

## Impact of Osteopathic Manipulative Treatment on Secretory Immunoglobulin A Levels in a Stressed Population

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**Context:** High levels of human secretory immunoglobulin A (sIgA) have been shown to decrease the incidence of acquiring upper respiratory tract infections. Osteopathic manipulative treatment (OMT) has been shown to improve cardiac indices, increase lymph flow rates through the thoracic duct, and decrease sympathetic tone in postoperative patients and those in intensive care. Therefore, we hypothesized that OMT may also increase sIgA levels in people under high levels of emotional and psychological stress, thereby enhancing immunity and potentially preventing subsequent infections.

**Objective:** To determine if OMT increases sIgA levels in highly stressed individuals.

**Methods:** Twenty-five second-year osteopathic medical students were randomly assigned to an experimental group (n=12) or a control group (n=13). All participants were scheduled to take their national board examination (Comprehensive Osteopathic Medical Licensing Examination-USA) within 2 to 3 weeks after the experiment. After each participant submitted a saliva sample for a baseline sIgA level assessment, the experimental group received 20 minutes of OMT while the control group sat quietly and relaxed in a separate area for 20 minutes. Participants in both groups rested quietly for 1 hour after the 20-minute session and then submitted a second saliva sample.

**Results:** A 2 × 2 repeated measures analysis of variance revealed that the experimental group displayed a statistically significant greater increase in postintervention sIgA levels than the control group ( $F_{1,23} = 5.92; P < .025$ ).

**Conclusion:** This study demonstrates the positive effect of OMT on sIgA levels in persons experiencing high stress. Results suggest that OMT may then have therapeutic preventive and protective effects on both healthy and hospitalized patients, especially those experiencing high levels of emotional or physiological stress and those at higher risk of acquiring upper respiratory tract infections.

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Secretory immunoglobulin A (sIgA, also referred to as salivary IgA) is the major immunoglobulin secreted by the mucosal system<sup>1</sup> and is found in saliva, intestinal fluids, bronchoalveolar lavage fluid, and other mucosal fluids.<sup>2</sup> Secretory IgA provides protection from pathogenic organisms by preventing attachment, replication, and colonization of such organisms.<sup>1,3</sup>

Recent literature has indicated an inverse relationship between stress and the level of mucosal immunity, in which increasing levels of stress—caused by either a perceived or a physical stress—cause a decrease in mucosal sIgA.<sup>4,5</sup> Levels of sIgA in humans have also been shown to indicate immune system potency. High levels of sIgA in humans have been shown to decrease the incidence of upper respiratory tract infections (URTIs).<sup>6</sup> Hospitalized patients, especially those under physiologic stress such as ventilated patients, have demonstrated lower levels of sIgA.<sup>7</sup> Lower levels of sIgA have been associated with an increased incidence of nosocomial pneumonia in critical care patients.<sup>8</sup>

Additional studies have demonstrated an indirect relationship between low levels of sIgA and high levels of stress. Jemmott and colleagues<sup>9</sup> found dental students who were exposed to high levels of stress were found to have decreased sIgA levels, and increased sIgA levels correlated with periods of relatively lower levels of stress. Bosch and colleagues<sup>10</sup> found that an increase in the amount of bacterial adherence to teeth accompanied low levels of salivary IgA following periods of increased stress.

In osteopathic patient care, OMT has been shown to improve lymphatic circulation and augment immunologic responses.<sup>11</sup> During the past 3 decades, the potential effect of OMT—particularly lymphatic pump techniques—on human immune response has been investigated.<sup>12</sup> Measel<sup>13</sup> reported a statistically significant enhanced immunologic response in

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subjects who received OMT as compared to a control group by measuring antibody response to pneumococcal polysaccharide assayed by bacterial agglutination and passive hemagglutination. Using a larger number of subjects and a readily measurable variable (serum antibody), Jackson et al<sup>14</sup> supported Measel's findings when they found that subjects who received OMT had an apparent enhancement in immunologic response after the application of the lymphatic and splenic pump techniques.

Further support for the usefulness of OMT and the lymphatic pump techniques in particular was reported by a group of collaborators who investigated the acute changes occurring in circulating blood cells and serum enzyme levels following lymphatic pump techniques. Despite the small number of subjects, results indicated a significant increase in circulating basophils in those subjects who were treated with 2 lymphatic pump techniques (pectoral traction and splenic pump) in contrast to the control group.<sup>15</sup> Basophils, which together with mast cells produce cytokines, are felt to play a more vital role in the immune response than had been thought previously.<sup>16</sup> In contrast, one study<sup>17</sup> found measuring interferon levels in 12 volunteers at various timed intervals within a 24-hour period showed no statistically significant difference in the serum concentrations between the OMT group and the control groups. Most recently, Henderson et al<sup>18</sup> showed no significant changes in salivary flow rate activity and salivary cortisol levels following OMT when compared to placebo procedure group.

