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REVIEW ARTICLE

THE IMPACT OF DRUG-INDUCED FATIGUE ON PHYSIOTHERAPY COMPLIANCE: A SYSTEMATIC LITERATURE REVIEW

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ABSTRACT

Fatigue induced by pharmacological interventions represents a significant yet understudied barrier to physiotherapy adherence, particularly in populations with chronic or complex medical conditions. While drug-induced fatigue is a well-documented side effect of numerous therapeutic agents, its specific impact on patient compliance with physiotherapy regimens remains poorly characterized, necessitating a systematic synthesis of existing evidence. This review aims to elucidate the relationship between drug-induced fatigue and physiotherapy compliance, identifying key mechanisms, risk factors, and potential mitigation strategies. A comprehensive search was conducted across multiple academic databases, focusing on peer-reviewed studies that examined fatigue as a drug-related adverse effect and its consequences on rehabilitation adherence. The inclusion criteria prioritized empirical investigations, clinical trials, and observational studies, while exclusion criteria eliminated non-relevant or low-quality sources. The findings reveal that drug-induced fatigue disproportionately affects older adults and individuals with neurological or cardiovascular conditions, often leading to reduced participation in prescribed physiotherapy. Common culprits include sedatives, opioids, and chemotherapeutic agents, which exacerbate fatigue through central nervous system depression or metabolic dysregulation. Notably, interdisciplinary approaches combining pharmacological adjustments and tailored rehabilitation strategies show promise in improving compliance. The review underscores the need for heightened clinical awareness and individualized interventions to address this interplay, ultimately optimizing therapeutic outcomes. Future research should focus on longitudinal studies to establish causal relationships and evaluate the efficacy of proposed management protocols.

Keywords: *Drug-induced fatigue, physiotherapy adherence, rehabilitation compliance, adverse drug reactions, chronic conditions, central nervous system depression, medication management, tailored rehabilitation.*

INTRODUCTION

Fatigue is a multifaceted symptom that significantly impacts patient quality of life and treatment adherence, particularly in the context of physiotherapy. While fatigue can arise from various physiological and psychological factors, drug-induced fatigue remains a critical yet often overlooked contributor to reduced compliance with rehabilitation programs [1]. The intersection of pharmacotherapy and physiotherapy presents a complex challenge, as medications prescribed to manage underlying conditions may inadvertently impair a patient's ability to engage in therapeutic exercises. This systematic review seeks to explore the mechanisms, prevalence, and clinical implications of drug-induced fatigue on physiotherapy compliance, with a focus on identifying evidence-based strategies to mitigate its effects.

The background of this research is rooted in the growing recognition of polypharmacy as a major public health concern, partically among geriatric and chronically ill populations [2]. As patients are prescribed multiple medications to manage comorbidities, the cumulative burden of side effects-especially fatigue-can hinder their capacity to participate in rehabilitation. Fatigue is a common adverse effect of numerous drug classes, including opioids, antidepressants, antihypertensives, and chemotherapeutic agents, each exerting distinct mechanisms that impair physical and cognitive function [3]. For instance, central nervous system depressants reduce alertness and motor coordination, while metabolic disruptors induce lethargy through mitochondrial dysfunction or hormonal imbalances. Despite its clinical relevance, the specific impact of drug-induced fatigue on physiotherapy adherence has not been systematically examined, leaving a gap in both research and clinical practice.

Research gaps persist in understanding the bidirectional relationship between pharmacotherapy and rehabilitation outcomes. While studies have investigated fatigue in isolation-either as a symptom of disease or a side effect of treatment-few have explored

its role as a mediator of physiotherapy non-compliance [4]. Additionally, existing literature often fails to differentiate between fatigue of pathological origin and that induced by medications, leading to generalized management approaches that may not address the root cause. The lack of standardized assessment tools for drug-induced fatigue further complicates its identification and management in clinical settings. These gaps highlight the need for a comprehensive synthesis of evidence to inform targeted interventions.

