

Furazolidone in Typhoid Fever

The communication from Latha(1) brings to fore the controversy regarding the role of furazolidone in the treatment of typhoid fever. I have attempted to address this issue by reviewing the relevant literature.

Furazolidone is poorly absorbed from the gastro-intestinal tract. The serum levels achieved (1.5 µg/ml or less) are far below than the minimum inhibitory concentration required for *Salmonella typhi* (2-5 µg/ml) (2,3). Post dose serum does not have clinically significant bactericidal activity even after using furazolidone in high dose(4). Though organisms like *E. coli*, *Klebsiella*, *Staphylococci*, etc. have been shown to be sensitive to furazolidone *in vitro* (3), systemic infections due to these organisms have never been successfully treated with furazolidone due to the poor serum levels achieved. At the same time furazolidone has been shown to be effective in treating enteric infections due to *E. coli*, *Shigella*, *Cholera*, etc.(5), proving its good action in the intestinal lumen. Thus it seems that though furazolidone has good action in the intestinal lumen, it has negligible systemic action.

Every pediatrician will agree that a proportion of patients with typhoid fever can be successfully treated with furazolidone. It is hypothesised that the action of furazolidone in the lumen of intestine effectively blocks the entero-systemic re-entry of the organisms reaching there in plenty from the bile(4). Thus the systemic bacteria load is

considerably reduced, helping the immune system to tackle the remaining bacteria. Whether the immune system can take care of this, is to be considered. Only 12-16% of patients with typhoid fever died in the pre-antibiotic era (6), meaning that the majority improved on their own. This process can be enhanced if furazolidone blocks the entero-systemic re-entry of organisms present in the intestine.

Majority of patients included in various studies using furazolidone consisted of Widal positive but blood culture negative children(4). This represents a later stage in the natural history of the disease when the immune system has already got an upper hand, thus reducing the bacterial load in the blood resulting in negative blood cultures. During this stage of the natural history, the stool cultures remain positive (6,7) indicating the presence of bacilli in the intestine. In this situation, furazolidone can bring about a cure by its action in the intestinal lumen.

Since the main traffic of organisms during secondary bacteremia is from blood to intestine(7), furazolidone can theoretically produce a response in blood culture positive immuno-competent host also. However treating a systemic infection with a non-absorbable drug may prove dangerous in some patients. This may have medico-legal implications also.

Since chloramphenicol is very well absorbed from the intestine, some clinicians combine it with furazolidone to take care of the organisms in the intestinal lumen. However, there are no well controlled studies comparing the efficacy of this combination with that of mono-

therapy. Addition of furazolidone is not indicated when ceftriaxone or ciprofloxacin is used as these drugs by themselves achieve very high concentrations in the bile and the intestinal lumen.

After reviewing the literature it seems reasonable to conclude that monotherapy with furazolidone should be avoided in all blood culture proved cases of typhoid fever.

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