

Mindfulness Meditation Eases Stress, Lowers ESR

BY NANCY WALSH
New York Bureau

SAN DIEGO — Participation in a program that incorporated mindfulness meditation and yoga resulted in a statistically significant reduction in psychological distress in a pilot study of patients with rheumatoid arthritis, Elizabeth Kimbrough Pradhan, Ph.D., reported at the annual meeting of the American College of Rheumatology.

A group of 63 adults with rheumatoid arthritis (RA) was randomized to either a 2.5-hour mindfulness-based stress reduction class once a week for 8 weeks or to a wait-list control group.

Mindfulness meditation involves the cultivation of moment-to-moment awareness and attention, against a backdrop of compassion for oneself and others, said Dr. Pradhan of the Center for Integrative Medicine, University of Maryland School of Medicine, Baltimore. Participants learned meditation techniques and hatha yoga postures, and were asked to practice at home for 45 minutes to an hour 6 days each week.

RA disease status was evaluated by Disease Activity Score (DAS) 28, while psychological distress was measured by the

Symptom Checklist-90-Revised. Patients were predominantly female, educated, and of mid to high socioeconomic status. All were under the regular care of a rheumatologist, with 74% taking disease modifying antirheumatic drugs, 15.9% being prescribed biologic agents, 50.8% taking nonsteroidal anti-inflammatory drugs, and 31.8% using corticosteroids.

In the meditation group, there was a 30% reduction in psychological distress at 2 months, which was a statistically significant change, Dr. Pradhan said. The 10% decrease seen in the control group was not significant.

At 6 months, a statistically significant 33% reduction in psychological distress was seen in the meditation group, compared with a nonsignificant 2% decrease in the control group.

The mean DAS28 at baseline was 3.1 in the treatment group and 3.3 in the control group, indicating moderate disease activity. Mean erythrocyte sedimentation rate (ESR) was 22.1 in both groups.

There was no change in disease activity

in either group by 2 months, but by 6 months there was an 11% decrease in the meditation group. This was statistically significant but would not be considered clinically significant by experts, Dr. Pradhan said. "Nonetheless, what was interesting was that of the four components in the DAS28, the one driving the change was

ESR," she said during a press briefing. There was a statistically significant 23% reduction in ESR from baseline to 2 months in the meditation group, and a statistically significant 33% decrease from baseline to 6 months.

At both of these time points, there were slight increases in ESR in the control group. As to why the ESR would have decreased in response to meditation, Dr. Pradhan offered several possible explanations. One was that the meditation group may have modified lifestyle factors.

"If participants in the meditation group were feeling better as a result of being in the mindfulness-based stress reduction course, it is possible that they could have changed their diets to include more fruits

and vegetables, reduced fried and sugary foods and so forth, which may have contributed to a decrease in general inflammation," she explained.

Another possible explanation could be a proinflammatory response to stress, involving activation of the hypothalamus-pituitary-adrenal (HPA) axis and the autonomic nervous system, she offered. Emotional responses to stress register in the hippocampus, causing the release of corticotropin-releasing hormone (CRH), which stimulates the HPA axis, ultimately resulting in the release of epinephrine and other hormones. CRH and norepinephrine are released peripherally through the response of the autonomic nervous system.

"A CRH receptor-dependent inflammatory response in RA synovial tissue has been observed, and CRH has been seen to up-regulate prostaglandin production in RA synovial tissue in a dose-response manner," she said.

CRH, norepinephrine, and epinephrine may also potentiate inflammation in RA by activating macrophages that release interleukin (IL)-1, IL-6, and tumor necrosis factor- α and through up-regulation of α -adrenoceptors for norepinephrine that results in increased IL-6 secretion, Dr. Pradhan added. ■

Participants in mindfulness meditation may have made positive lifestyle changes, thereby contributing to a decrease in general inflammation.

Once-Abandoned Knee Surgery Sees Renewed Use in Arthritis

BY BRUCE K. DIXON
Chicago Bureau

CHICAGO — The once-dismissed unicompartmental knee arthroplasty is regaining popularity due to its specific advantages in certain patients, compared with total knee arthroplasty, according to Dr. Bryan J. Nestor of the Hospital for Special Surgery in New York.

"It's an operation that's seen renewed interest over the last 10 years and I think for some good reasons," Dr. Nestor said at a symposium sponsored by the American College of Rheumatology.

