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Diabetes Update

Vol. 2 | Issue 31| 2021

Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you "DIABETES UPDATE" which contains latest and interesting news in the field of Diabetes and Endocrinology.

- The use of microbiological cultures from remnant bone in the treatment of diabetic foot osteomyelitis
- A study on self-monitoring of blood glucose associated with therapeutic interventions that unstructured self-monitoring: Prism trial
- A study on the ratio of albumin to creatinine in the urine is associated to

The use of microbiological cultures from remnant bone in the treatment of diabetic foot osteomyelitis

The aim of this study was to examine culture results from the proximal and distal portions of bone excised intraoperatively as part of DFO therapy, as well as their impact on antibiotic selection and duration.

Each patient's age, gender, date of operation, operation site, date when bone segment samples were received in the microbiology laboratory, germs isolated, and antibiotics administered were all entered into a database. Only individuals who had both infected and residual bone

samples cultured were included in the study. The bone fragment samples were taken aseptically in the operating room and brought to the laboratory, where they were tested for Gram stain, culture, and antibiotic sensitivity. Based on existing literature and commonly recognised understanding of the pathogenicity of microorganisms in skin, soft tissue, and bone infections, the microbial isolates were classified as definite pathogens, likely pathogens, and un-likely pathogens. The antibiotics prescribed and the length of time they were given was then compared to hospital prescribing guidelines and microbiologists' recommendations.

A total of 47 patients were enrolled in the study during the time period. Prior to the surgery, all of the patients got antibiotic medication. Antibiotics were given until the findings of the bone culture were known. All patients had their footwear evaluated by physiotherapists and podiatrists to allow for unloading. Mixed anaerobes and Enterococcus faecalis were the pathogens that were isolated the most from diseased tissues. Within 12 months of surgery, 11% of the individuals required a severe amputation.

Pathogen classification	Organisms cultured
Definite pathogens	Gram positive cocci: *Staphylococcus aureus*, beta-haemolytic streptococci (such as Group B streptococcus, Group G streptococcus), *Streptococcus anginosus*
Likely pathogens	Gram negative rods (*E. coli, Pseudomonas aeruginosa, Proteus* spp, etc), anaerobes
Unlikely pathogens	Enterococci, Coagulase negative staphylococci

Table 1: Classification of pathogens cultured from bone samples

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In all cases, the remaining bone was infected, and 80 percent of the cases grew probable and/or confirmed pathogens from both segments of the bone. Patients who developed definite pathogens had a below-the-knee amputation in 27% of cases within 10 days, while patients who developed likely pathogens had a below-the-knee amputation in 8% of cases within 11 months.

Isolated pathogen		Bone specimen site (n=47)	
		Proximal (remnant) bone sample	Distal bone sample
Gram positive cocci	Coagulase negative staphylococci	9 (19.1)	10 (21.3)
	Staphylococcus aureus	5 (10.6)	6 (12.8)
	Group B streptococcus	4 (8.5)	4 (8.5)
	Group G streptococcus	3 (6.4)	0
	Streptococcus anginosus	3 (6.4)	2 (4.3)
Gram negative rods	*Proteus mirabilis*	8 (17)	8 (17)
	Escherichia coli	6 (12.8)	6 (12.8)
	Morganella morganii	5 (10.6)	6 (12.8)
	Pseudomonas aeruginosa	3 (6.4)	4 (8.5)
	Citrobacter freundii	2 (4.3)	3 (6.4)
	Proteus spp.	2 (4.3)	2 (4.3)
	Citrobacter koseri	2 (4.3)	1 (2.1)
	Providencia rettgeri	1 (2.1)	2 (4.3)
	Klebsiella pneumoniae	1 (2.1)	1 (2.1)
	Proteus vulgaris	1 (2.1)	0
	Klebsiella oxytoca	1 (2.1)	0
	Mixed anaerobes (not speciated)	5 (10.6)	10 (21.3)
	Peptostreptococci	1 (2.1)	1 (2.1)
	Bacteroides fragilis	0	1 (2.1)
Entero-cocci	*Enterococcus faecalis*	9 (19.1)	10 (21.3)
	Enterococcus spp.	1 (2.1)	2 (4.3)
	Vancomycin-resistant *Enterococcus*	1 (2.1)	0
	Enterococcus avium	0	1 (2.1)

