Varenicline Reduces Delayed Union Rates in Nicotine-Dependent Adults with Cervical Fractures

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INTRODUCTION:

High serum nicotine levels are associated with increased risk of delayed union and nonunion. Varenicline, a nicotinic receptor partial agonist used in smoking cessation, has been shown to mitigate the adverse effects of nicotine use in rodent models. However, its impact on human adult cervical fracture patients is not known.

METHODS: The PearlDiver database was queried to identify nicotine-dependent adults with cervical fracture. Patients were stratified by preoperative varenicline use within one year of surgery and matched 1:1 by age, sex, and Charlson Comorbidity Index (CCI). Comparative analyses were performed on demographics, comorbidities, and medical and surgical complications up to two years postoperatively. Multivariate logistic regression analyses, accounting for significant variables, were utilized to further characterize the role of varenicline on fracture healing.

RESULTS:

In total, 1,883 non-varenicline and varenicline users were included. Mean age was 53.6 years, 47.0% were female, and mean CCI was 2.5. Varenicline users reported lower rates of blood loss anemia (Varenicline User = 5.4% vs Non-Varenicline User = 7.8%) but higher rates of chronic pulmonary disease (69.1% vs 55.7%), obesity (38.8% vs 34.2%), osteoarthritis (44.1% vs 39.3%), and depression (73.6% vs 67.7%), all p<0.05. At 90-day follow-up, varenicline users had lower rates of infection (0.3% vs 1.1%, p=0.011) and anterior (0.6% vs 1.6%, p=0.003) or posterior (0.5% vs 1.5%, p=0.003) fusion and but comparable rates of wound dehiscence (0.5% vs 0.7%, p=0.403) and hematoma (0.5% vs 0.3%, p=0.422). At 6-month follow-up, varenicline users had lower rates of delayed fracture union (0.4% vs 1.4%, p=0.002). Finally, at 2-year follow-up, varenicline users had lower rates of fracture sequelae (2.8% vs 4.3%, p=0.013) but comparable rates of pseudoarthrosis (1.2% vs 1.3%, p=0.882) as non-varenicline users. Multivariate regression analysis, accounting for age, gender, CCI, and significant comorbidities, revealed that varenicline users have lower odds of delayed union (OR=0.41, 95%CI=0.34-0.48, p<0.001) and pseudoarthrosis (OR=0.79, 95%CI=0.69-0.90, p<0.001).

DISCUSSION AND CONCLUSION:

In cervical fracture patients, varenicline use was associated with lower rates of infection, delayed fracture union, fracture sequelae, and subsequent anterior or posterior fusion. In addition, pseudoarthrosis and delayed fracture union patients were less likely to report varenicline use preoperatively. Pharmacotherapy may be beneficial in mitigating associated risks and optimizing outcomes in nicotine users with spinal pathologies.

Variable	Non-Varenicline Users (N = 1,883)	Varenicline Users (N = 1,883)	P-value
Demographics			
Age	53.64 (12.21)	53.64 (12.21)	1.000
Female Sex	889 (47.21)	889 (47.21)	1.000
CCI	2.52 (2.30)	2.52 (2.30)	1.000
Comorbidities			
Asthma	418 (22.20)	488 (25.92)	**0.009**
Blood Loss Anemia	147 (7.81)	102 (5.42)	**0.004**
Cerebrovascular Disease	722 (38.34)	725 (38.50)	0.947
Chronic Kidney Disease	365 (19.38)	347 (18.43)	0.479
Chronic Pulmonary Disease	1050 (55.76)	1302 (69.14)	**<0.001**
COPD	943 (50.08)	1204 (63.94)	**<0.001**
Congestive Heart Failure	152 (8.07)	170 (9.03)	0.322
Coronary Artery Disease	604 (32.08)	704 (37.39)	**<0.001**
Depression	1274 (67.66)	1385 (73.55)	**<0.001**
Diabetes	781 (41.48)	724 (38.45)	0.062
Hypertension	1448 (76.90)	1475 (78.33)	0.309
Obesity	643 (34.15)	731 (38.82)	**0.003**
Osteoarthritis	739 (39.25)	831 (44.13)	**0.003**
Peripheral Vascular Disease	611 (32.45)	595 (31.60)	0.600

Variable	Non-Varenicline Users (N = 1,883)	Varenicline Users (N = 1,883)	P-value
90-Day Complications			
Infection	20 (1.06)	6 (0.32)	**0.011**
Wound Dehiscence	14 (0.74)	9 (0.48)	0.403
Surgical Site Complications	16 (0.85)	7 (0.37)	0.094
Hematoma	5 (0.27)	9 (0.48)	0.422
Anterior Fusion	31 (1.61)	11 (0.58)	**0.003**
Posterior Fusion	28 (1.49)	9 (0.48)	**0.003**
6-Month Complications			
Delayed Union	27 (1.43)	8 (0.42)	**0.002**
2-Year Complications			
Pseudoarthrosis	24 (1.27)	22 (1.17)	0.882
Fracture Sequelae	81 (4.30)	52 (2.76)	**0.013**