DRUG-RELATED CAUSES AND MANAGEMENT OF COMMON GERIATRIC SYMPTOMS

Geriatric patients frequently experience medication-induced symptoms that complicate physiotherapy compliance, with fatigue emerging as a predominant concern. The interplay between polypharmacy and physiological decline in aging populations creates a high-risk environment for drug-related adverse effects, particularly those affecting energy levels and functional capacity. As shown in Table 1, the included studies highlight several drug classes implicated in fatigue, alongside their mechanistic pathways and clinical management strategies.

Table 01: Drug-Induced Fatigue in Geriatric Populations: Causes and Management Approaches

Drug Class	Mechanism of Fatigue Induction	Associated Symptoms	Management Strategies	Sources
Anticholinergics	Central muscarinic receptor blockade	Cognitive decline, drowsiness	Dose reduction, alternative agents	[7]
Benzodiazepines	GABAergic CNS depression	Sedation, impaired balance	Tapering protocols, non-pharmacological sleep aids	[7]
Opioids	μ-opioid receptor activation	Lethargy, reduced motivation	Multimodal pain management	[8]
Beta-blockers	Reduced cardiac output, CNS effects	Exercise intolerance	Switch to vasodilating alternatives	[9]
Thyroid hormones	Metabolic dysregulation	Weight loss, muscle weakness	Dose titration, monitoring TSH	[10]

The table underscores the multifactorial nature of drug-induced fatigue, where pharmacological action (e.g., GABAergic suppression by benzodiazepines) intersects with age-related vulnerabilities (e.g., reduced hepatic metabolism). Notably, anticholinergics and benzodiazepines not only induce fatigue but also elevate fall risk, creating a dual barrier to physiotherapy participation [7]. This is particularly problematic in geriatric rehabilitation, where balance and mobility exercises are often central to treatment plans.

Management strategies must address both pharmacological and rehabilitative dimensions. For example, [8] demonstrates that opioid-induced fatigue in elderly patients with chronic pain can be mitigated through stepped pharmacotherapy-replacing long-acting opioids with adjuvant therapies like gabapentin-while simultaneously adapting physiotherapy intensity to match fluctuating energy levels. Similarly, [9] highlights the therapeutic competition between heart failure medications (e.g., beta-blockers) and rehabilitation goals, advocating for personalized dosing schedules that align with peak patient stamina.

A critical gap identified across studies is the lack of standardized protocols for monitoring drug-induced fatigue in rehabilitation settings. While [10] emphasizes the role of thyrotoxicosis in fatigue-related non-compliance, it also notes the absence of routine thyroid screening in geriatric physiotherapy cohorts. This observation aligns with broader literature calling for integrated pharmacovigilance in rehabilitation programs, where routine medication reviews could preemptively identify fatigue-inducing agents. The studies collectively advocate for interdisciplinary collaboration, where physiotherapists work closely with pharmacologists to tailor regimens that balance therapeutic efficacy and functional capacity. For instance, [7] proposes deprescribing algorithms for high-risk medications like benzodiazepines, coupled with graded exercise programs to counteract withdrawal-related fatigue. Such approaches not only address the immediate symptom burden but also optimize long-term adherence to rehabilitation.

Emerging evidence suggests that non-pharmacological interventions-such as light therapy for circadian rhythm disruption or nutritional support for metabolic fatigue-may complement traditional strategies. However, these approaches remain underrepresented in the reviewed literature, indicating a need for further research into integrative management models. The heterogeneity of geriatric populations also necessitates individualized assessments, where factors like renal function, cognitive status, and comorbidities modulate both drug effects and rehabilitation potential.

MANAGEMENT OF DRUG-INDUCED DISEASES AND SIDE EFFECTS

The management of drug-induced diseases and side effects requires a multifaceted approach that integrates pharmacological adjustments, supportive care, and

rehabilitation strategies. As shown in Table 2, the included studies highlight diverse drug-induced conditions and their corresponding management approaches, emphasizing the need for tailored interventions to mitigate adverse effects while maintaining therapeutic efficacy.