Table 2: Pathogens isolated from bone cultures

It is difficult to accurately estimate intraoperatively whether clear surgical margins have been attained when resecting diseased bone, sampling of eftover bone culture can assist patients reduce the length of antibiotic treatment (27 percent of instances in cohort).

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A study on self-monitoring of blood glucose associated with therapeutic interventions that unstructured self-monitoring: Prism trial.

The efficacy of self-monitoring of blood glucose (SMBG) in type 1 diabetes and insulin-treated type 2 diabetes (T2D) is well established, and it is recommended in current guidelines. Although a recent meta-analysis revealed that SMBG may be related with better short-term glycemic control in non-insulin-treated T2D, data on the benefits of SMBG in non-insulin-treated T2D have been debated for years.

The aim of this study is to evaluate the benefits of intensive structured SMBG (ISM) vs. active control (AC) in non-insulin-treated type 2 diabetes and association between specific treatment interventions and glycemic control indices (T2D).

Patients were randomised to ISM (n = 501) or AC (n = 523) in the 12-month PRISMA study, which was a prospective, multicenter, open-label, parallel-group, controlled clinical research. The data was collected at four time points, corresponding to months 3, 6, 9, and 12 and visits 2, 3, 4, and 5, respectively. Regardless of the drug used, all therapeutic interventions were divided into four categories: I no change in drug therapy; ii) intensification of drug therapy (i.e. drug adjunct and/or dose increment); iii) de-intensification of drug therapy (i.e. drug discontinuation and/or dose reduction); and iv)

redistribution of drugs and/or dose reduction (i.e. any other type of drug therapy change).

At each visit, data on HbA1c levels and the number of hypoglycemia episodes were evaluated. Each HbA1c measurement at the planned appointment was considered to reflect the therapeutic change from the previous visit; as a result, any visits where the prescribed therapy was discovered to be different (presumably reflecting inter-visit therapeutic changes) were excluded. A mixed linear model with the model response variable "HbA1c changes from the preceding visit" was used to evaluate the association between the type of treatment adjustments and changes in HbA1c.

The proportion of therapeutic changes in the two groups at each visit, including intensification of drug therapy, de-intensification of drug therapy, and redistribution of drugs and/or dose, was significantly higher in the ISM group at visits 2–4 compared to the AC group (visit 2: $p = 0.0144$; visit 3: $p = 0.0068$; visit 4: $p = 0.0068$). When no modification, intensification, de-intensification, or redistribution of medication therapy occurred, median entry HbA1c levels were 7.00%, 7.26%, 6.95%, and 7.50%, respectively, in the entire study cohort. In both groups, intensification of pharmacological therapy resulted in substantial decreases in HbA1c compared to the previous visit, whereas de-intensification of medication resulted in a significant increase in HbA1c only in the AC group.

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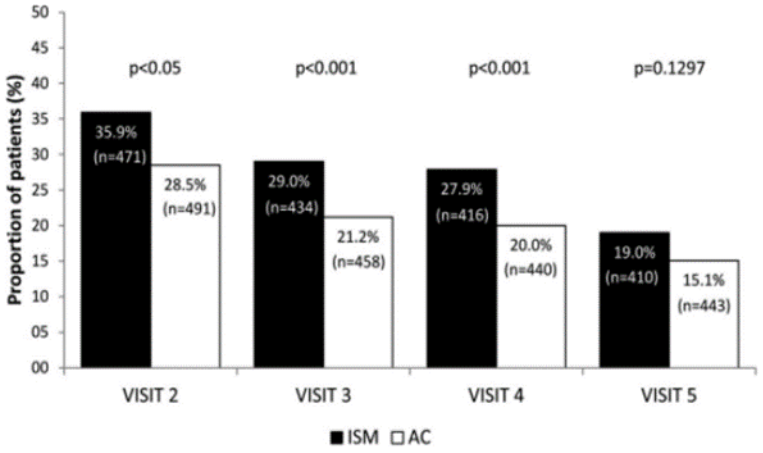

