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ORIGINAL ARTICLE

Advanced Oxidation Protein Products Aggravate Inflammation of Henoch-Schönlein Purpura Nephritis Through the RAGE-NF-κB Pathway

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SUMMARY

Background: **Henoch-Schönlein purpura nephritis (HSPN) is the most serious complication of allergic purpura (HSP). Advanced oxidized protein products (AOPPs) are an important damage factor in chronic kidney disease, and its expression level is also closely related to the pathogenesis of HSP. However, the role of AOPPs in HSPN reminds unclear. In the present study, we aimed to investigate the expression of AOPPs and its mechanism of inducing inflammation during the pathogenesis of HSPN in children.**
Methods: **We collected 20 patients with HSPN and 20 age- and gender-matched healthy controls in our hospital. ELISA, western blot, and immunofluorescence technique were performed to verify the above aim.**
Results: **Results showed that, as compared with the control group, serum levels of AOPPs in the HSPN increased significantly ($p < 0.05$). Serum IL-1β, IL-6 and TNF-α levels in the HSPN were also significantly higher than in the control group ($p < 0.05$). Moreover, the results showed that there was a positive correlation between serum AOPPs and inflammatory factor TNF-α, IL-6 and IL-1β level in children with HSPN. AOPPs treatment was found to significantly increase expression of RAGE, and p-P65, while the IκB was obviously reduced. Immunofluorescence showed that AOPPs significantly induce P65 nuclear metastasis. We further demonstrated that FPS-ZM1 (a selective RAGE inhibitor) and/or BAY 11-7082 (a selective NF-κB signaling pathway inhibitor) inhibited AOPPs-induced inflammation in HBZY-1 through blocking RAGE-NF-κB signaling pathway.**
Conclusions: **Collectively, these results implicated that AOPPs may be related to the pathogenesis of HSPN, AOPPs might induce or aggravate inflammation of HSPN through regulating RAGE-NF-κB signaling pathway. Above all, it has important clinical guiding significance for the prognosis judgment of HSPN, and can also provide new therapeutic targets for the HSPN.**
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KEYWORDS

AOPPs, HSPN, inflammation, NF-κB signaling pathway

INTRODUCTION

Henoch-Schönlein purpura (HSP) is a common systemic vasculitis syndrome that affects organs such as joints, skin, and kidneys. The main pathological manifestation of HSP is the deposition of immune complexes in blood vessels. HSP nephritis (HSPN) may be the most serious

complication of HSP, which damages the kidneys and even endangers the patient's life. HSPN is relatively common in pediatrics, and listed as the most common secondary glomerulopathy in children [1]. Although most have a good prognosis, some children may have suffered from prolonged illness, and about 15 - 20% of children develop chronic renal insufficiency [2]. Therefore, it is urgent to explore the pathogenesis of HSPN for providing new targets for the treatment of HSPN. Oxidative stress is involved in the pathogenesis of HSP. AOPPs are one of the hallmark products of oxidative stress and their uremic toxins are found in the blood of patients with chronic renal failure. Studies have suggested that AOPPs is not only the product of oxidative stress response, but may also actively participate in the induction and aggravation of oxidative stress damage [3]. AOPPs can stimulate monocyte nuclear neutrophils to synthesize, release IL-8 and other inflammatory cytokines, and induce vascular endothelial cells to produce reactive oxygen species (ROS), thereby inducing tissue cell damage and apoptosis [4]. Recent studies have confirmed that AOPPs are elevated in circulating blood in patients with IgA nephropathy and diabetic nephropathy, and is closely related to the severity of the disease [5,6]. In addition, some studies have shown that the expression level of AOPPs is also elevated in patients with HSP, and it is involved in the pathogenesis of HSP through various pathways [7]. However, there are few studies on the roles of AOPPs in HSPN, so it is of great significance to explore the expression and related mechanism of AOPPs in HSPN.

In this study, we aim to explore whether the expression level of AOPPs is increased in the serum of HSPN patients, whether it affects the expression of inflammatory factors, and whether AOPPs can enhance the inflammatory responses, thus promoting the occurrence and development of HSPN. Serum AOPPs and the expression levels of inflammatory factors IL-1β, IL-6 and TNF-α were measured and compared between HSPN patients and healthy patients. Changes in inflammatory factors after induction of glomerular mesangial cells by AOPPs were examined at the cellular level. Western blot was performed to detect the expression of receptors for intermediate and late glycosylation end products (RAGE), phosphorylated nuclear factor-κB (NF-κB) P65 and IκB after induction of AOPPs in glomerular mesangial cells.