Table 02: Taxonomy of Drug-Induced Conditions and Management Strategies

Drug-Induced Condition	Management Strategy	Sources
Lupus-like Syndromes	Monitoring and supportive care (e.g., rest periods, physiotherapy)	[11]
Gastrointestinal Diseases	Adjusting drug regimens to improve compliance	[12]
Myopathies	Diagnosis and discontinuation of causative drugs	[13-15].
Neurological Side Effects	Dose adjustment and symptom monitoring	[16]
Hepatotoxicity	Supportive care (e.g., physical therapy) and drug regimen adjustments	[17]
Fatigue	Evaluation of coexisting causes (e.g., anemia) and supportive care	[18]
Cardiovascular Side Effects	Case-specific management (e.g., QT prolongation monitoring)	[19]
General Drug Toxicity	Technological frameworks for mitigation (e.g., digital dispensary systems)	[20]
Cutaneous T-cell Lymphoma Side Effects	Supportive care to improve treatment adherence	[18]

Drug-induced lupus, as described in [11], necessitates careful monitoring due to its potential to mimic systemic lupus erythematosus (SLE) while exhibiting distinct clinical features. The study highlights the importance of rest periods and physiotherapy in managing fatigue, a common symptom that can hinder rehabilitation compliance. Similarly, gastrointestinal drug-induced diseases, as discussed in [12], often require regimen adjustments to enhance patient adherence, particularly when myopathies induced by medications such as statins or minocycline present unique challenges. [13] and [15] emphasize the need for prompt diagnosis and discontinuation of offending agents, followed by rehabilitative measures to restore muscle function. In cases where statin-induced myositis unmasks underlying metabolic disorders like McArdle disease, as reported in [14], a multidisciplinary approach involving pharmacologists and physiotherapists becomes critical.

Neurological side effects, including rare manifestations like excessive yawning with escitalopram dose escalation [16], underscore the importance of dose titration and symptom surveillance. Hepatotoxicity, particularly in drug-resistant tuberculosis management [17], requires a balance between therapeutic efficacy and supportive interventions, including physical therapy to maintain functional capacity during prolonged treatment. Fatigue management remains a recurring theme, with [18] advocating for comprehensive evaluations to identify contributing factors such as anemia or metabolic disturbances. The study also highlights the role of supportive care in improving adherence to treatment regimens, particularly in conditions like cutaneous T-cell lymphoma where drug-induced fatigue is prevalent. Technological advancements, as proposed in [20], offer promising solutions for mitigating general drug toxicity through digital dispensary systems that enhance monitoring and reduce adverse events. These innovations could be particularly valuable in polypharmacy management, where drug interactions often exacerbate side effects. The studies collectively demonstrate that effective management of drug-induced diseases requires an integrated approach, combining pharmacovigilance with rehabilitative support.

THE ROLE OF REHABILITATION IN DISEASE-SPECIFIC MANAGEMENT

Rehabilitation programs play a pivotal role in mitigating disease progression and improving functional outcomes across various medical conditions, yet their efficacy is often compromised by drug-induced fatigue. The included studies demonstrate how tailored physiotherapy interventions address disease-specific impairments while navigating the challenges posed by medication-related fatigue.

Table 03: Rehabilitation Strategies Across Disease Contexts with Drug-Induced Fatigue Considerations

Disease Context	Rehabilitation Focus	Fatigue-Related Challenges	Adaptive Strategies	Sources
Cancer (Older Adults)	Functional status and QoL improvement	Chemotherapy-induced fatigue	Energy conservation techniques, graded activity	[21]
Parkinson's	Motor symptom	Medication 'off'	Heart rate-	[22]

Disease	management	periods, exercise intolerance	monitored group therapy, rest intervals	
Cerebral Palsy (Pediatric)	Mobility and coordination	Sedation from spasticity medications	Integrative medicine approaches (e.g., acupuncture + PT)	[23]
Cancer-Related Fatigue	Aerobic / resistance exercise	Multifactorial fatigue etiology	Supervised, dose-adjusted exercise protocols	[24]

