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SHORT COMMUNICATION

Effect of Indomethacin on Selected Immune Parameters in Different Age Groups of Mice

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Summary

The authors studied the effect of indomethacin on the phagocytic activity of polymorphonuclear leucocytes (PMNL) and on haemolytic antibody formation (plaques) by lymphoid cells of the spleen in 3-, 6- and 12-month-old mice. In 3- and 12-month-old animals the phagocytic activity of the PMNL was significantly inhibited. Plaque formation was likewise significantly inhibited in 3-month-old mice, but it was significantly raised in 6- and 12-month-old animals.

Key words:
Indomethacin – Phagocytic activity of polymorphonuclear leucocytes – Plaque-forming cells

Indomethacin, a synthetic non-steroidal antiphlogistic, is often employed in clinical practice for its anti-inflammatory and antirheumatic effects. The finding of alteration of certain immune functions in patients treated over long periods with non-steroidal antiphlogistics (NSA) led to a speculation about the effect of NSA on the immune system. In recent years, attention has been turned to the ability of NSA to influence certain functions of "immunoinflammatory" cells (Ngwenyh and Yamamoto 1986), which have become a model for studying the NSA effects(Raghoeber *et al.* 1989).

The data in the literature on the action of indomethacin are often controversial. Since too little attention has been paid to age relationships in the effect of these drugs, we studied the presumed effect of indomethacin on the cells of the immune system in three groups of experimental animals of different ages.

The experimental animals were female C 57 BL 6 mice (VELAZ) aged 3, 6 and 12 months. Groups consisting of nine animals were formed and indomethacin was administered i.p. for one month in doses of 1, 2, 3 and 4 mg/kg body weight; the controls were given 0.9 % NaCl solution.

Phagocytic activity of the PMNL was evaluated as the percentage of phagocytic cells per 100 cells of the same type by means of a set with microspherical hydrophylic particles (Institute for the Research, Development and Utilization of Radioisotopes, Prague). For the direct demonstration of lymphoid cells releasing specific antibodies we used the so called plaque method (as modified by Šterzl and

Mandel 1964). The effect of indomethacin on the phagocytic activity of the PMNL and on plaque formation in the different mouse age groups is illustrated graphically as the phagocytic activity percentage and the number of plasmatic cells per 10^8 spleen cells in respect of the dose.

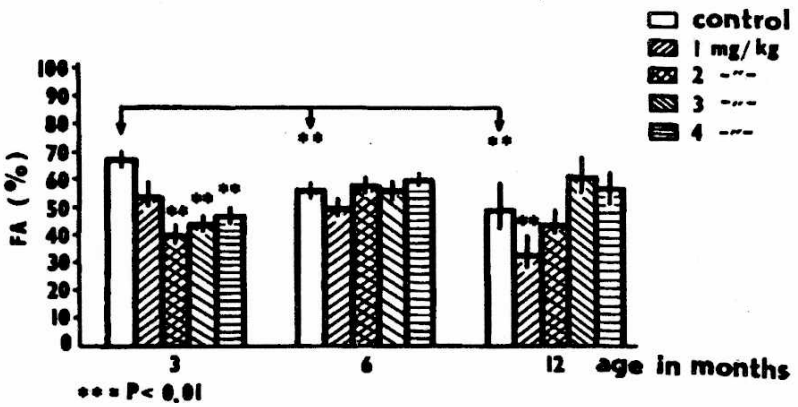

Fig. 1
Effect of indomethacin on the phagocytic activity of the polymorphonuclear leucocytes in different age groups of C 57 BL 6 mice. Statistical significance: ++ = $p<0.01$ (Student's t-test).

