Prevalence of Muscle Cramps in Patients With Diabetes

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There are limited epidemiological studies addressing the prevalence of muscle cramps in the general population and diseases like diabetes (1). Common long-term complications of diabetes, such as neuropathy and nephropathy, have been associated with higher rates of muscle cramps (2).

We aimed to determine the prevalence and characteristics of muscle cramps in patients with diabetes compared with healthy volunteers. Frequency, severity (using visual analog scale [VAS]), duration, and disability due to muscle cramps were evaluated, as is standard in clinical trials. Information about each patient's clinical status was collected, including patient demographics, neuropathy (diagnosed using established clinical and electrophysiological criteria and quantitated using the Toronto Clinical Neuropathy Score) (3), diabetes complications, duration and type of diabetes, concurrent cramp-inducing (β-blockers, diuretics, statins) and cramp-protecting (quinine, calcium channel blockers, antiepileptics) medications, and markers of glycemic control (HbA_{1c}).

Baseline demographics and cramp characteristics for 269 patients with diabetes (type 1 diabetes, $n = 87$; type 2 diabetes, $n = 144$) or healthy volunteer ($n = 38$) status are presented in Table 1. The age-adjusted prevalence of cramps was higher in patients with type 2 diabetes (65.2 vs. 45.5%; $P = 0.009$) but not type 1 diabetes (61.2 vs. 45.5%; $P = 0.13$) compared with healthy volunteers. Patients with type 1 diabetes (5.8 vs. 3.8 out of 10 on VAS; $P = 0.006$) and type 2 diabetes (6.7 vs. 3.8 out of 10 on VAS; $P < 0.001$) had more severe cramps than healthy volunteers. More type 2 diabetes patients reported that cramps were disabling compared with healthy volunteers (33.3 vs. 0%; $P = 0.0008$). In patients with diabetes, neuropathy (odds ratio, 3.34; 95% CI 1.62–7.11; $P = 0.0009$) and type of diabetes (odds ratio, 2.80; 95% CI 1.29–6.24 in type 2 vs. type 1 diabetes; $P = 0.0095$) were independent predictors of muscle cramps, while age, sex, and nephropathy were not.

Studies evaluating prevalence of neuropathy in diabetes have come from observational studies or treatment trials where there has not been characterization of cramps or adjustment for confounders (1,4). The unadjusted prevalence of cramps in our patients was consistent with these reports: 75.5% in type 2 diabetes (range, 45–78%) and 57.5% in type 1 diabetes (range, 24–34%). Neuropathy, a risk factor for development of cramps on the basis of peripheral nerve hyperexcitability (5) was found to be the most important factor determining development of cramps in our diabetic cohort. Nephropathy, which also occurs at a high rate in diabetes and has been associated with cramps, was not an independent predictor in our cohort. Limitations include lack of a validated questionnaire for cramps, younger control group, and lack of data on factors relevant to cramps such as pregnancy, hepatic dysfunction, arterial hypertension, vitamin levels, and electrolyte status. In spite of these limitations, the current study shows that muscle cramps are prevalent, severe, and disabling in patients with type 2 diabetes. Muscle cramps do not appear to be more prevalent or disabling in patients with type 1 diabetes; however, more studies are needed to confirm these findings and evaluate mechanisms underlying the development of cramps in diabetes. We recommend that treatment trials in patients with diabetes include muscle cramps as an outcome measure.

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Table 1—Demographics and cramp characteristics in healthy volunteers, type 1 diabetes, and type 2 diabetes

Factor	Type 1 diabetes $n = 87$	*P* value (type 1 diabetes vs. healthy volunteers)	Type 2 diabetes $n = 144$	*P* value (type 2 diabetes vs. healthy volunteers)	Healthy volunteers $n = 38$
Age, years	44.9 (18–81)	0.13	62.7 (32–88)	<0.0001	40.1 (19–75)
Sex (female), %	56.3	0.91	36.6	0.04	55.3
Nephropathy, %	11.9	0.005	20.8	<0.0001	0.0
TCNS (#/19)	5.4 (0–19)	<0.0001	9.8 (0–19)	<0.0001	1.2 (0–10)
Neuropathy, %	38.6	<0.0001	66.2	<0.0001	0.0
Neuropathic pain, %	24.1	0.001	34.0	<0.0001	2.6
Neurotropic medication, %	16.0	0.88	30.1	0.19	14.3
Duration of diabetes, years	25.4 (1–74)	—	11.1 (0–45)	—	—
HbA_{1c} level, %	7.7 (5.4–14.8)	<0.0001	7.4 (4.7–13.5)	<0.0001	5.7 (5.0–6.6)
HbA_{1c} level, mmol/mol	61 (36–138)	<0.0001	57 (28–124)	<0.0001	39 (31–49)
Cramp experience (yes), %	57.5	0.063	75.5	<0.0001	39.5
Age-adjusted (yes) %	61.2	0.13	65.2	0.009	45.5
Sex-adjusted (yes), %	57.5	0.24	74.7	<0.0001	35.7
Frequency (per month)	5.2 (0–40)	0.062	11.2 (0–180)	0.081	1.1 (0–5)
Duration (min)	3.2 (0–30)	0.58	2.4 (0–90)	0.29	2.4 (0.5–20)
Severity (#/10)	5.8 (1–10)	0.006	6.7 (0–10)	<0.0001	3.8 (1–8)
Disabling (yes), %	12.0	0.07	33.3	0.0008	0.0
ower limbs (yes), %	98.0	0.52	96.2	0.37	100.0
Upper limbs (yes), %	32.7	0.20	35.2	0.13	15.4
Cramp-inducing medication (yes), %	42.7	0.0002	74.8	<0.0001	9.1
Cramp-protecting medication (yes), %	21.0	0.005	30.9	<0.0001	2.9

Data are proportion or mean (range). TCNS, Toronto Clinical Neuropathy Score.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. H.K. created the questionnaire evaluating the frequency, severity, and duration of muscle cramps and disability due to muscle cramps; contributed to the statistical analyses; and wrote the manuscript. S.K. and C.B. contributed to the statistical analyses and edited the manuscript. E.H. maintained the database and edited the manuscript. E.L. maintained the database, helped with the statistical analyses, and reviewed the manuscript. D.H. maintained the database and reviewed the manuscript. V.B. contributed to the study design and edited the manuscript. B.P. contributed to the study design, overlooked the study, took responsibility for financial/funding support, and edited the manuscript. H.K. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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