In oncological rehabilitation, [21] underscores the dual burden of malignancy-related and treatment-induced fatigue in older patients. Chemotherapeutic agents like anthracyclines exacerbate fatigue through mitochondrial dysfunction, necessitating rehabilitation programs that incorporate energy conservation principles. The study advocates for prehabilitation-structured exercise regimens initiated pre-chemotherapy-to enhance physiological reserve and subsequent treatment tolerance. For Parkinson's disease, [22] identifies fatigue as a critical barrier during medication 'off' periods when dopaminergic therapy efficacy wanes. The described group physical therapy program employs real-time heart rate monitoring to modulate exercise intensity, pausing sessions when cardiovascular stress signals emerge. This approach aligns medication pharmacokinetics with rehabilitation timing, optimizing motor benefits while minimizing exhaustion-related dropout.

Pediatric populations present unique challenges, as illustrated by [23] in cerebral palsy management. Sedating effects of antispasticity drugs (e.g., baclofen) often conflict with active participation in physiotherapy. The trial protocol combines conventional physiotherapy with acupuncture, hypothesizing that reduced medication doses may be achievable through synergistic effects, thereby attenuating fatigue. Cancer-related fatigue management, as examined in [24], reveals the efficacy of structured exercise in breaking the cycle of inactivity and fatigue. The meta-analysis demonstrates that supervised aerobic training at 60-80% of peak heart rate, performed 3x weekly, significantly reduces fatigue severity compared to standard care. Notably, programs incorporating pharmacologic review (e.g., adjusting antidepressant doses) show superior adherence rates, highlighting the importance of concurrent medication optimization.

The studies collectively emphasize three rehabilitation paradigms for fatigue mitigation: temporal adaptation (aligning sessions with peak medication efficacy), pharmaco-exercise synergy (using physical activity to reduce drug dependence), and graded exposure (progressively increasing activity tolerance). Emerging insights suggest that rehabilitation timing relative to drug administration critically influences outcomes. For instance, Parkinson's patients exhibit better exercise adherence when physiotherapy coincides with peak levodopa plasma concentrations, whereas cancer patients tolerate afternoon sessions better post-morning chemotherapy. These nuances underscore the need for individualized scheduling informed by pharmacokinetic profiles.

Technological integration emerges as a promising frontier, with [22]'s heart rate monitoring model offering a template for real-time fatigue assessment. Future directions include wearable devices that dynamically adjust exercise prescriptions based on continuous vital sign feedback, potentially bridging the gap between clinical supervision and home-based rehabilitation. The reviewed evidence consistently demonstrates that effective rehabilitation in the context of drug-induced fatigue requires interdisciplinary coordination. Physiotherapists must collaborate with prescribing clinicians to reconcile therapeutic goals with pharmacological realities, ensuring that rehabilitation plans are both physiologically achievable and pharmacologically sustainable.

MANAGEMENT OF NEUROLOGICAL DISEASES AND THEIR COMPLICATIONS

The management of neurological diseases presents unique challenges due to the interplay between disease progression, pharmacological interventions, and rehabilitation needs. Drug-induced fatigue emerges as a critical factor influencing treatment compliance, particularly in conditions such as Parkinson's disease and Wilson's disease, where motor symptoms and medication side effects often converge to impair functional capacity.

Table 04: Neurological Disease Management Strategies Addressing Drug-Induced Fatigue

Disease	Primary Management Approach	Fatigue-Related Considerations	Rehabilitation Integration	Sources
Parkinson's Disease	Dopaminergic therapy optimization	Medication 'off' periods reduce exercise tolerance	Physiotherapy timed with peak drug efficacy	[25-28].

Wilson's Disease	Copper chelation therapy	Drug-induced neurological deterioration	Physiotherapy and speech therapy adjuncts	[29]
Late-Stage Parkinsonism	Pragmatic medication adjustments	Dementia and drug-induced psychosis complicate compliance	Baseline PT assessments to guide care plans	[30], [31]
Psychosis	Antipsychotic pharmacotherapy	Sedation and motor impairment from neuroleptics	Activity-based rehabilitation strategies	[32]
Psychogenic Movement Disorders	Multidisciplinary evaluation	Fatigue from diagnostic uncertainty and polypharmacy	Physical therapy as diagnostic and therapeutic tool	[33]

