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 and is found in saliva, intestinal fluids, bronchoalveolar lavage fluid, and other mucosal fluids. Secretory IgA provides protection from pathogenic organisms by preventing attachment, replication, and colonization of such organisms.

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. 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). Hospitalized patients, especially those under physiologic stress such as ventilated patients, have demonstrated lower levels of sIgA. Lower levels of sIgA have been associated with an increased incidence of nosocomial pneumonia in critical care patients.

Additional studies have demonstrated an indirect relationship between low levels of sIgA and high levels of stress. Jemmott and colleagues 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 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. During the past 3 decades, the potential effect of OMT—particularly lymphatic pump techniques—on human immune response has been investigated. Measel reported a statistically significant enhanced immunologic response in
subjects who received OMT as compared to a control group by measuring antibody response to pneumococcal polysaccha-
ride assayed by bacterial agglutination and passive hemag-
glutination. Using a larger number of subjects and a readily mea-
surable variable (serum antibody), Jackson et al\textsuperscript{14} 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 tech-
niques.

Further support for the usefulness of OMT and the lymph-
atic 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 sub-
jects, results indicated a significant increase in circulating baso-
phil in those subjects who were treated with 2 lymphatic pump
techniques (pectoral traction and splenic pump) in con-
trast to the control group.\textsuperscript{15} 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.\textsuperscript{16}
In contrast, one study\textsuperscript{17} found measuring interferon levels in 12
volunteers at various timed intervals within a 24-hour period
showed no statistically significant difference in the serum con-
centrations between the OMT group and the control groups.
Most recently, Henderson et al\textsuperscript{18} showed no significant changes
in salivary flow rate activity and salivary cortisol levels fol-
lowing 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 experi-
ence 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 med-
ical students at New York College of Osteopathic Medicine of
New York Institute of Technology (NYCOM) and were sched-
uled 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:

\begin{itemize}
\item vigorous exercise for more than 10 hours per week
\item immunosuppressive syndromes (human immunodeficiency
\hspace{0.5cm}virus or AIDS, cancer, mononucleosis, or any other immuno-
\hspace{0.5cm}suppressive syndrome not listed)
\item steroid use
\item radiation or chemotherapy within the past 3 years
\item diagnosis of lupus, asthma, or any other autoimmune dis-
\hspace{0.5cm}ease not stated above\textsuperscript{3,4}
\end{itemize}

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 deter-
mine their suitability for inclusion in the study based on the pre-
viously 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 elec-
tronic 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 con-
trol 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 osteo-
pathic manipulative medicine fellows (called “operators”) per-
formed the following OMT techniques for 20 minutes: occipitoatlantal release for 5 minutes, rib raising for 5 min-
utes, 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 stan-
dardize 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 qui-
elty for 1 hour. A second 1-mL saliva specimen was collected
after that hour. Gregory et al\textsuperscript{19} investigated breast milk IgA and
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.\textsuperscript{4,5} Decreases in sIgA levels have shown to have deleterious

| Table. Changes in Mean (SD) sIgA Levels From Pre- to Postintervention * |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| 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.
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’ slgA. Although OMT has previously been reported to increase lymphatic flow through the thoracic duct, increase peripheral circulation, improve cardiac indices, and decrease sympathetic tone in postsurgical and intensive-care patients, our study may be the first to describe its effect on slgA levels.

The present pilot study demonstrates that OMT significantly increases the slgA levels in persons under apparent high levels of stress. As the Table demonstrates, the level of slgA 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 slgA postintervention.

High levels of human slgA, 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. 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 slgA.

Limitations
While our results clearly demonstrated a statistically significant increase in slgA 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 slgA 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 slgA? 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 slgA 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.