MATERIALS AND METHODS

Reagents

Rat glomerular mesangial cells (HBZY-1) were purchased from Procell Life Science & Technology Co., Ltd. Fetal bovine serum, basic medium DMEM, penicillin, streptomycin, trypsin (0.25% trypsin + 0.02% EDTA) were obtained from Thermo Fisher Scientific Technology (China) Co., Ltd. Human Advanced Oxidation Protein Products (AOPPs), IL-1β, IL-6 and TNF-α ELISA Kit were purchased from Shanghai Enzyme-linked Biotechnology Co., Ltd. BCA kit, goat anti-rabbit IgG antibody, goat anti-mouse IgG antibody, and GAPDH antibody were purchased from Shanghai Beyotime Biotechnology Co., Ltd., and RAGE antibody, phosphorylated (p)-NF-κB P65 antibody, NF-κB P65 antibody, and IκB antibody from Cell Signaling Technology, USA. FPS-ZM1 (a selective RAGE inhibitor) and BAY 11-7082 (a selective NF-κB signaling pathway inhibitor) were obtained from Med Chem Express (MCE).

Clinical sample collection

Serum of 20 patients with HSPN and 20 age- and gender-matched healthy controls were collected from the affiliated hospital of Putian University (January 2020 to August 2022). Our experimental protocol was approved by the Ethics Committee of the affiliated hospital of Putian University (No.: 202038). Our work was performed in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans found at https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/.

Cell culture and treatment

HBZY-1 were cultured in DMEM containing 10% FBS, 100 U/mL penicillin and 0.1 mg/mL streptomycin, and then placed in an incubator at 37°C, 5% CO_2 + 95% air.

Cells were passaged with trypsin every two days

Cells were seeded in 96-well plates with 104 cells/well, and then stimulated with different concentrations of AOPPs. Cell viability was measured by CCK8. The cells were seeded in 6-well plates with 2 x 10^5 cells/well and then stimulated with a certain concentration of AOPPs for a specific time. The supernatant was collected for ELISA detection, and the cells were used for protein extraction for subsequent WB.

Cellular immunofluorescence

Cells were treated with AOPPs for 24 hours. Following treatment, cells were washed three times with phosphate-buffered saline (PBS), fixed with 4% paraformaldehyde for 15 minutes at room temperature, and permeabilized with 0.5% Triton X-100 for 20 minutes. After blocking with normal goat serum for 30 minutes, the cells were incubated overnight at 4°C with primary antibody against p-NF-κB (diluted 1:100). Subsequently, cells were incubated with the appropriate fluorescent secondary antibody for 1 hour at room temperature in the dark. After washing with PBS containing 0.1% Tween-20 (PBST), the nuclei were counterstained with DAPI for 5 minutes in the dark. The cells were then washed three times with PBST (5 minutes each) to remove excess DAPI. Finally, the slides were mounted with anti-fade mounting medium. Fluorescence images were captured using a fluorescence microscope.

Determination of AOPPs, IL- 1β, IL-6 and TNF-α
The cell serum and supernatant were collected and the concentrations of AOPPs, IL-1β, IL-6 and TNF-α content in the serum and supernatant of each treatment group were detected using an ELISA kit according to the kit instructions.

Western blot detection of RAGE, p-NF-κB, and p-IκB protein expression in glomerular thylakoid cells
The treated cells were collected, and the protein solution was collected by centrifugation of lysed cells according to the whole protein extraction kit; protein concentration was determined by BCA method; SDS-PAGE gels were prepared, protein sample was loaded, electrophoresed, and wet transferred to PVDF membranes; the membranes were blocked with 5% skim milk for 1 hour at room temperature and incubated with the corresponding RAGE antibody (1:1,000), p-NF-κB P65 antibody (1:1,000), p-IκB antibody (1:1,000), and GAPDH antibody (1:2,000). Samples were incubated overnight at 4℃; TBST was added and shaken 3 times for 5 minutes each time; the corresponding goat anti-rabbit IgG antibody or goat anti-mouse IgG antibody (1:5,000) was incubated at room temperature for 1 hour. TBST was added and shaken 3 times for 5 minutes each time, then ECL developer was added, developed, and pictures were taken. The expression levels of RAGE, p-NF-κB, and p-IκB were calculated as the grayscale values of the target protein bands compared to GAPDH.

Statistical analysis
SPSS 20.0 software was used for analyzing the data, and the data were expressed as $x \pm s$. The means of multiple groups were compared by chi-squared test and one-way ANOVA, and differences were considered statistically significant at $p < 0.05$. Spearman's correlation analysis was used to investigate the relationship.