The present pilot study was designed to investigate the influence of OMT on levels of sIgA. Due to the link between stress and sIgA, the use of OMT may cause research participants to experience a greater increase in sIgA compared to participants who did not receive OMT. A greater increase in sIgA among patients receiving OMT would suggest OMT could be used to increase immunity in vulnerable populations.

### Hypothesis

We hypothesized that participants in the experimental group would experience an increase in sIgA levels after receiving OMT and that participants in the control group would experience no change in sIgA levels.

### Materials and Methods

Men (n=12) and women (n=13) between the ages of 18 and 40 years who had no underlying medical problems were included in the present study. All participants were second-year medical students at New York College of Osteopathic Medicine of New York Institute of Technology (NYCOM) and were scheduled to take their national board examination (Comprehensive Osteopathic Medical Licensing Examination-USA Level 1) 2 to 3 weeks after their participation in the present study. Based on the repeated and almost constant feedback from students scheduled to take the examination, we proceeded with the study under the assumption that the participants were under considerable "pre-high-stakes examination" stress. We felt

this to be a considerably stressful time in the participants' lives.

Potential participants were excluded if they met any of the following criteria:

- vigorous exercise for more than 10 hours per week
- immunosuppressive syndromes (human immunodeficiency virus or AIDS, cancer, mononucleosis, or any other immunosuppressive syndrome not listed)
- steroid use
- radiation or chemotherapy within the past 3 years
- diagnosis of lupus, asthma, or any other autoimmune disease not stated above<sup>3,4</sup>

The study was reviewed and approved by the NYCOM Institutional Review Board, and all subjects provided informed consent.

### Procedures

Participants were provided a screening questionnaire to determine their suitability for inclusion in the study based on the previously mentioned inclusion and exclusion criteria. Twenty-five students were randomly selected from those who met the inclusion criteria. Based on a power analysis, a sample size of 25 was deemed justified. Each participant received an electronic mail message that included their study identification number and instructions for the day of the study (eg, do not chew gum). Participants were randomly placed into a control group or an experimental group. Participants were block randomized so there was a fairly equal distribution of men and women in each group.

After screening and randomization, the study was carried out in a single day. All participants were asked to report to the research laboratory at 10 AM the morning of the study. Upon entrance to the testing site, each participant submitted a 1-mL saliva specimen in a sterile container.

Participants in the experimental group were then escorted to an area where attending osteopathic physicians and osteopathic manipulative medicine fellows (called "operators") performed the following OMT techniques for 20 minutes: occipitoatlantal release for 5 minutes, rib raising for 5 minutes, and a thoracic pump technique for 10 minutes. These OMT techniques are described in *Figure 1*. The day before the study, the operators received 1 hour of instruction to standardize treatment. Each participant in experimental group was treated by 1 of 12 treatment operators. Control group participants were escorted to a quiet area of the laboratory and were asked to rest calmly while sitting at individual tables that were separated from the experimental group by large, solid room dividers.

After the 20-minute OMT or rest protocol was completed, all participants remained either seated or supine and rested quietly for 1 hour. A second 1-mL saliva specimen was collected after that hour. Gregory et al<sup>19</sup> investigated breast milk IgA and

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|---------------------------------|--|
| <b>occipitoatlantal release</b> | During this treatment, the operator cradles the subject's head with both hands. The tips of the operator's fingers remain at the level of the subject's bilateral occipital sulci bilaterally. The subject's neck is bent slightly forward throughout the treatment. The operator applies linear traction slowly as his or her fingers are rolled laterally away from the midline.   |
| <b>rib raising</b>              | The subject lies supine on a treatment table while the operator sits facing the subject's side. The operator uses gentle pressure and traction forces to disengage ribs that may be held down by tight muscle.   |
| <b>thoracic pump</b>            | The operator places his or her hands at the foremost portion of the subject's chest (the subject is lying supine on a treatment table with the operator seated at the subject's head). The heels of the operator's hands are on ribs 2 thru 4. A rhythmic pumping action is induced in a cephalad caudad vector in sync with the natural response of the subject's body tissues. The subject is instructed to breathe normally throughout the treatment. |

**Figure 1.** Descriptions of the osteopathic manipulative treatment techniques used in the protocol of the present study. Operators received 1 hour of instruction to standardize treatment.

strenuous exercise and found that breast milk IgA levels dropped with strenuous exercise within 30 minutes and returned to baseline at approximately 60 minutes. Based on that finding, we chose a 60-minute interval as a safe measurement point post-OMT in the current study.

Each specimen was immediately sealed, placed on ice, and shipped to an independent facility (Saliva Testing and Reference Lab Inc, Seattle, Washington) for analysis. Each sample was subject to 2 independent measurements of sIgA, and the average of those 2 measures was obtained for each sample.