Parkinson's disease management exemplifies the delicate balance between pharmacological control and rehabilitation feasibility. As reported in [25], neuropsychiatric complications such as depression and anxiety frequently accompany motor symptoms, exacerbating fatigue through both disease mechanisms and psychotropic medication effects. The study emphasizes the need for regular medication reviews to identify agents contributing to excessive daytime sleepiness, particularly dopamine agonists and anticholinergics [26]. Further highlights the role of surgical interventions like deep brain stimulation in reducing medication burden, thereby indirectly mitigating drug-induced fatigue and enhancing physiotherapy participation.

Wilson's disease presents distinct challenges, where [29], demonstrates that copper-chelating agents like penicillamine can paradoxically worsen neurological symptoms in some patients, necessitating drug switches to alternatives like trientine. The study underscores the importance of concurrent physiotherapy to maintain motor function during these pharmacological transitions, particularly for patients developing dysarthria or dystonia. Rehabilitation in this context serves not only to counteract drug side effects but also to preserve functional independence during prolonged treatment courses.

Late-stage parkinsonism management requires special consideration of cognitive decline and drug-induced psychosis, as detailed in [30] and [31]. These studies reveal how dementia complicates medication adherence and physiotherapy compliance, with caregivers often struggling to maintain treatment schedules. The proposed solution involves structured physical therapy assessments to establish baseline function, enabling tailored interventions that account for fluctuating cognitive capacity and medication-related sedation. Notably, [31], identifies drug-induced psychosis as a major barrier to rehabilitation, recommending antipsychotic dose adjustments before initiating physiotherapy to improve engagement. Psychosis management introduces different challenges, where [32], describes the tension between antipsychotic efficacy and their fatigue-inducing properties. Second-generation antipsychotics like quetiapine, while having fewer extrapyramidal effects, often cause significant sedation that impedes participation in rehabilitation activities. The study advocates for integrating physical therapy with psychosocial interventions, using graded activity programs to gradually build tolerance while monitoring for medication side effects.

For psychogenic movement disorders in pediatric populations, [33], highlights the dual role of physiotherapy in both diagnosis and treatment. The study notes that drug-induced fatigue from unnecessary medications (often prescribed before accurate diagnosis) can obscure clinical presentation and hinder rehabilitation progress. A key recommendation involves medication reconciliation as part of the initial physiotherapy assessment to identify and deprescribe superfluous agents that may contribute to fatigue.

The studies collectively identify three critical strategies for managing neurological complications: pharmacovigilance (regular review of drug regimens for fatigue contributors), temporal coordination (aligning rehabilitation with optimal medication states), and functional prioritization (focusing therapy on preserving independence in activities of daily living). [27]'s randomized trial of late-stage parkinsonism management provides compelling evidence that pragmatic medication adjustments-reducing polypharmacy while maintaining symptom control-can significantly improve both fatigue levels and physiotherapy adherence rates.

Emerging approaches emphasize the role of technology in bridging pharmacological and rehabilitative care. [28]'s evaluation of safinamide as an add-on therapy for Parkinson's disease demonstrates how newer agents with lower fatigue profiles can expand the window for effective physiotherapy. Future directions include the development of integrated monitoring systems that track both medication pharmacokinetics and functional performance, enabling dynamic adjustments to rehabilitation plans based on real-time patient status. The evidence consistently demonstrates that successful neurological rehabilitation requires ongoing collaboration between neurologists, pharmacists, and physiotherapists.

CONSIDERATIONS IN RESPIRATORY AND CARDIOVASCULAR TREATMENT STRATEGIES

The management of respiratory and cardiovascular conditions presents unique challenges when addressing drug-induced fatigue and its impact on physiotherapy compliance. These systems are particularly vulnerable to medication-related side effects due to their physiological roles in oxygen delivery and energy metabolism. The included studies reveal critical considerations for optimizing treatment while maintaining rehabilitation adherence.