RESULTS

Comparison of serum concentrations of AOPPs and inflammatory factors in children with HSPN and healthy children and their relationships
The concentration of AOPPs in children with HSPN was 191.988 to 393.317 μmol/L, with an average of 271.835 ± 61.3194 μmol/L (Figure 1A). The concentration of AOPPs in healthy children ranged from 66.157 to 193.505 μmol/L, with an average of 122.761 ± 37.301 μmol/L (Figure 1A). The concentration of AOPPs in HSPN children were significantly higher than those in healthy children, and the difference was statistically significant ($p < 0.001$).
Similarly, the concentrations of inflammatory cytokines (TNF-α, IL-6, and IL-1β) in children with HSPN were 107.808 ± 27.894, 85.739 ± 15.558, 80.919 ± 16.946 pg/mL, respectively (Figure 1B - C). The concentrations of inflammatory cytokines (TNF-α, IL-6, and IL-1β) in healthy children were 63.976 ± 17.488, 30.265 ± 8.856, 33.790 ± 8.613 pg/mL, respectively (Figure 1B - C). Compared with healthy children, the serum levels of IL-1β, IL-6 and TNF-α in children with HSPN were significantly increased ($p < 0.001$).
We further used Spearman's correlation analysis to investigate the relationship between AOPPs and the expression levels of inflammatory factors in children with HSPN. The results showed that there was a positive correlation between serum AOPPs and inflammatory factor TNF-α level in children with HSPN and the correlation coefficient: $R^2 = 0.6097$, $p < 0.001$ (Figure 2A). As for IL-6, IL-6 was positively correlated with AOPPs levels ($R^2 = 0.4215$, $p < 0.001$) (Figure 2B); IL-1β was also positively correlated with AOPPs levels ($R^2 = 0.4726$, $p < 0.001$) (Figure 2C).

Cell viability of AOPPs stimulated mesangial cells for 24 hours
The results of the CCK-8 experiment after AOPPs stimulated mesangial cells (HBZY-1) for 24 hours showed that, compared with the negative control, when the concentration of AOPPs was ≥ 400 μg/mL, the difference in cell activity was statistically significant ($p < 0.05$) (Figure 3A). When the concentration of AOPPs was ≤ 200 μg/mL, the difference in cell activity was not statistically significant ($p > 0.05$) (Figure 3A). Thus, we choose 200 μg/mL as the maximum concentration for further experiments.

AOPPs treatment induce inflammation of HSPN *in vitro*
We used the ELISA kit to measure the concentrations of IL-1β, IL-6 and TNF-α in HBZY-1 cells treated with AOPPs. Results showed that the concentrations of IL-1β, IL-6, and TNF-α in the AOPPs-treated group was significantly higher than the PBS group ($p < 0.05$) (Figure 3B - C). In addition, the concentrations of IL-1β, IL-6 and TNF-α increased in an AOPPs concentration-dependent manner (Figure 3B - C).

Effect of AOPPs on the expression of RAGE/NF-κB signal axis related proteins in glomerular cells
Compared with the normal group, the expression levels of RAGE and p-NF-κB P65 in AOPPs group were significantly increased ($p < 0.05$) (Figure 4A - C). Compared with the PBS group, the expression of IκB protein in AOPPs group was significantly decreased ($p < 0.05$) (Figure 4D). In immunofluorescence, AOPPs treatment obviously induced the transfer of P65 from cytoplasm to nucleus (Figure 4E).

AOPPs promote IL-1β, IL-6 and TNF-α production and secretion via RAGE/NF-κB signal axis
We further proved that the inflammatory cytokines IL-1β, IL-6 and TNF-α were induced selectively via RAGE/NF-κB signal. Results showed that, in BAY 11-7082 (a selective NF-κB signaling pathway inhibitor) treatment group, the concentration of IL-1β, IL-6 and TNF-α was significantly decreased (Figure 5A - C),