At the completion of the study a \$10 Starbucks gift card was given to all subjects as compensation for their time.

## Results

Data were analyzed in a  $2 \times 2$  analysis of variance (ANOVA) with repeated measures on the second factor. The between-participant factor was group assignment: control group or experimental group. The within-participants factor was time: before intervention or after intervention. There was no significant effect of group, indicating that the sIgA levels from the control

group and the experimental group were generally the same ( $F_{1,23}=1.376$ ;  $P>.05$ ). There was a statistically significant main effect for time ( $F_{1,23}, 16.486$ ;  $P<.001$ ) and a statistically significant interaction effect between time and group ( $F_{1,23}, 5.931$ ;  $P=.027$ ). These findings indicate that the sIgA level before intervention and after intervention differed in general, and the change of sIgA levels from before intervention to after intervention differed in the control group and the experimental group.

The Table displays means and standard deviations (SD) for both groups, as well as the main effect of time on each group's mean sIgA measures. The sIgA level for the experimental group increased an average of 139%, while the control group's sIgA level increased an average of only 32%. Figure 2 and Figure 3 display changes in average sIgA measures at the participant level.

## Comment

Previous literature has demonstrated that there is an inverse relationship between an individual's level of stress and sIgA level.<sup>4,5</sup> Decreases in sIgA levels have shown to have deleterious

| Group        | Preintervention | Postintervention | Mean Difference | % Change |
|--------------|-----------------|------------------|-----------------|----------|
| Experimental | 99.83 (66)      | 238.83 (134)     | 139             | 139      |
| Control      | 109.46 (77)     | 144.23 (126)     | 35              | 32       |

\* Secretory immunoglobulin A (sIgA) measured in mg/L.

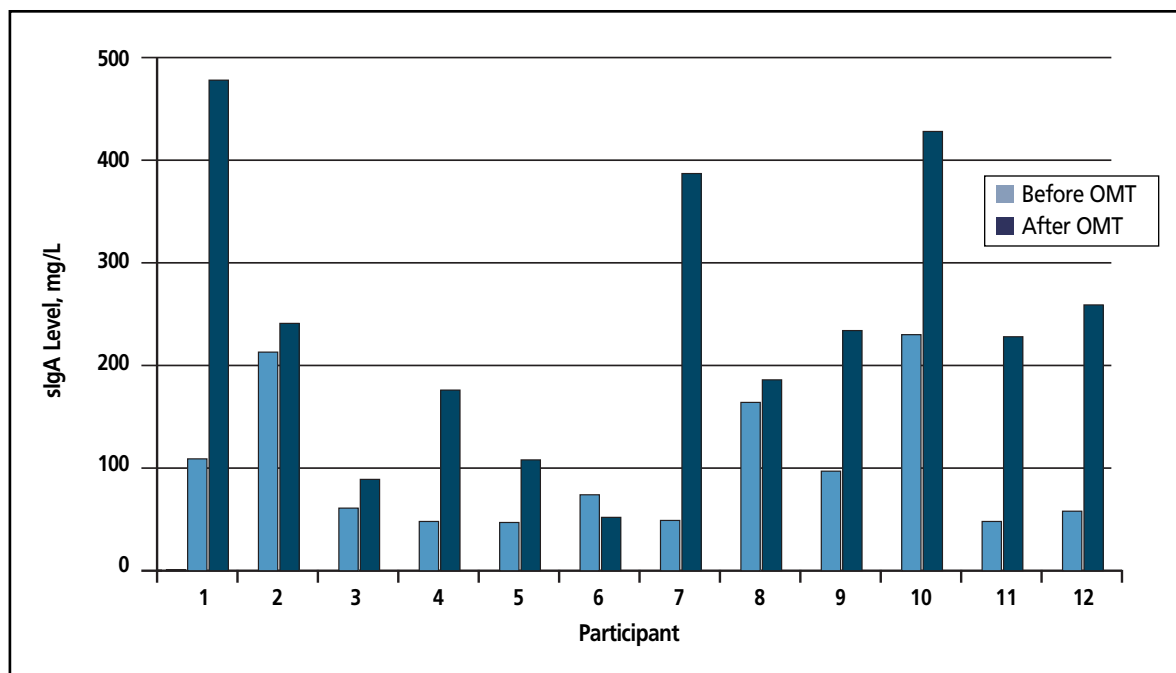


Figure 2. Changes in experimental group participants' mean secretory immunoglobulin A (sIgA) levels. As predicted, the average sIgA levels of experimental group participants increased after osteopathic manipulative treatment (OMT). Only one experimental group participant had a decrease in sIgA posttreatment.

effects on the immune system, which leads to an increased risk of infection. Such findings demonstrate the importance of discovering osteopathic clinical practices that increase the level of patients' sIgA. Although OMT has previously been reported to increase lymphatic flow through the thoracic duct,<sup>20</sup> increase peripheral circulation, improve cardiac indices, and decrease sympathetic tone<sup>21</sup> in postsurgical and intensive-care patients, our study may be the first to describe its effect on sIgA levels.

