

Use of Long-Acting Injectable Paliperidone to Increase Medication Compliance in Individuals with ESRD and Schizophrenia

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Background

Patients with end-stage renal disease (ESRD) and schizophrenia are vulnerable to the medical effects associated with psychiatric decompensation.

Uncontrolled psychosis can lead to missed hemodialysis (HD) appointments, electrolyte disturbances, and risk of mortality.

Given concerns about renal clearance and toxicity, ESRD often limits the pharmacologic armamentarium.

We describe the successful use of long-acting injectable (LAI) paliperidone in a patient with schizophrenia and ESRD requiring HD, and discuss the evidence regarding its safety in ESRD.

Case

First Hospitalization: A 61-year-old man with schizophrenia and ESRD on HD presented for suicidal ideation (SI), stating that he “no longer want[s] to live to avoid the mafia.”

Exam revealed repetitive tongue movements consistent with tardive dyskinesia (TD). He was admitted and given aripiprazole to avoid worsening TD.

Paranoia did not improve. He was switched to oral risperidone, which resolved psychotic symptoms.

He became medication non-adherent in the community.

Second Hospitalization: Two weeks later, he presented again to the ED after lacerating his forearms to avoid “being killed by the mafia.”

Labs revealed a creatinine of 3.64mg/dL and a creatinine clearance of 16.88mL/min.

Psychiatry was consulted for SI and paranoid delusions in the context of the patient declining dialysis.

Given worsening of TD with haloperidol and inefficacy of aripiprazole, oral risperidone was restarted, which again led to improvement in paranoid delusions and HD compliance.

He consented to administration of LAI paliperidone palmitate at a reduced loading dose of 156mg. Psychotic symptoms continued to improve, and he denied any side effects.

One week later, he received a second loading dose at 78mg, and was discharged with outpatient psychiatric follow up with a recommended monthly maintenance dose of 78mg. He has not required hospitalization since.

Discussion

Risperidone remains a popular neuroleptic given its strong D2 antagonism and availability in oral and LAI formulations.

Clearance of paliperidone (the active metabolite of risperidone) may be reduced in ESRD; however, associated clinical risk has yet to be established (Snoeck, 1995).

A small number of case reports have demonstrated clinical efficacy and absence of side effects in ESRD patients receiving the LAI formulation of risperidone (Xiong, 2018; Tourtellotte, 2019).

Given that paliperidone/risperidone is poorly dialyzable, reduction in dose is recommended.

