumption of tramadol; Literature says that dialysis removes tramadol and redosing may be necessary after a dialysis session, indicating more number of tramadol consumers will be in patients undergoing dialysis three times a week.<sup>11</sup> We found that the number

of patients undergoing two times dialysis was more consumers than those undergoing three times dialysis/week. However, the observed difference was only apparent and not statistically significant ( $p>0.05$ ). The explanations for such a finding could be possibly multifactorial.

## Limitations

Since our study was conducted at one centre, and with a fewer number of samples, theoretically limiting generalisability. Additionally, the retrospective nature of the study and critical analysis of data could have introduced bias. We did not quantify the pain intensity because of a retrospective study.

## CONCLUSION

In our study, Tramadol consumption was more (56%) in patients undergoing hemodialysis. We also noticed analgesic interaction between clonidine and tramadol. Further studies are needed to assess the beneficial and harmful interactions between clonidine and tramadol when used concurrently in hemodialysis patients.

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