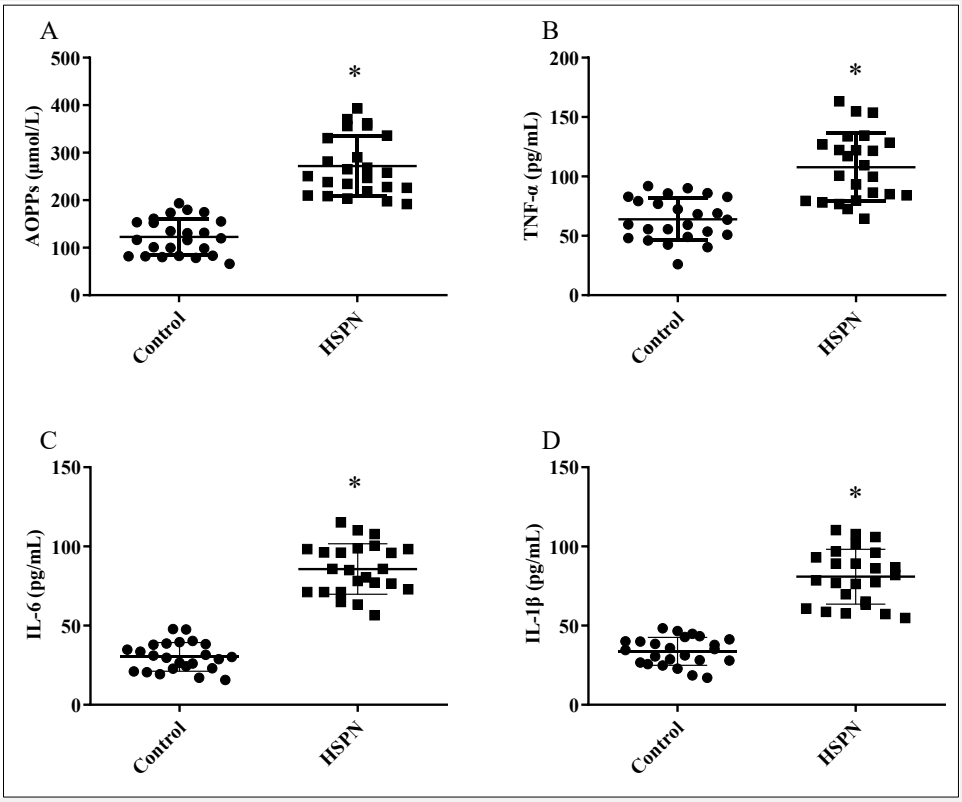

Figure 1. The levels of AOPPs and inflammatory cytokines in the serum of HSPN patients.

A) The concentration of AOPPs, B) The concentration of TNF-α, C) The concentration of IL-6, D) The concentration of IL-1β compared with the control group, * $p < 0.05$.

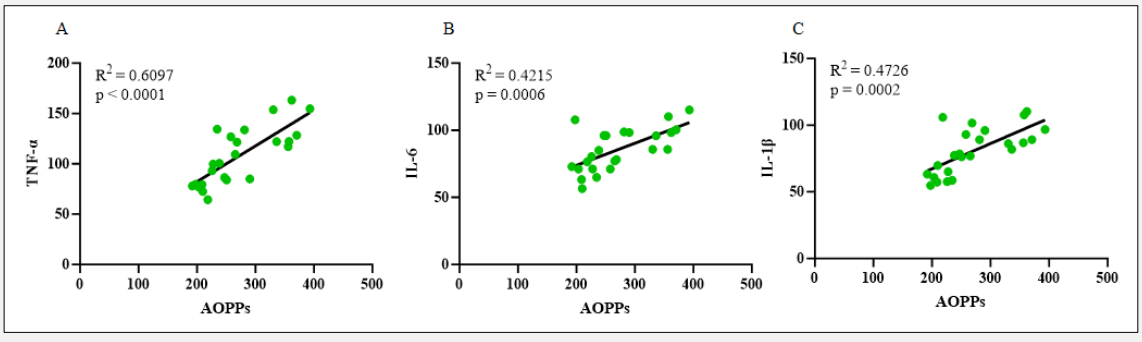

Figure 2. Correlation analysis between AOPPs and inflammatory cytokines in serum.

A) The correlation between AOPPs and TNF-α, B) The correlation between AOPPs and IL-6, C) The correlation between AOPPs and IL-1β.

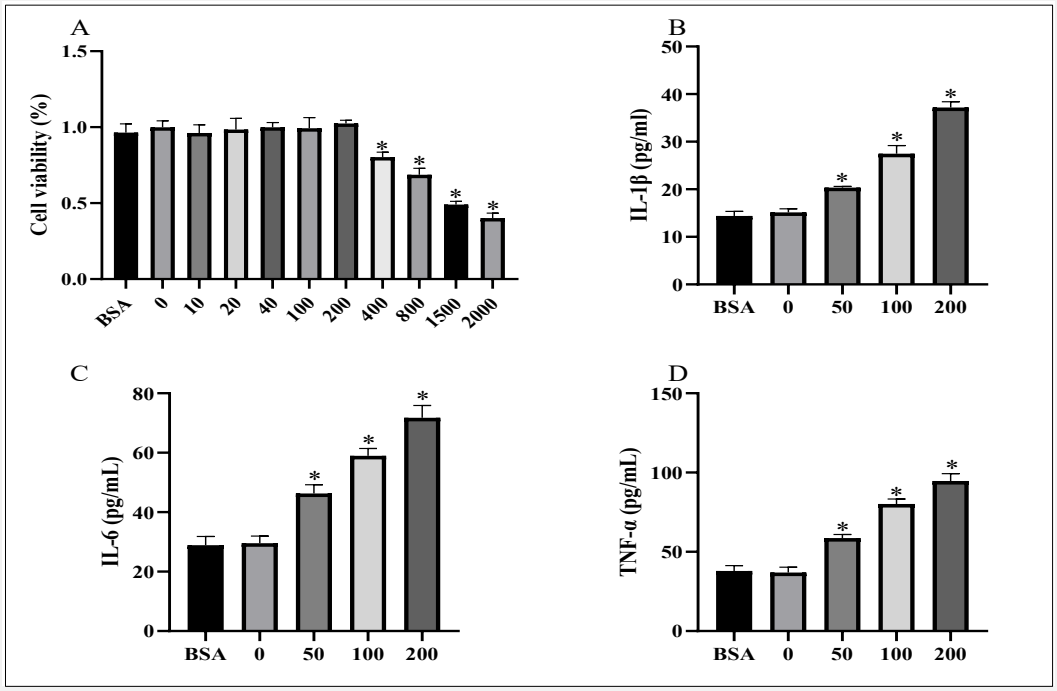

Figure 3. The effect of AOPPs on the viability and inflammatory factors of mesenchymal cells.

