DRUG REVIEW

Chloramphenicol : A Comeback

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Chloramphenicol, a potent inhibitor of protein synthesis, is extremely active against a variety of organisms including bacteria, spirochetes, rickettsiae, chlamydiae, and mycoplasmas. It has bacteriostatic activity against most pathogens but is bactericidal for Haemophilus influenzae, Streptococcus pneumoniae, and Neisseria meningitidis. Resistance to chloramphenicol has been documented to occur through several mechanisms: reduced permeability or uptake, ribosomal mutation, and acetylation to an inactive derivative. Most reports of resistance were in cases of Salmonella typhi, while anaerobic bacteria, including Bacteroides fragilis, retained 100% susceptibility. Respiratory pathogens such as H. influenzae and S. pneumoniae have also retained high susceptibility rates, with 99.2% and 99.4% of H. influenzae isolates in Canada and the United States respectively, and 91% susceptibility of S. pneumonia isolates. The high susceptibility rates noted for chloramphenicol might be due to the very limited use of this drug for many years in the developed world (1).

However, the use of chloramphenicol has reduced over a period of time due to the adverse effects like bone marrow depression or in some cases severe aplastic anaemia. Overuse and abuse of antibiotics can increase the risk ; however, the underlying mechanisms of chloramphenicol in carcinogenesis are still unclear (2). This effect is either dose dependent or idiosyncratic. The overall risk of developing aplastic anemia after oral Chloramphenicol is 1:30000 to 1:5000015 (2). Based on limited evidence of carcinogenicity from human cancer studies, it was listed in the first annual report on carcinogens in 1980 as a human carcinogen but it was removed from the second annual report on carcinogens in 1981, based on re-evaluation of the carcinogenic potential of the drug by International Agency for Research on Carcinogens.(IARC) (3).

As the effects are seen on the bone marrow cell, it was intended to find out if these adverse effects could be used for the benefits in leukaemia patients, using in-vitro study on leukaemic cell lines. Lokhande *et al* (4) found that Chloramphenicol alone caused about 50 % inhibition of growth of almost all cancer cell lines. The study showed inhibition of growth of the leukaemia cells by chloramphenicol which was comparable to or better than daunorubicin in some cell lines (4).Combination of Chloramphenicol with other anticancer drugs showed higher inhibition of cancer cells than the anticancer drugs used alone (4).

If these results are confirmed in future studies, Chloramphenicol may be used as an anticancer agent with a distinct advantage. Its actions are specific to the bone marrow, thus there will be lesser incidence of adverse effects. Moreoever, its antimicrobial actions will be beneficial in the neutropenic patients suffering from high temperature and malaise, not responding to high doses of gentamicin, cephalothin and carbenicillin to lower the fever (5). Recently reported cardio protective effect of Chloramphenicol make it further useful in clinical practice. Structural changes of chloramphenicol can make it a more potent and reliable cost effective anticancer drug.

In an era of increasing resistance to many antibiotics, chloramphenicol might have a role in the treatment of intraabdominal infections and respiratory tract infections caused by multidrug-resistant pathogens.Moreover, it has a potential to be used as an anticancer drug.However, more studies are needed to evaluate the usefulness of its anticancer potentials.Thus, it represents a great comeback in clinical practise.

References

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