Figure 1: Proportion of patients with at least one therapy change in the ISM and AC groups.

The incidence of hypoglycemia per visit was rather low, even after adjusting for stratification factor and previous visit incidence. The ISM group had a significantly greater incidence of hypoglycemia than the AC group (4.3 vs.1.7 occurrences per visit every 100 patients, $p < 0.001$), which was associated with no change in pharmacological therapy but not with any other type of treatment.

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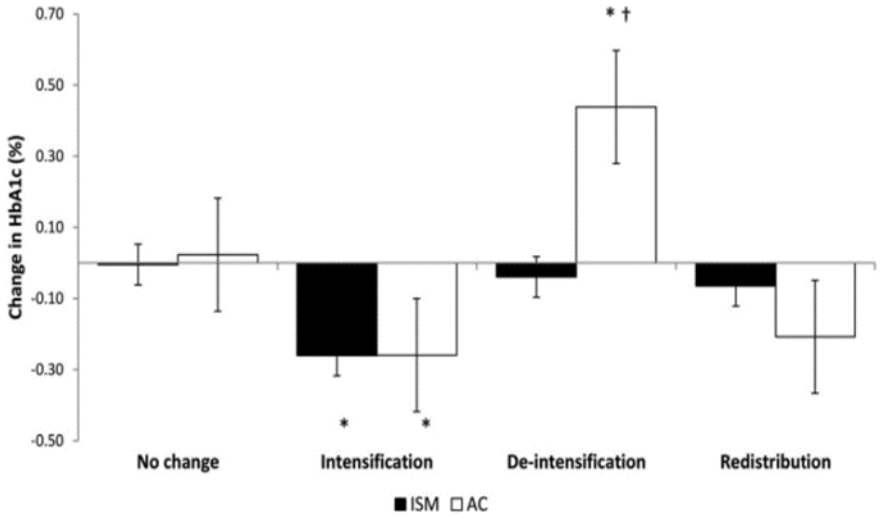

Figure 2: Change in HbA1c vs. baseline according to therapeutic intervention in the ISM and AC groups. * $p < 0.05$ vs baseline; $p < 0.05$ vs ISM. The results of the study strongly suggested that structured SMBG has therapeutic utility in lowering HbA1c in non-insulin-treated T2D patients, and that this clinical effect could be mediated by more suitable and prompt pharmacological therapy modifications.

Reference:

Di Molfetta S, Bosi E, Ceriello A, Cucinotta D, Tiengo A, Scavini M, Piccolo C, Bonizzoni E, Acmet E, Giorgino F; PRISMA STUDY GROUP. Structured self-monitoring of blood glucose is associated with more appropriate therapeutic interventions than unstructured self-monitoring: A novel analysis of data from the PRISMA trial. Diabetes Res Clin Pract. 2021 Sep 27;181:109070.

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A study on the ratio of albumin to creatinine in the urine is associated to prognosis in patients with diabetic foot osteomyelitis

Albuminuria is a symptom of diabetic neuropathy (DN) that appears early on. Many investigations on albuminuria have been conducted to predict the prognosis of DN. In diabetic individuals, albuminuria is a major predictor of renal insufficiency and cardiovascular events.

This study aimed to evaluate the correlation between albuminuria and all-cause mortality, major cardiovascular adverse events (MACE), and mixed end-point events in diabetic foot osteomyelitis (DFO) patients to see if there was a link between albuminuria and clinical outcomes.