Table 05: Respiratory and Cardiovascular Treatment Considerations in the Context of Drug-Induced Fatigue

Treatment Focus	Key Considerations	Impact on Physiotherapy Compliance	Management Strategies	Sources
Respiratory Muscle Training	Drug-induced respiratory depression may limit training efficacy	Reduced ability to perform inspiratory loading exercises	Adjust medication timing relative to therapy sessions	[34]
Cardiovascular Pharmacology	Antihypertensives may cause exercise intolerance	Decreased stamina for aerobic rehabilitation components	Consider vasodilating alternatives with fewer fatigue effects	[35]
Pulmonary Tuberculosis Rehabilitation	Drug-induced hepatotoxicity complicates adherence	Fatigue from second-line agents reduces participation in chest physiotherapy	Monitor liver function and adapt percussion techniques	[36]
Poisoning-Related Respiratory Complications	Sedating antidotes impair respiratory drive	Limits capacity for breathing retraining exercises	Balance antidote efficacy with respiratory support needs	[37]
Antihistamine Use in Active Populations	H1-blockade reduces exercise performance	Impairs achievement of target heart rates in cardiac rehab	Time dosing to minimize interference with peak activity periods	[38]

Respiratory muscle training requires special attention to pharmacological interactions, as demonstrated in [34]. Opioids and benzodiazepines commonly prescribed for comorbid conditions can depress respiratory drive, reducing the effectiveness of inspiratory loading exercises. The study recommends scheduling physiotherapy sessions during periods of lowest respiratory suppression, typically before doses of long-acting sedatives reach peak plasma concentrations. For patients on continuous oxygen therapy, gradual titration of supplemental oxygen during respiratory training may counteract medication-induced hypoventilation.

Cardiovascular pharmacotherapy presents competing priorities between disease management and rehabilitation potential. [35], identifies beta-blockers as particularly problematic, with their negative chronotropic and inotropic effects limiting achievement of target heart rates during aerobic conditioning. The meta-analysis suggests that switching to angiotensin receptor blockers or calcium channel blockers in appropriate patients can maintain blood pressure control while reducing exercise-induced fatigue. Notably, the study found that nebivolol, a beta-blocker with vasodilating properties, showed better preservation of exercise capacity compared to traditional agents.

The rehabilitation of pulmonary tuberculosis survivors illustrates the complex interplay between drug toxicity and physiotherapy adherence. [36] reveals that second-line antitubercular drugs like pyrazinamide frequently cause hepatotoxicity, inducing fatigue that compounds the disease's metabolic burden. The study emphasizes the need for modified chest physiotherapy techniques-replacing vigorous percussion with postural drainage and controlled coughing-when patients exhibit medication-related lethargy. Serial monitoring of liver enzymes helps identify individuals who may benefit from temporary dose reductions to facilitate rehabilitation participation.

Poisoning management introduces unique challenges, where [37], describes how lifesaving antidotes like naloxone can paradoxically hinder respiratory rehabilitation. While effectively reversing opioid toxicity, naloxone's short half-life often necessitates repeated dosing that creates fluctuating respiratory drive. The authors propose synchronized breathing exercises during periods of stable antidote coverage, combined with incentive spirometry to maintain lung expansion between therapy sessions. This approach acknowledges the primacy of acute toxicity

management while preserving long-term pulmonary function.

Athletic populations receiving antihistamines for allergic conditions face distinct performance limitations. [38] demonstrates that first-generation H1-antagonists impair exercise capacity through both central sedative effects and peripheral vasodilation. For cardiovascular patients requiring antihistamines, the study recommends second-generation agents like fexofenadine that minimally cross the blood-brain barrier. Timing doses to avoid peak plasma concentrations during prescribed exercise periods can further mitigate interference with rehabilitation goals.

The studies collectively identify three critical adaptation strategies for respiratory and cardiovascular rehabilitation: chronotherapeutic alignment (coordinating medication peaks with rest periods), alternative agent selection (choosing drugs with lower fatigue profiles), and modality adjustment (modifying physiotherapy techniques to accommodate medication limitations). [36]'s findings on tuberculosis management particularly highlight the importance of flexible rehabilitation protocols that can be scaled in intensity based on daily fluctuations in drug-related fatigue.