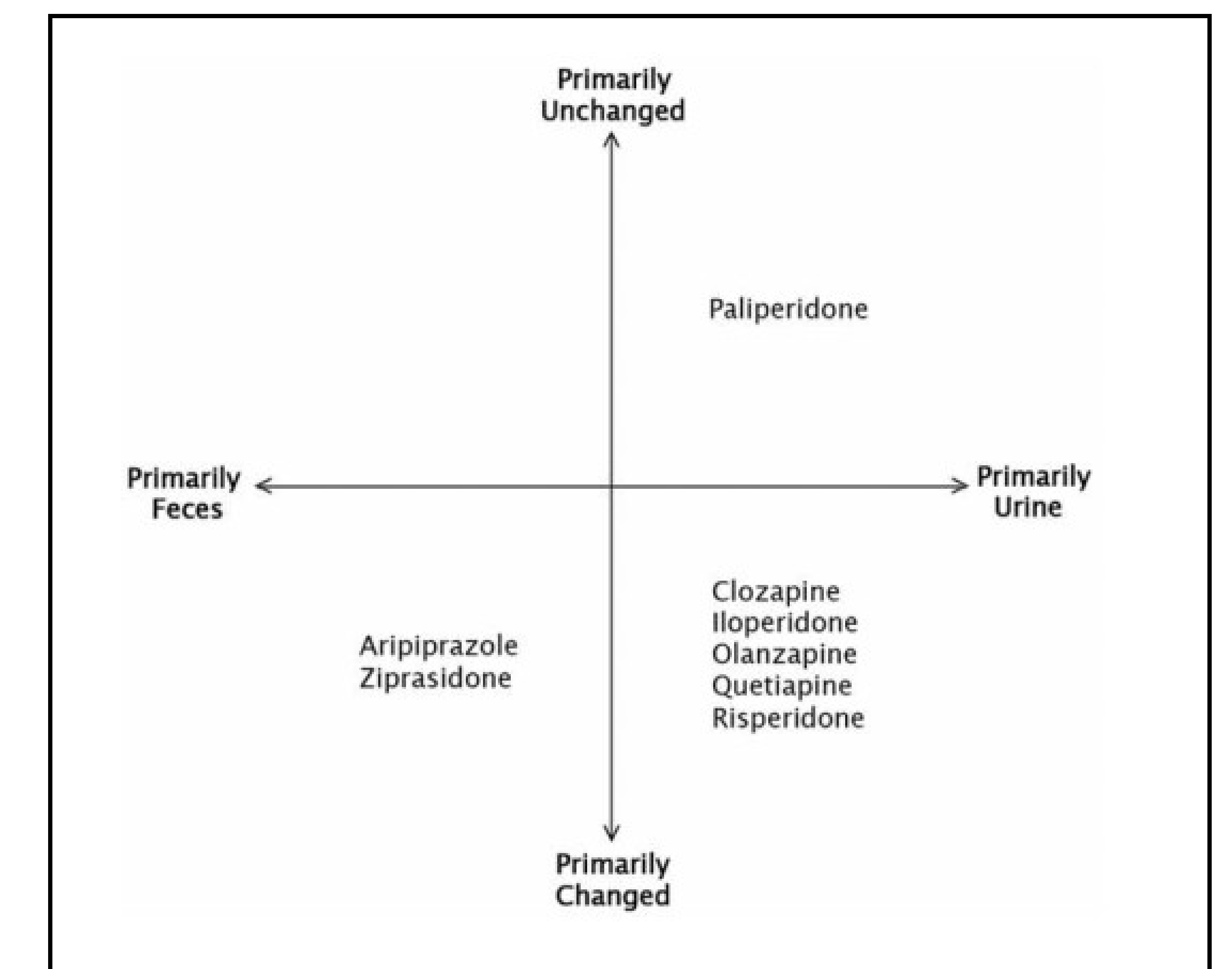


Figure 3: Primary Route of Elimination of Each Atypical Antipsychotic Agent (Sheehan, 2010)

