

Sodium Hyaluronate (SPH) のマウス, ラットおよび ウサギにおける急性毒性試験

長野 聖, 後藤 幸子, 岡部 良治
佐野 章子, 山口敏二郎*

Acute Toxicity Test of Sodium Hyaluronate (SPH) in Mice, Rats and Rabbits

Kiyoshi Nagano, Sachiko Goto, Yoshiharu Okabe,
Akiko Sano and Toshijiro Yamaguchi*

(*Tokyo Research Institute, Seikagaku Kogyo Co., Ltd.,
3-1253, Tateno, Higashiyamato, Tokyo 189)

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Acute toxicity test was performed using 3% sodium hyaluronate (SPH) solution in 10 mice, 10 rats and 5 rabbits of both sexes per a group by oral, subcutaneous and intraperitoneal administration.

1. The LD₅₀ value of SPH were higher than the highest dose possible by any of the three routes of administration in any of the three species.
2. Administered orally, there were no deaths or no specific signs of toxicity during 7 or 14 days period of observation in any of the species.
3. Administered subcutaneously, retention of SPH in the local site was observed for several days, but there were no deaths or no specific signs of toxicity during 10 or 28 days period of observation in any of the species.
4. Administered intraperitoneally, retention of SPH in the local site was observed for several days in any of the species.

Some in the high dose groups of mice and rats showed sedation and rolling with torticollis and a few of them died. In rabbits, one died after sedation. Autopsy revealed retention of the drug in the abdominal cavity in all dead animals. In those dead rats, there were brain hemorrhage, a slight accumulation of viscous fluid in the thoracic cavity, hepatic hypertrophy, and renal swelling. In that dead rabbit, there were accumulation of viscous fluid in the thoracic cavity, renal swelling, and dilatation of mesenteric vessels. The surviving animals were sacrificed, the autopsy indicated no remarkable changes in these animals except for one rat after 14 or 28 days period of observation.

Key words: Sodium hyaluronate—Acute toxicity test (mouse, rat, rabbit).

緒 言

hyaluronic acid (HA と略) は哺乳動物の結合組織に広く分布する代表的な glycosaminoglycan の一種である。

HA 溶液は, その物理化学的な性質として高い粘性と保水性を有し (Laurent, 1970), 生体内での HA の生理的機能もこれらの物理化学的な性質に負うところ

が大きい。Dorfman (1958) は HA の生理学的機能として関節においては潤滑に, 硝子体においてはその構造保持や透明度維持に, 皮膚においては創傷治癒や感染防御に関与し, また細胞外液の水分や電解質の調整に重要な役割を果していることを報告している。

HA のこれらの特性に着目し, Balazs *et al.* (1967) は早くから HA の医学的応用を目的として検討を進めてきた。Rydell *et al.* (1970) は競走馬の外傷性関節炎の治療に HA が有用であることを報告し, また Peyron *et al.* (1974) はヒト変形性関節症の治療にも

* 東京都東大和市立野 3-1253 (〒189) 生化学工業株式会社東京研究所