A total of 202 patients with DFO who were hospitalized were included in this study and according to the urine albumin-creatinine ratio (UACR), the patients were split into three groups: normoalbuminuria (UACR 30 mg/g; n = 111), microalbuminuria (30 UACR 300 mg/g; n = 50), and macroalbuminuria (UACR > 300 mg/g; n = 41). Type 2 diabetes mellitus (T2DM), hypertension, coronary heart disease (CHD), cardiovascular diseases (CVD), sepsis, and amputation were all part of the patients' medical history. The ratio of ankle to brachial systolic blood pressure was used to establish the ankle-brachial index (ABI). In addition, the area, depth, position (forefoot, midfoot, or hind foot), number (single or many), and presence of infection were all used to assess foot health. All-cause mortality, MACE, and mixed endpoint events are the key outcomes. Myocardial infarction, stroke, or coronary heart disease (CHD) were defined as MACE. All-cause death, MACE, and hospitalisation for coronary artery disease were among the mix endpoint events. For normally distributed values, the mean and standard deviation (SD) were used, and for

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non-normally distributed variables, the median (quartiles) was used. Variables that were not continuous were expressed as a frequency. P < 0.05 was considered statically significant.

The average age was 60.3 years, 62.9 percent of the participants were male, and 45.05 percent tested positive for urine protein. Patients with DFO had significantly higher rates of all-cause death, MACE, and mixed endpoint events due to elevated UACR (all P for trend 0.01). After controlling for covariates, the risk of all-cause mortality, MACE, and mixed endpoint events in the microalbuminuria group increased by 81.8 percent, 135.4 percent, and 136.4 percent, respectively, as compared to the normoalbuminuria group. In the macroalbuminuria group, the risk of all-cause mortality, MACE, and mixed endpoint events increased by 246.2 percent, 145.1 percent, and 252.3 percent, respectively.

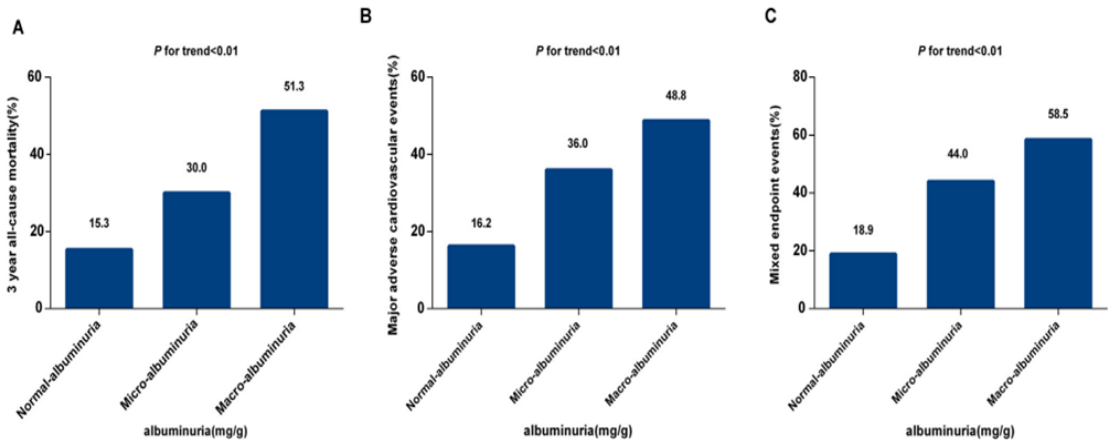

Figure 1: Comparison of all-cause mortality, MACE and mixed events among three groups

The high UACR was found to be responsible for 50.16 percent of all-cause mortality, 47.85 percent of MACE, and 59.11 percent of mixed endpoint events, according to the population attributable risk percentage (PAR percent). Meanwhile, those with microalbuminuria or macroalbuminuria have lower apoA1 and ABI, greater SCr, and a higher incidence rate of CHD, hindfoot infection, and severe infection (all P 0.05) than those with normoalbuminuria.