A) Cell viability, B) The concentration of IL-1β, C) The concentration of IL-6, D) The concentration of TNF-α, n = 5, X ± SD, compared with the BSA group, * p < 0.05.

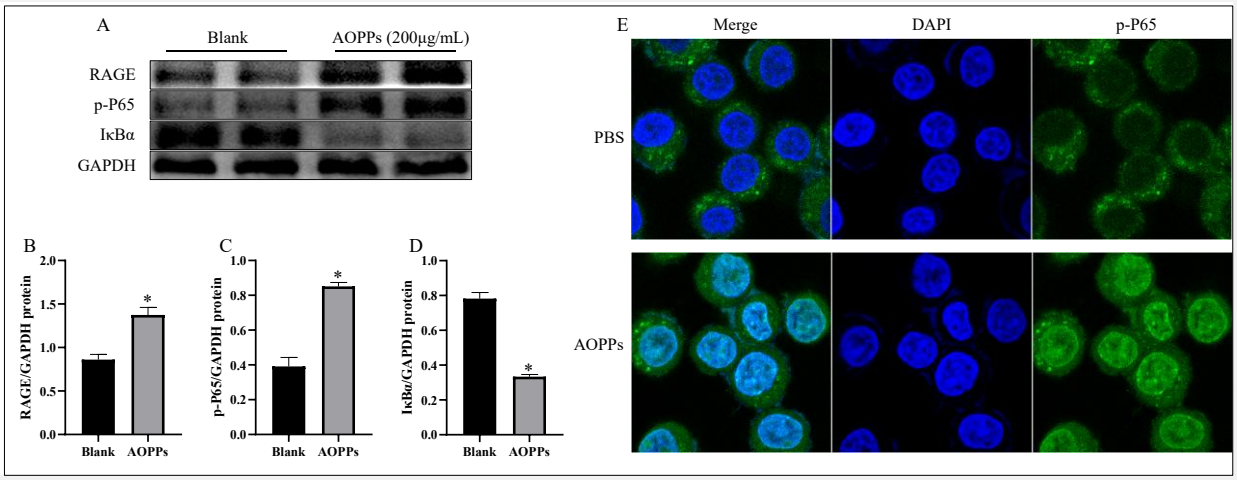

Figure 4. The effect of AOPPs on RAGE/NF-κB signal pathway.

A) Representative protein bands of RAGE, p-P65, and IκBα, B) Relative quantitative image of RAGE, C) Relative quantitative image of p-P65, D) Relative quantitative image of IκBα, E) Fluorescence images of p-P65, n = 3, X ± SD, compared with the blank group,* p < 0.05.

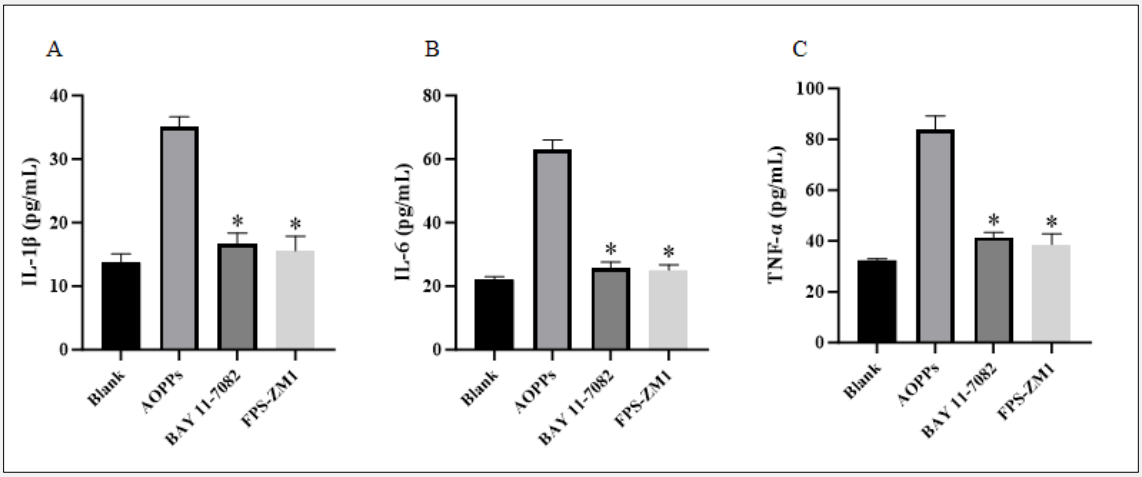

Figure 5. AOPPs promote IL-1β, IL-6, and TNF-α production through RAGE/NF-κB signaling.