Indications for unicompartmental knee replacement (UKR), also called minimally invasive partial knee surgery, include:

- ▶ Isolated medial or lateral joint disease.
- ▶ Minimal and correctable deformity.
- ▶ Flexion contracture less than 5 degrees.
- ▶ Flexion greater than 115 degrees.
- ▶ Patient weight under 200 pounds.

"That leaves about 10% of the patients I see who have severe arthritis of the knee and are candidates for unicompartmental knee replacement," said Dr. Nestor. He described the procedure as less invasive than total knee arthroplasty (TKA).

"If you're only bending to 110 degrees preoperatively, you're not going to gain that motion postoperatively and are bet-

ter served with a TKA. However, if you're bending 130-135 degrees, which we sometimes see with isolated unicompartmental arthritis, doing a total knee [arthroplasty] may cause the patient to lose motion and I have to counsel him accordingly, as the average motion after total knee replacement is only about 115 degrees. With a unicompartmental knee I can feel pretty comfortable that I will preserve that 130-degree arc of motion," he said.

Within 6 weeks of UKR, patients feel improvement. After total knee arthroplasty, it can take 3 months.

DR. NESTOR

beyond 90 degrees and can do outpatient rehabilitation. Further, many feel better by the 6th week, "whereas with total knee replacement we don't usually see that much self-reported improvement until 3 months," he said. "More importantly, patients will tell you that the knee feels like a normal knee."

"This technique is associated with a failure rate of 10%-15% at 10 years, compared with 2% or less for TKA. The unicompartmental procedure can now be revised. Today, a revision of a failed unicompartmental knee replacement approaches the results of a total knee arthroplasty, so we're not burning a bridge and that's why I think the renewed interest in UKR for selected patients is justified." ■



Sulfasalazine Induced Falsely Positive Urinary Catecholamines

BY NANCY WALSH
New York Bureau

GLASGOW, SCOTLAND — Sulfasalazine should be added to the list of drugs that can interfere with assays of urinary catecholamines and their metabolites, Dr. Clive Kelly reported at the annual meeting of the British Society for Rheumatology.

Several medications—including tricyclic antidepressants, antipsychotics, and levodopa—can cause false-positive results when assays for normetanephrine and metanephrine are undertaken to rule out pheochromocytoma. The effect of sulfasalazine on the results of urinary catecholamine assays has not thus far been reported in the literature or to the manufacturers, according to Dr. Kelly, who heads the department of rheumatology, Queen Elizabeth Hospital, Gateshead, Tyne and Wear, England.

In one such case of a false-positive pheochromocytoma result, a 48-year-old man with well-controlled rheumatoid arthritis was admitted with a blood pressure reading of 210/130 mm Hg. He had been taking sulfasalazine for 6 years and was then on 1 g/day. His other medications included Calcichew D3 (calcium carbonate plus vitamin D₃), cimetidine, and thyroxine. Initial investigations found nothing remarkable, Dr. Kelly said, but following a 24-hour urine collection, a high-performance liquid chromatography assay found significantly increased levels of normetanephrine at

60.8 $\mu\text{mol/day}$ (the normal range is less than 3.2 $\mu\text{mol/day}$).

Three repeated analyses during the subsequent 5 months produced similar results, despite that neither MRI nor metaiodobenzylguanidine scintigraphy showed any evidence of a pheochromocytoma, Dr. Kelly wrote in a poster.

To further examine the influence of sulfasalazine on urine collections for fractionated metanephrines, he and his colleagues then prospectively recruited 10 rheumatoid arthritis patients on sulfasalazine who were not hypertensive and were not taking antihypertensive drugs, and 10 age- and sex-matched controls who also were not hypertensive but were not taking sulfasalazine. Both groups provided 24-hour urine collections, which were then analyzed using standard techniques.

The mean level of normetanephrine in the sulfasalazine group was 17.3 $\mu\text{mol/day}$, compared with 2.4 $\mu\text{mol/day}$ in the control group. The pheochromocytoma false-positive rate was 80% in the sulfasalazine group and 20% in the control group, Dr. Kelly reported. Normetanephrine elevations were not dose dependent.

"We suspect that a metabolite of sulfasalazine forms a peak on the chromatogram close to the position of normetanephrine and is therefore easily misidentified," he wrote. An alternative explanation is that sulfasalazine may increase endogenous loads of catecholamines or their metabolites. ■