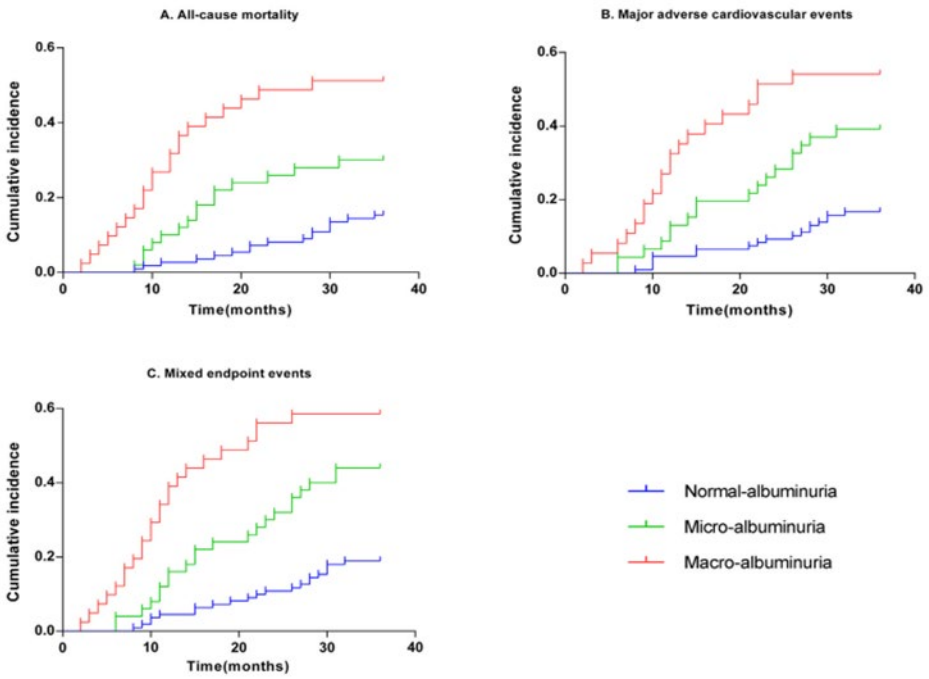

Figure 2: Cumulative incidence of all-cause mortality, MACE and mixed endpoint events by albuminuria level.

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Adjustment Strategy*	All-cause mortality	MACE	Mixed events
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Non-adjusted			
Microalbuminuria	2.212 (1.104–4.430)	2.700 (1.404–5.192)	2.729 (1.500–4.965)
Macroalbuminuria	4.903 (2.582–9.312)	4.782 (2.523–9.062)	4.882 (2.711–8.791)
Model I			
Microalbuminuria	2.009 (1.001–4.031)	2.545 (1.320–4.907)	2.513 (1.378–4.583)
Macroalbuminuria	4.666 (2.165–10.054)	3.883 (1.808–8.338)	4.510 (2.233–9.106)
Model II			
Microalbuminuria	1.818 (0.890–3.716)	2.354 (1.198–4.623)	2.364 (1.286–4.345)
Macroalbuminuria	3.462 (1.541–7.782)	2.451 (1.066–5.638)	3.523 (1.694–7.325)

Table 1: Univariate and mutivariate Cox proportional-hazard models assessing the association between main outcomes and albuminuria.

The study concluded showing, The UACR level is linked to all-cause mortality, MACE, and mixed endpoint events in patients with DFO, and an elevated UACR level raises the risk of all-cause mortality, MACE, and mixed endpoint events.

Reference:

Yang J, Huang J, Wei S, Zhou X, Nong Y, Sun J, Zhai Z, Li W, Lu W. Urine Albumin-Creatinine ratio is associated with prognosis in patients with diabetic foot osteomyelitis. Diabetes Res Clin Pract. 2021 Sep 9;180:109043.