A) The concentration of IL-1β, B) The concentration of IL-6, C) The concentration of TNF-α, n = 5, X ± SD, compared with the BSA group, * p < 0.05.

compared with the AOPPs treatment group. Similarly, compared with the AOPPs treatment group, RAGE inhibitor also obviously reduced the expression of IL-1β, IL-6 and TNF-α (Figure 5A - C).

DISCUSSION

HSPN is an immune complex nephropathy, with hematuria and proteinuria as the main clinical manifestations. It is mainly mesangial proliferative glomerulonephritis, often accompanied by crescent formation, stage glomerular capillary loop necrosis and other vasculitis manifestations. Its pathological basis is excessive deposition of extracellular matrix and mesangial cell proliferation. Its renal pathological features are mesangial cells and mesangial matrix hyperplasia, IgA and other immune complexes deposited in the glomerular mesangial area, which can be manifested as minimal lesions, mesangial hyperplasia or sclerosis, crescent formation, membranous hyperplasia and other lesions. It can also lead to renal interstitial fibrosis, renal tubular atrophy, inflammatory cell infiltration, etc. [8-10].

It has been demonstrated the role of AOPPs in immune inflammatory diseases such as coronary heart disease, diabetes, obesity or metabolic syndrome, active Crohn's disease, ulcerative colitis, systemic lupus erythematosus and rheumatoid arthritis [11]. AOPPs in patients with membranous nephropathy act on the receptor for advanced glycation end products (RAGE) on the cell membrane of podocytes, promoting intracellular NADPH-dependent oxidative stress, leading to increased reactive oxygen species (ROS) in the cell membrane of podocytes, further activation of NF-kB, MAPK, JAK-STAT and other downstream pathways, resulting in podocyte injury or triggering apoptosis pathway [12,13]. Furthermore, it was found that serum AOPPs and Gd-IgA 1 were strong risk factors for the progression of IgA nephropathy, and the two synergistically caused renal damage [14]. A large number of studies have shown that oxidative stress plays a key role in the development of HSPN [15]. In this study, serum AOPPs levels were found to be significantly higher in HSPN patients, compared with healthy controls, and statistically different. It is suggested that AOPPs play an important role in the pathogenesis of HSPN.

AOPPs are not only the products of oxidative stress, but also can induce monocytes and neutrophils to produce ROS. At the same time, AOPPs can induce or aggravate oxidative stress and chronic inflammation through oxidative cascade reaction. It is well known that the inflammatory response is a protective response in which the immune system is activated, inflammatory cells infiltrate, and secrete many cytokines when the body and tissue are damaged or some pathogenic microorganisms invade. Inflammatory response is beneficial to protect the body to a certain extent, but excessive inflammatory response and (or) persistent inflammation (chronic inflammation) are an adverse effect for the body, which is not conducive to the repair of the body and tissues. HSP is a systemic vasculitis with multi-organ involvement, and HSPN is one of the most serious complications in patients with HSP. In patients with HSPN, especially in children, the early glomerular lesions are characterized

by acute inflammation caused by an influx of leukocytes and proliferation of capillary endothelial cells [16]. It is suggested that inflammatory response is involved in the occurrence and development of HSPN. Inflammatory cytokines such as interleukin-1 (IL-1), IL-6, IL-8, IL-10, chemokines such as monocyte chemoattractant protein-1 (MCP- 1) and ICAM are involved in the pathogenesis of HSPN [17]. These factors promote vascular inflammatory response, mediate damage to vascular endothelial cells, increase vascular permeability and fragility, induce necrotizing vasculitis, and lead to tissue and organ damage. This study showed that inflammatory cytokines in serum including IL-1β, IL-6, and TNF-α were significantly higher in HSPN patients, compared with healthy controls, and statistically different. These inflammatory factors damage the kidney to promote the development of HSPN.

One of the main pathological changes of HSPN is the proliferation of mesangial cells. The proliferation of mesangial cells can secrete a large number of cytokines, activate a variety of immune response mechanisms, promote the occurrence of inflammatory response, lead to the infiltration of a large number of inflammatory cells, and cause glomerular damage [18]. Rat mesangial cells (HBZY-1) are commonly used in clinical research on the mechanism of nephropathy, and can also be used to construct animal models. In our study, we used HBZY-1 cells as an in vitro HSPN research model to study the possible potential pathogenesis of HSPN, in order to provide new strategies and new targets for clinical prevention and treatment of HSPN. AOPPs could stimulate HBZY-1 to secrete higher levels of inflammatory factors, IL-1β, IL-6, and TNF-α, compared with the negative control (PBS), the difference was statistically significant ($p < 0.05$). In addition, these inflammatory factors increased in an AOPPs concentration-dependent manner. Although some studies have shown that IGA abnormalities are the pathological basis of HSPN [19], our study found that AOPPs are also abnormally expressed in HSPN. Previously, it is known that AOPPs not only promote oxidation, but also promote inflammation and damage tissues or cells [20]. In our clinical data, it was found that the expression of AOPPs was high in HSPN patients and was positively correlated with the expression of inflammatory factors, IL-1β, IL-6, and TNF-α. Similarly, *in vitro* experiments also showed that AOPPS could promote the secretion of inflammatory factors by glomerular mesangial cells. Therefore, we hypothesize that AOPPs can promote HSPN inflammation and aggravate kidney damage.