MANAGEMENT OF CHRONIC DISEASES AND THEIR COMORBIDITIES

Chronic disease management necessitates a comprehensive approach that addresses both primary conditions and their associated comorbidities, with particular attention to drug-induced fatigue as a barrier to physiotherapy compliance. The included studies demonstrate diverse strategies for managing these complex cases, emphasizing the need for personalized care plans that balance pharmacological efficacy with functional rehabilitation goals.

Table 06: Chronic Disease Management Strategies Addressing Drug-Induced Fatigue and Comorbidities

Disease Context	Primary Challenge	Drug-Induced Fatigue Contributors	Integrated Management Approach	Sources
Chronic Heart Failure	Malnutrition-related fatigue	Loop diuretics, beta-blockers	Nurse-led nutritional support + medication review	[39]
End-Stage Renal Disease & Stroke	Polypharmacy burden	Phosphate binders, antihypertensives	Personalized deprescribing protocols	[40]
Pulmonary Tuberculosis & Neuropathy	Dual pathology complexity	Second-line TB drugs (neurotoxic)	Concurrent neurological rehabilitation	[41]
Knee Osteoarthritis	Pain-fatigue cycle	NSAID-induced gastrointestinal blood loss	Physical therapy + iron supplementation	[42]
Cirrhosis	Metabolic fatigue	Diuretics, lactulose	Symptom-targeted pharmacotherapy	[43]
Familial Mediterranean Fever	Exercise intolerance	Colchicine myopathy	Graded exercise programming	[44]
Chronic Venous Insufficiency	Activity-related discomfort	Venoactive drugs (sedation)	Compression therapy + lifestyle modification	[45]
Stress Urinary Incontinence	Medication side effects	Duloxetine (CNS effects)	Pelvic floor training + dose optimization	[46]

The management of malnutrition in chronic heart failure patients illustrates the intersection of pharmacological and non-pharmacological interventions. [39], highlights how loop diuretics, while essential for volume control, exacerbate nutritional deficiencies by promoting electrolyte wasting and anorexia. The nurse-led care model described combines close monitoring of serum albumin and micronutrient levels with strategic diuretic timing-administering furosemide after meals to minimize appetite suppression. This approach demonstrates a 32% improvement in physiotherapy attendance when combined with tailored protein supplementation, addressing both the iatrogenic and disease-related components of fatigue.

For patients with end-stage renal disease and stroke, [40] presents a case where polypharmacy reduction directly enhanced rehabilitation potential. The study details how phosphate binders and multiple antihypertensives compounded fatigue in a hemodialysis patient, limiting participation in post-stroke gait training. Through systematic deprescribing-prioritizing renally cleared medications and eliminating redundant agents-the care team achieved a 40% reduction in fatigue scores while maintaining adequate metabolic control. This case underscores the importance of regular medication reconciliation in chronically ill populations undergoing rehabilitation.

The concurrent management of pulmonary tuberculosis and peripheral neuropathy, as described in [41], reveals the challenges of balancing antimicrobial

efficacy with neurological preservation. Second-line TB drugs like linezolid were found to exacerbate neuropathy symptoms, reducing tolerance for balance exercises. The implemented strategy involved splitting the daily antibiotic dose to lower peak plasma concentrations while maintaining total therapeutic exposure, coupled with sensory re-education physiotherapy. This dual approach allowed continued TB treatment without compromising neuropathy rehabilitation. In knee osteoarthritis, [42] identifies NSAID-induced anemia as an underrecognized contributor to exercise intolerance. Chronic gastrointestinal blood loss from non-selective COX inhibitors was shown to reduce hemoglobin levels by an average of 1.2 g/dl in long-term users. The study protocol combines COX-2 selective inhibitors with iron supplementation and aquatic therapy, demonstrating superior adherence to weight-bearing exercises compared to conventional NSAID regimens.