The present pilot study demonstrates that OMT significantly increases the sIgA levels in persons under apparent high levels of stress. As the *Table* demonstrates, the level of sIgA in participants who did not receive OMT had an average increase of 32%. Likewise, participants who received OMT experienced an average increase of 139% in their level of sIgA postintervention.

High levels of human sIgA, in both the clinical and non-clinical settings, have been shown to benefit the immune system by decreasing the risk of acquiring upper respiratory tract infections.<sup>6</sup> These simple OMT treatments may increase immunity and lower the incidence of nosocomial infections in populations that are subject to high levels of emotional and physiological stress and low levels of sIgA.

### Limitations

While our results clearly demonstrated a statistically significant increase in sIgA levels in the participants receiving OMT,

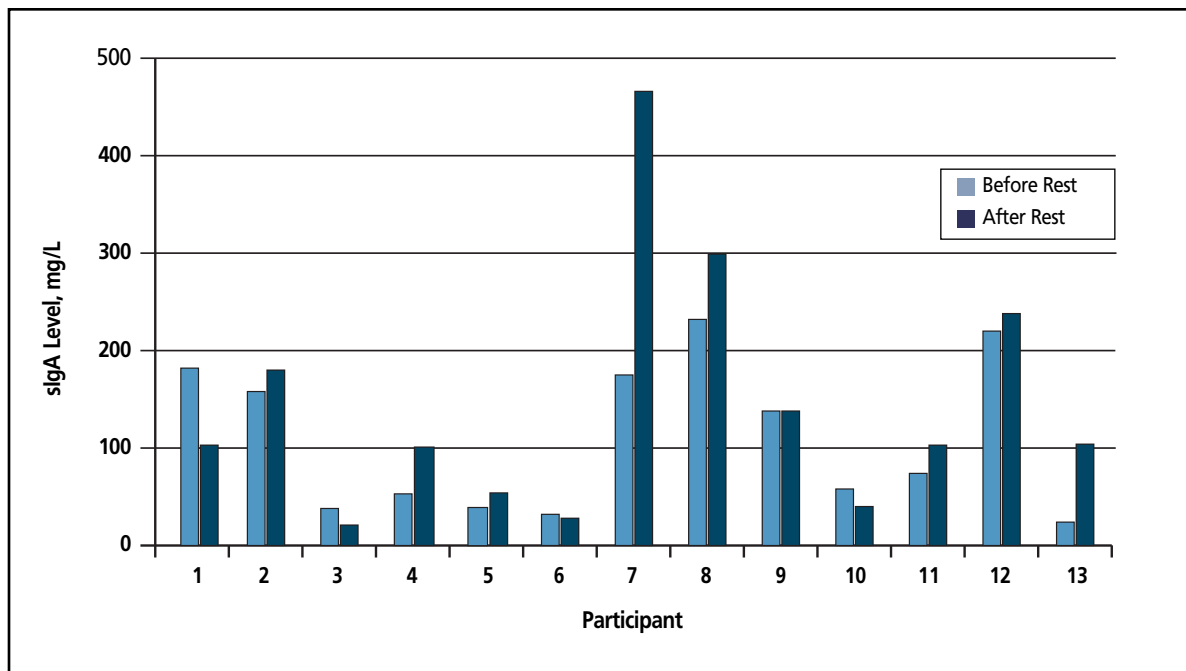
the authors recognize certain limitations. The present study provides evidence for the potential of measurement in saliva of total sIgA concentrations for this population, additional studies with a larger number of participants are needed to expand on these results. It is also feasible to apply the same rationales to different populations such as hospitalized patients and critically ill patients and, more importantly, to applying OMT for preventive care. While this study has assessed what was presumed to be a generalized stress situation shortly before a high-stakes national medical board examination, using simultaneous detailed stress assessment tools would be a next rational step. Another question raised by the present study is which OMT technique was responsible for the increase in sIgA? Was it 1 particular OMT technique or a physiologic accumulative or additive effect of combining all 3 techniques?

### Conclusion

Our findings demonstrate OMT's ability to increase sIgA and to potentially improve immune system function, in stressed but otherwise healthy individuals. Our encouraging results demonstrate the need for further investigation into the application of OMT to increase the immune system's response in healthy and immunocompromised patients.

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**Figure 3.** Changes in control group participants' mean secretory immunoglobulin A (sIgA) levels. In contrast to the experimental group participants, only 8 of the control group participants had an increase in sIgA; 5 control participants had a decrease in sIgA level.

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