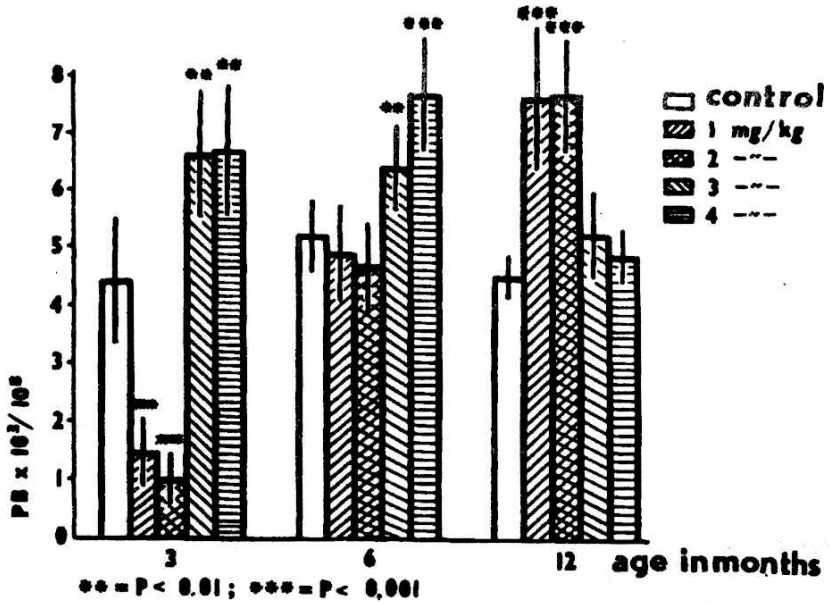

Fig. 2
Effect of indomethacin on the haemolytic antibody formation by the spleen cells in mice of different age groups. Statistical significance: ++ = $p<0.01$, +++ = $p<0.001$

Changes in the phagocytic activity of PMNL in the individual mouse age groups, in relation to the dose of indomethacin, are given in Fig. 1. It can be seen that phagocytic activity in the 3-month-old controls varied from 60 to 70 %. After

a dose of 2, 3 or 4 mg indomethacin/kg, phagocytic activity fell significantly ($p<0.01$). In the 6-month-old controls, phagocytic activity varied from 50 to 60 % and was significantly lower than in 3-months-old ones. In this group, none of administered doses of indomethacin caused significant changes in phagocytic activity. In the 12-month-old controls, phagocytic activity ranged from 40 to 60 %, i.e. it was significantly lower than in 3-months-old animals. In this group, phagocytic activity fell significantly only after a dose of 1 mg indomethacin/kg.

The effect of plaque formation in relation to age is illustrated in Fig. 2. In the control group, the number of plaque-forming cells was about 4.5×10^3 *per* 10^8 spleen cells. After doses of 1 and 2 mg indomethacin/kg, a significant decrease in the number of plaques was observed ($p<0.001$). Plaque formation in the 12-month-old controls did not differ significantly from the control values in 3-month-old ones. After 1 and 2 mg indomethacin/kg, antibody production rose significantly ($p<0.001$) as compared with the control.

The data on the effects of indomethacin on certain functions of the immune system are often contradictory, possibly owing to inter-species and inter-strain differences as well as due to differences in the methods used. Goodwin *et al.* (1978), Goodwin (1984) and Gay *et al.* (1985) pointed out the stimulant effect of therapeutic doses of indomethacin on the activation of neutrophilic leucocytes and on monocyte secretion of proteinase in humans. According to Boorman *et al.* (1982) and Koga *et al.* (1985) high but non-toxic doses of indomethacin cause a marked increase in the proliferative activity of spleen cells and haemopoiesis in mice. An increase in the proliferative activity in lymphocytes, in plaque formation and in antibody levels was observed in pigs in correlation to the dose of indomethacin (Kingston *et al.* 1984). On the other hand, there are reports on the negative effect of therapeutic doses of indomethacin on the complement activation and human polymorphonuclear leucocytes migration (Keiko *et al.* 1982). When administered *per os* in high but not toxic doses (4–8 mg/kg), indomethacin inhibited the immune response of mice to sheep erythrocytes (Rojo *et al.* 1981, Badger *et al.* 1982). The significant stimulation of antibody production by the lymphoid cells of the spleen in 3- and 6-month-old mice given doses of 3 and 4 mg indomethacin/kg and in 12-month-old mice given doses of 1 and 2 mg/kg presented in our study call the attention to the ability of indomethacin to modify the activity of cells of the immune system. Our results further indicate that this effect undergoes sensitivity changes in relation to age. Our next studies will concern the reactivity of older age groups.

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