In vitro studies, it has been reported that AOPPs can induce neutrophils and monocytes to synthesize and release inflammatory cytokines such as IL-8 and TNF-α, trigger respiratory bursts, and induce vascular endothelial cells to produce reactive oxygen species (ROS), thereby inducing inflammatory injury and apoptosis in various tissue cells. ROS can directly or indirectly act on p53, Jun, Akt and other transcription factors to regulate MAPK and NF-κB signaling pathways to mediate T and B lymphocyte differentiation, proliferation, and signal transduction [21,22]. Glomerular mesangial cells have many functions, including their function as mononuclear macrophages to phagocytose and removing macromolecules deposited in the mesangial area, and secretion and production of various cytokines to mediate various immune responses [23]. *In vitro*, we have proved that AOPPs treatment induce inflammatory response in glomerular mesangial cells. However, there are few studies on how do AOPPs induce inflammation in glomerular mesangial cells. In our study, we detected the RAGE-NF-κB signaling pathway using western blot. Our results showed that AOPPs treatment significantly upregulated the RAGE-NF-κB signaling pathway. Immunofluorescence results also showed that AOPPs treatment induces NF-κB P65 nuclear translocation. The activation of RAGE receptors can induce inflammation, and the NF-κB signaling pathway is a key pathway mediating inflammation. Further, we used FPS-ZM1 (a selective RAGE inhibitor) and BAY 11-7082 (a selective NF-κB signaling pathway inhibitor) to find that AOPPs-induced inflammation through blocking the RAGE-NF-κB signaling pathway. Thus, AOPPs may induce or aggravate inflammation of HSPN selectively via modulating RAGE-NF-κB signaling pathway.

CONCLUSION

In summary, all of the results in this study demonstrated that AOPPs show a promoting role in HSPN; AOPPs may induce or aggravate inflammation of HSPN through inducing activation of the RAGE-NF-κB signaling pathway. Our findings may offer a new understanding of the relationship of AOPPs and inflammatory damage in HSPN, which has important clinical guiding significance for the prognosis judgment of HSPN and can also provide new therapeutic targets and theoretical basis for the prevention and treatment of HSPN. However, further study needs to be performed on animals to support this conclusion.

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Declaration of Interest:
The authors declare that they have no conflict of interest.

References:

1. Chen L, Wang X, Yin L, Ma K, Liu X. Effects of dexamethasone and gamma globulin combined with prednisone on the therapeutic effect and immune function of Henoch-Schonlein purpura nephritis in children. J Clin Lab Anal 2021 Jan;35(1):e23580. (PMID: 33174652)

2. Hou L, Zhang Z, Du Y. Leflunomide therapy for IgA vasculitis with nephritis in children. BMC Pediatr 2021 Sep 8;21(1):391. (PMID: 34496826)

3. Azouaou Toualbi L, Adnane M, Ballouti W, et al. Mo602 high levels of Advanced oxidative protein products (aopp) help to predict the progression of atherosclerosis in chronic kidney disease with vitamine e treatement might stabilize aopp levels. Nephrol Dial Transpl 2021;36(Supplement_1):gfab089.0015. (https://doi.org/10.1093/ndt/gfab089.0015)

4. Li W, Jiang WS, Su YR, et al. PINK1/Parkin-mediated mitophagy inhibits osteoblast apoptosis induced by advanced oxidation protein products. Cell Death Dis 2023 Feb 7;14(2):88. (PMID: 36750550)

5. Shelbaya SEA, Ali HM, Ibrahim RH, Sawirs NS. Podocalyxin as an early marker predicting diabetic nephropathy and its correlation with stages of diabetic nephropathy in type two diabetic patients. QJM 2021;114:hcab100.097. (https://doi.org/10.1093/qjmed/hcab100.097)

6. Conti G, Caccamo D, Siligato R, et al. Association of Higher Advanced Oxidation Protein Products (AOPPs) Levels in Patients with Diabetic and Hypertensive Nephropathy. Medicina (Kaunas) 2019 Oct 7;55(10):675. (PMID: 31591338)

7. Liu Q, Yang Y, Ge S, et al. Serum level of advanced oxidation protein products (AOPPs) in patients with Henoch-Schonlein purpura and its relationship with aberrant glycosylation of IgA1 and Cosmc mRNA expression. Int J Dermatol 2019 Sep;58(9):1092-7. (PMID: 31250447)