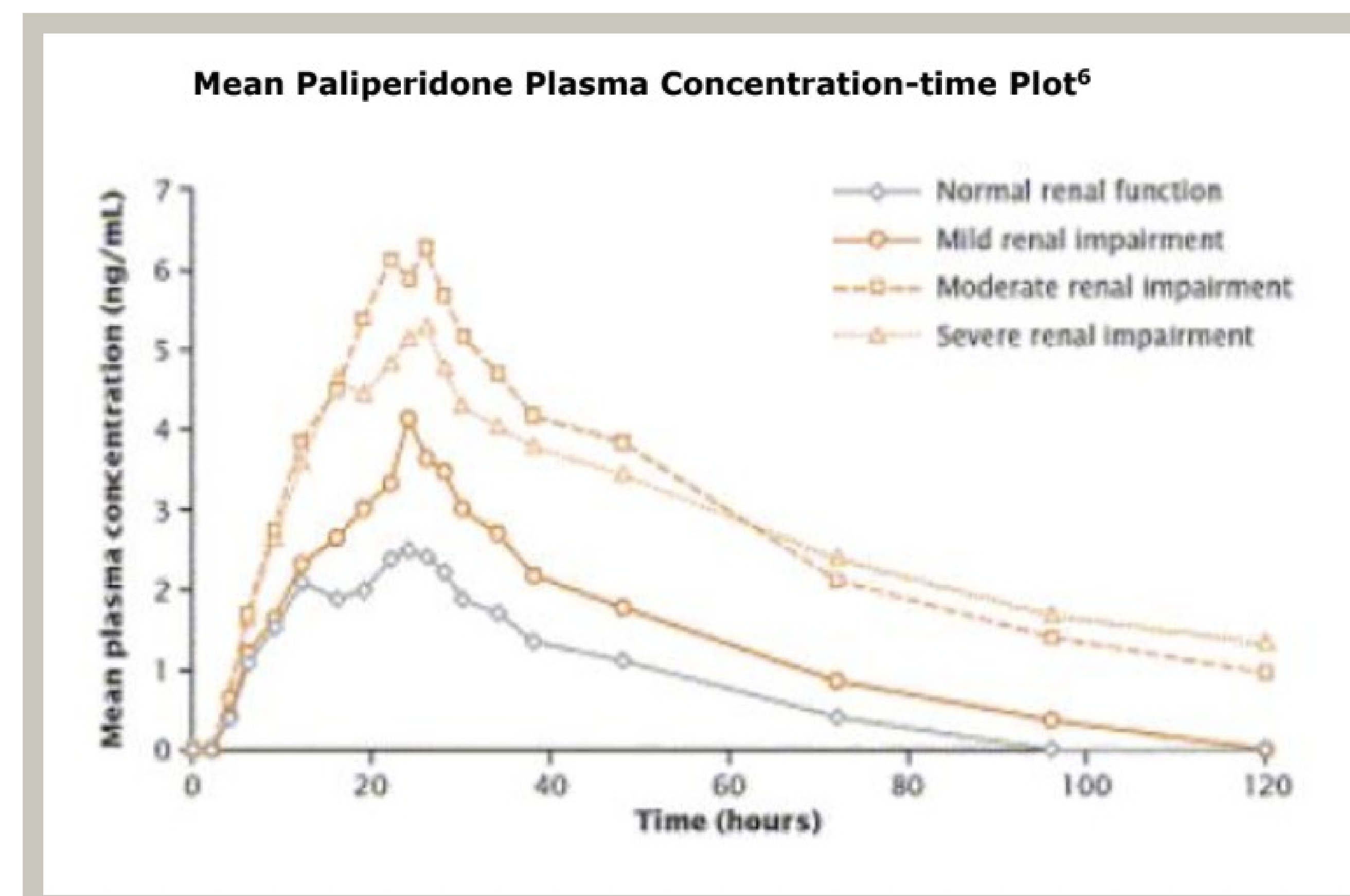


Figure 2: Mean Paliperidone Plasma Concentration-Time Plot Based on Renal Function (Thyssen, 2007)

References

- Sheehan JJ, Sliwa JK, Amatniek JC, Grinspan A, Canuso CM. Atypical antipsychotic metabolism and excretion. *Curr Drug Metab.* 2010 Jul;11(6):516-25
- Snoeck E, et al. Influence of age, renal and liver impairment on the pharmacokinetics of risperidone in man. *Psychopharmacology (Berl).* 1995 Dec.
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- Tourtellotte R, and Schmidt R. Use of therapeutic drug monitoring of risperidone microspheres long-acting injection in hemodialysis: A case report. *Ment Health Clin.* 2019 Nov 27.
- Xiong Y, et al. Injectable Risperidone During Hemodialysis. *Prim Care Companion CNS Disord.* 2018 Apr 19.

Chemical Structure	Excretion
	<ul style="list-style-type: none"> urine unchanged: <1% urine changed: 24-25% feces unchanged: 18% feces changed: 37% unrecovered: 20%
	<ul style="list-style-type: none"> urine unchanged: 0.5% urine changed: 48.5% feces unchanged: 2% feces changed: 28% unrecovered: 21%
	<ul style="list-style-type: none"> urine unchanged: <1% urine changed: 57-58% feces unchanged: <1% feces changed: 19-20% unrecovered: 22%
	<ul style="list-style-type: none"> urine unchanged: 7% urine changed: 50% feces unchanged: 2% feces changed: 28% unrecovered: 13%
	<ul style="list-style-type: none"> urine unchanged: 60% urine changed: 20% feces changed: 11% unrecovered: 9%
	<ul style="list-style-type: none"> urine unchanged: <0.5% urine changed: 72.5% feces unchanged: 0.5% feces changed: 19.5% unrecovered: 7%
	<ul style="list-style-type: none"> urine unchanged: 5% urine changed: 65% feces changed: 14% unrecovered: 16% <p>* Note: These excretion parameters are specific to patients who are extensive CYP2D6 metabolizers.</p>
	<ul style="list-style-type: none"> urine unchanged: <1% urine changed: 19-20% feces unchanged: <4% feces changed: 63-67% unrecovered: 13%

Figure 1: Summary of the Chemical Structures and Excretion Profiles of the Atypical Antipsychotics (Sheehan, 2010)