The Effects of Saccharin, Sodium Chloride, Aspirin and Gastrojejunostomy on Gastric Carcinogenesis of N-methyl-N'-nitro-N-nitrosoguanidine in Rats

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The incidence of gastric cancer in Japan, Chile and northern Europe has been increased while decreasing in United States recently. Especially the intestinal type of gastric cancer was selectively increased or decreased.

It has been known that intestinal type cancer is related with diet factor, nitrites and nitroso compounds such as N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) or N-nitrosotaurocholic acid (NOTC).

Many investigators have reported the gastric carcinogenesis by administration of MNNG and promoting effect of saccharin, sodium chloride, gastrojejunostomy or inhibition effect of aspirin in animal experiments. Also preneoplastic changes such as preneoplastic hyperplasia, adenomatous hyperplasia, atypical glands, intestinal metaplasia are known to relate with experimental carcinogenesis in animal experiments.

On the other hand, non-specific immunity is decreased in advanced cancer patients and normal or slightly decreased in early stage of cancer patients, but it is not clearly documented yet.

In order to observe the gastric carcinogenesis in rats by oral administration of MNNG and the effects of saccharin, sodium chloride, aspirin and gastrojejunostomy, the experimental animals were divided into six groups: water and basal diet only (control = Group 1), supplemented with MNNG 100 mg/L in water for 8 weeks (Group 2), supplemented with MNNG 100 mg/L for 8 weeks and 5% saccharin in water for 40 weeks (Group 3), supplemented with MNNG 100 mg/L for 8 weeks and 10% sodium chloride for 40 weeks (Group 4), supplemented with MNNG 100 mg/L for 8 weeks and 1% aspirin for 40 weeks (Group 5), gastrojejunostomy and MNNG 100 mg/L for 8 weeks (Group 6), and all animals were fed for 40 weeks.

The authors observed peripheral blood lymphocyte counts, PHA, Con A, PWM stimulated lymphocyte blastogenesis and histopathological findings at the end of the experiment.
The results obtained were as follows:

1) 40% of preneoplastic hyperplasia, 40% of atypical glands, 30% of intestinal metaplasia and 10% of adenocarcinoma with one case of pancreas cancer were observed in group 2.

2) In group 3, preneoplastic hyperplasia (43%), atypical glands (43%), intestinal metaplasia (30%), adenocarcinoma (13%) were observed which was slightly higher than group 2.

3) 100% of preneoplastic hyperplasia and atypical glands, 71% of intestinal metaplasia and adenocarcinoma with each one case of jejunal cancer and cystic liver tumor were observed which findings were much higher than the other groups.

4) In group 4 and 5, only below 20% of preneoplastic hyperplasia and atypical glands, 11% of intestinal metaplasia were observed which was lower than group 2.

5) The peripheral blood lymphocyte count in group 1 was $6,898 \pm 829/ul$ and no significant differences were observed between each group except slight increase in group 5 $(8,292 \pm 795/ul)$.

6) PHA stimulated lymphoblastogenesis were significantly decreased in group 2 to 6 $(3,312 \pm 727.4, 4 \times 10^6 cells - 4,451 \pm 522.3, 4 \times 10^6 cells)$ than control $(5,215 \pm 489.5, 5 \times 10^6 cells)$, and Con A lymphoblastogenesis were significantly increased in group 2.4 and 6 $(4,285 \pm 609.6, 6 \times 10^6 cells - 5,372 \pm 960.6, 6 \times 10^6 cells)$ than control $(3,524 \pm 337.3, 6 \times 10^6 cells)$. But there were no significant differences between group 2 to 6.

With above results, authors inferred that oral administration of MNNG induce gastric carcinogenesis in rats and saccharin, gastrojejunosotomy promote but aspirin inhibits the effects of MNNG.

서론

위암의 발생은 일본, 질병 및 복음에서는 늑은 빈도를 보이고 있지만 미에서의 근거에 그 빈도가 현저하게 감소하는 경향을 보이고 있다. 이론적으로 위암의 발생은 여러 요인에서 관계되는 것으로 알려져 있지만 최근 특히 섭取영양으로서 아질산염 (nitrites), 니트로소 화합물 (nitroso compounds) 등이 발암과 관계되므로 알려져 있으며, 사카린, 고농도 식염수, 위-공장 유흥은 이러한 발암작용을 촉진시키고 아스피린은 억제시킨다고 하였다.

실험적으로 니트로소 화합물을 경구투여하여 발생시킨 위암용암이 보고되었으며, 이러한 실험적 위암 발생은 그 전암변화 (preneoplastic changes)로서 위관암 세포의 전암증상 (preneoplastic hyperplasia) 또는 전암증상 (adenomatous hyperplasia)18,20 이 형성되어 전암변화 (atypical gland)4,6,21,22, 정상성 (intestinal metaplasia)16,21이 관계가 있는 것으로 알려져 있다.

한편 암환자에서의 비특이성 면역은 진단된 경우 감소되어 있고 초기 암환자에서는 정상이거나 약간 감소되어 있으나 암종증에 따라 차이가 있다고 하였으나 아직 확실히 규명되지 못하고 있다.

저자들은 환자를 이용하여 강력한 위암전 위암용 약물로 알려진 N-methyl-N-nitro-N-nitrosoguanidine (이하 MNNG)를 경구투여하고 이에 사카린, 고농도 식염수, 아스피린 두여 또는 위-공장 유흥을 시행하여 32주 내지 40주간 사육한 후 말초혈액 반응계수, phytohemagglutinin (이하 PHA), concanavalin A (이하 Con A), pokeweed mitogen (이하 PWM) 자극 염증가체로 변형를 촉진한 조직적검사 등을 시행하여 위암의 전암변화, 발암, 말초혈액 반응계수의 기능과 사카린, 고농도 식염수, 아스피린 또는 위-공장 유흥이 이에 미치는 영향을 관찰하고자 본 실험을 시도하였다.

재료 및 방법

1) 실험 동물

실험동물은 8주 대비 10주되는 Sprague-Dawly 개에 8주 청구중 체중 200g 내지 300g의 건강한 새끼들만을 사용하였다.

2) 방법

모든 실험동물은 6군으로 나누어 MNNG, 사카린,