

RESEARCH LETTER

Nikolai Bolibok ORCID iD <https://orcid.org/0000-0002-4087-4007>

Estradiol E2 as a possible solution for therapy of severe viral infections with significant sex differentials in morbidity and mortality.

There are two viral infections with a significant sex differential in mortality: rabies and coronavirus COVID-2019. A teenage girl is the only person survived from rabies using Milwaukee protocol.

And only 36.2 % of 1023 coronavirus victims were female in Mainland China as of February 11, 2020 (15% in the beginning of outbreak) [4].

The explanation of that is action of estradiol on Ig production and internalisation by target cell.

As reported in 1985 by Michael J. Myers, Bruce H. Petersen, estradiol exerts a direct effect on B cells resulting in increased synthesis of IgM antibodies[1].

In 1988 F Furukawa, M B Lyons, L A Lee, S N Coulter, D A Norris proved that estradiol enhances binding to cultured human keratinocytes of antibodies [3].

N Kanda, K Tamaki in 1999 studied the in vitro effects of 17beta-estradiol (E2) on spontaneous immunoglobulin production by human PBMCs[2]. PBMCs from healthy human volunteers were cultured with E2. Immunoglobulin production of E2 -treated B cells was slightly higher than that of control cells; IgG production was 161% of control cells, and that of IgM was 157%. E2 increased IL-10 production of monocytes up to 250% of control level, but it did not affect that of T cells or B cells. Exogenous IL-10 (1 U/mL) further enhanced E2 -induced increase of immunoglobulin production by B cells, although this level of IL-10 alone was ineffective for B cells.

Also reported that 17β-Estradiol restores antibody responses to an influenza vaccine in a postmenopausal mouse model [5].

In the most recent research authors consider that targeted manipulations of ERα binding within enhanceosomes or switchosomes may improve antibody activities when pathogen-specific responses are weak [6].

CONCLUSION

17beta-estradiol hormone therapy in male and menopausal female patients can significantly improve survival rate.

Patients in risk group with possibly lethal form of infection by COVID-19 should be administered oral estradiol valerate in standard hormone therapy doses as benefits of treatment are more valuable than possible harm.

In case of clinical rabies higher allowed therapy doses of estradiol and Milwaukee protocol I should be used.

REFERENCES

1. Michael J. Myers, Bruce H. Petersen, Estradiol induced alterations of the immune system— I. Enhancement of IgM production, International Journal of Immunopharmacology, Volume 7, Issue 2,

1985,Pages 207-213,ISSN 0192-0561,[https://doi.org/10.1016/0192-0561\(85\)90028-1](https://doi.org/10.1016/0192-0561(85)90028-1).

2. Kanda N, Tamaki K. Estrogen enhances immunoglobulin production by human PBMCs.

J Allergy Clin Immunol. 1999 Feb;103(2 Pt 1):282-8. PubMed PMID: 9949320.

[https://doi.org/10.1016/s0091-6749\(99\)70503-8](https://doi.org/10.1016/s0091-6749(99)70503-8)

3. Estradiol enhances binding to cultured human keratinocytes of antibodies specific for SS-A/Ro and SS-B/La. Another possible mechanism for estradiol influence of lupus erythematosus.

F Furukawa, M B Lyons, L A Lee, S N Coulter, D A Norris

The Journal of Immunology September 1, 1988, 141 (5) 1480-1488;

4. The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) — China, 2020[J]. China CDC Weekly, 2020, 2(8): 113-122.

5. Doan C. Nguyen, Feda Masseoud, Xiuhua Lu, Franco Scinicariello, Suryaprakash Sambhara, Roberta Attanasio,17β-Estradiol restores antibody responses to an influenza vaccine in a postmenopausal mouse model,Vaccine,Volume 29, Issue 14,2011,Pages 2515-2518,ISSN 0264-410X,
<https://doi.org/10.1016/j.vaccine.2011.01.080>.

6. Bart G. Jones, Rhiannon R. Penkert, Sherri L. Surman, Robert E. Sealy, Stephane Pelletier, Beisi Xu, Geoff Neale, Robert W. Maul, Patricia J. Gearhart, J.L. Hurwitz, Matters of life and death: How estrogen and estrogen receptor binding to the immunoglobulin heavy chain locus may influence outcomes of infection, allergy, and autoimmune disease,Cellular Immunology,Volume 346,2019,103996,ISSN 0008-8749, <https://doi.org/10.1016/j.cellimm.2019.103996>.