Cirrhosis management presents unique metabolic challenges, where [43] details how lactulose-induced diarrhea and diuretic-related electrolyte imbalances synergistically impair physical function. The proposed stepped pharmacotherapy approach adjusts lactulose dosing to achieve 2-3 soft stools daily (rather than strict titration to ammonia reduction), combined with tailored potassium-sparing diuretics. This regimen showed a 28% improvement in endurance test performance when paired with resistance training, suggesting that modest compromises in biochemical targets may yield substantial functional benefits.

For autoimmune conditions like familial Mediterranean fever, [44] examines colchicine's dual role as both preventive therapy and myopathy risk factor. The study implements electromyography-guided dosing, reducing colchicine by 0.5 mg/day when subclinical myopathic changes appear on testing. This precision approach maintained attack prevention while allowing progressive resistance training, with patients achieving 18% greater strength gains compared to fixed-dose protocols.

Chronic venous insufficiency management, as explored in [45], demonstrates how venoactive drugs like horse chestnut extract can cause sedation that conflicts with compression therapy adherence. The trial compares conventional stockings with intermittent pneumatic compression, finding the latter better tolerated by medicated patients due to reduced reliance on active patient participation. The duloxetine experience in stress urinary incontinence, detailed in [46], reveals how CNS side effects can undermine pelvic floor rehabilitation. Nearly 40% of patients discontinued therapy due to medication-related drowsiness in standard protocols. The optimized regimen introduces duloxetine at 20 mg/day (half typical starting dose) with weekly 10 mg increments, synchronized with progressive pelvic floor exercises. This slow titration achieved equivalent continence outcomes with 58% lower dropout rates.

8. Impact and Management of Fatigue Across Disease Contexts

Fatigue manifests as a debilitating symptom across various disease states, often exacerbated by pharmacological interventions and significantly impacting patients' ability to engage in physiotherapy. The included studies demonstrate how disease-specific mechanisms interact with drug-related fatigue pathways, creating unique challenges for rehabilitation compliance.

Table 07: Disease-Specific Fatigue Profiles and Rehabilitation Considerations

Disease Context	Primary Fatigue Mechanism	Drug Contributors	Rehabilitation Adaptation	Sources
HIV / AIDS	Chronic immune activation + mitochondrial toxicity	Antiretrovirals (NRTIs)	Graded aerobic exercise with viral load monitoring	[47]
Head / Neck Cancer	Radiation-induced tissue damage + anemia	Chemotherapy (cisplatin)	Swallowing therapy timed to drug clearance	[48]

In HIV/AIDS management, [47] identifies nucleoside reverse transcriptase inhibitors (NRTIs) as key contributors to fatigue through mitochondrial DNA depletion. The study reveals that zidovudine and stavudine particularly impair oxidative phosphorylation in skeletal muscle, reducing exercise tolerance. Rehabilitation programs must account for this metabolic limitation by incorporating frequent rest intervals and monitoring for lactic acidosis during aerobic training. Head and neck cancer patients present distinct challenges, where [48] demonstrates that cisplatin-based chemoradiation induces fatigue through multiple concurrent pathways. The cytotoxic agent not only causes anemia through bone marrow suppression but also damages oropharyngeal musculature, complicating swallowing rehabilitation. The study's pulmonary function data reveal significant reductions in maximal inspiratory pressure (MIP) following treatment, indicating respiratory muscle weakness that compounds general fatigue. Adaptive strategies include scheduling swallowing exercises during periods of peak drug clearance and incorporating inspiratory muscle training to counteract chemotherapy-induced diaphragmatic dysfunction.

CONCLUSION

This systematic review has synthesized current evidence on the impact of drug-induced fatigue on physiotherapy compliance, revealing critical insights into pharmacological and rehabilitative interactions.

The findings demonstrate that medication-related fatigue significantly impedes rehabilitation adherence across diverse clinical populations, particularly in geriatric, neurological, and chronic disease contexts. Key mechanisms include central nervous system depression, metabolic dysregulation, and neuromuscular impairment, each requiring tailored management strategies. The review underscores the necessity of interdisciplinary collaboration to optimize pharmacotherapy while preserving functional capacity for rehabilitation. By integrating pharmacovigilance with rehabilitation planning, healthcare providers can enhance treatment adherence and improve patient outcomes.

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