8. Davin JC, Coppo R. Henoch-Schönlein purpura nephritis in children. Nat Rev Nephrol 2014 Oct;10(10):563-73. (PMID: 25072122)

9. Su Q, Jiang L, Chai J, et al. Changes of Peripheral Blood Lymphocyte Subsets and Immune Function in Children with Henoch-Schönlein Purpura Nephritis. Iran J Immunol 2021 Sep;18(3): 259-67. (PMID: 34596591)

10. Fengyong Z, Zhixiang F, Jiajia P, et al. Increased CD8+ T cells in patients with Henoch-Schonlein purpura nephritis exhibit suppressive immune activity. Immunol Lett 2022 Oct;250:23-8. (PMID: 36174770)

11. Cristani M, Speciale A, Saija A, Gangemi S, Minciullo PL, Cimino F. Circulating Advanced Oxidation Protein Products as Oxidative Stress Biomarkers and Progression Mediators in Pathological Conditions Related to Inflammation and Immune Dysregulation. Curr Med Chem 2016;23(34):3862-82. (PMID: 27593960)

12. Tanji N, Markowitz GS, Fu C, et al. Expression of advanced glycation end products and their cellular receptor RAGE in diabetic nephropathy and nondiabetic renal disease. J Am Soc Nephrol 2000 Sep;11(9):1656-66. (PMID: 10966490)

13. Zhu SY, Zhuang JS, Wu Q, et al. Advanced oxidation protein products induce pre-osteoblast apoptosis through a nicotinamide adenine dinucleotide phosphate oxidase-dependent, mitogen-activated protein kinases-mediated intrinsic apoptosis pathway. Aging Cell 2018 Aug;17(4):e12764. (PMID: 29659123)

14. Descamps-Latscha B, Witko-Sarsat V, Nguyen-Khoa T, et al. Early prediction of IgA nephropathy progression: proteinuria and AOPP are strong prognostic markers. Kidney Int 2004 Oct;66(4): 1606-12. (PMID: 15458457)

15. Jiang J, Duan W, Shang X, et al. Inducible nitric oxide synthase gene polymorphisms are associated with a risk of nephritis in Henoch-Schönlein purpura children. Eur J Pediatr 2017 Aug;176 (8):1035-45. (PMID: 28593405)

16. Arai M, Mii A, Kashiwagi T, Shimizu A, Sakai Y. The severity of glomerular endothelial cell injury is associated with infiltrating macrophage heterogeneity in endocapillary proliferative glomerulonephritis. Sci Rep 2021 Jun 25;11(1):13339. (PMID: 34172770)

17. Liu Q, Liu J, Du Y, Guo W, Mi J, Guo Y. Network Pharmacology and Molecular Docking Analysis to Explore the Mechanism of Huaiqihuang-Mediated Alleviation of Henoch-Schönlein Purpura Nephritis. Biomed Res Int 2022 Nov 4;2022:2798217. (PMID: 36389115)

18. Liu Y, Li X, Zhao M, et al. Macrophage-derived exosomes promote activation of NLRP3 inflammasome and autophagy deficiency of mesangial cells in diabetic nephropathy. Life Sci 2023 Oct 1;330:121991. (PMID: 37524161)

19. Torun Bayram M, Heybeli C, Yıldız G, et al. Comparison of clinical, pathological and long-term renal outcomes of children with Henoch-Schonlein purpura nephritis and IgA nephropathy. Int Urol Nephrol 2022 Aug;54(8):1925-32. (PMID: 34846620)

20. Xue K, Wang Y, Wang Y, Fang H. Advanced Oxidation Protein Product Promotes Oxidative Accentuation in Renal Epithelial Cells via the Soluble (Pro)renin Receptor-Mediated Intrarenal Renin-Angiotensin System and Nox4-H2O2 Signaling. Oxid Med Cell Longev 2021 Nov 26;2021:5710440. (PMID: 34873430)

21. Xie Y, Deng Q, Guo M, Li X, Xian D, Zhong J. Proanthocyanidins: A novel approach to Henoch-Schonlein purpura through balancing immunity and arresting oxidative stress via TLR4/MyD88/NF-κB signaling pathway (Review). Exp Ther Med 2023 May 9;25(6):300. (PMID: 37229322)

22. Xun T, Lin Z, Wang X, et al. Advanced oxidation protein products downregulate CYP1A2 and CYP3A4 expression and activity via the NF-κB-mediated signaling pathway *in vitro* and *in vivo*. Lab Invest 2021 Sep;101(9):1197-209. (PMID: 34031539)

23. Zhao Y, Li Q, Ouyang Q, Wu L, Chen X. Activated mesangial cells acquire the function of antigen presentation. Cell Immunol 2021 Mar;361:104279. (PMID: 33422698)