胎生期PCB曝露ラットの精子形成障害

Testicular Toxicology of Rats Prenatally Exposure to 3,3',4,4',5-Pentachlorobiphenyl

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Abstract: The present study investigated the dose-response relationship in testicular toxicology of 7 (pubescent)- and 17 (adult)-week-old Sprague-Dawley rats whose dams had been injected (i.g.) with 25 pg, 2.5 ng, 250 ng, or 7.5 μg of 3,3',4,4',5-pentachlorobiphenyl (PCB126)/kg or the vehicle on days 13 to 19 post-conception. At 7 and 17 weeks old of the 7.5 μg group and at 7 weeks old of the 250 ng group showed an increase in the percentage of seminiferous tubules at Stages VII-VIII. At 7 and 17 weeks old, the 7.5 μg group showed a decrease in preleptotene spermatocytes with spermatids at all Stages; while the 250 ng group also showed a decrease in preleptotene spermatocytes, but round spermatids increased at Stages VI-VII and elongated spermatids decreased at Stage VIII. At 7 weeks old, the 2.5 ng group showed an increase in round spermatids at Stages VI-VII. The formation of spermatogenic cells in the 25 pg group was similar to that of the vehicle group. The number of Sertoli cells and cauda epididymal sperms in the PCB126 groups were similar to those of the vehicle group. Prenatal PCB126 exposure induced dose-related defective spermatogenesis. A high dose PCB126 group affected the development of spermatogonia and spermatids in puberty and adulthood, while a low dose group affected the conversion of spermatids at puberty, although this was recovered in adulthood. Because the serum testosterone levels were similar in the PCB126 and vehicle groups in puberty and adulthood, a direct endocrine cause for the observed effects was unlikely.

1. 目　的

ダイオキシン類による汚染は地球規模で広がっている。ダイオキシン類は水・堆積物・魚・野生動物，およびヒトの脂肪組織・ミルクならびに血清を含む地球の生態系のほとんどすべての構成要素に汚染物質として検出されている。また他のダイオキシン類に比べその生物濃縮性が高いことが知られている，さらに，胎盤・授乳を介して次世代に移行するため，次世代への影響が示唆されている。しかし，PCB126胎生期曝露が次世代の精子形成へ可逆的・非可逆的影響を与えるかについては検討させていない。我々はPCB126胎生期曝露が思春期から成獣期のラット精子形成サイクルにどの様な影響をおよぼすかについて検討することを目的とし，環境汚染化学物質であるPCB126の生体への可逆・非可逆的影響を検討した。

2. 方　法

SD（slc）ラット妊娠13～19日目までPCB126を7.5 ug/kg/day（7.5 ug群），250 ng/kg/day（250 ng群），25 ng/kg/day（25 ng群），25 pg/kg/day（25 pg群），0 g/kg/day（対照群）連日経口投与を行う。出生後，7週齢，17週齢に安楽死後に剖検し精巣を剖出する。

各精巣はH&E，PAS染色を施し，精細管における精子形成サイクルにおけるステージ分類を観察し各対照群と比較検討をおこなった。

3. 結　果

生後7週齢・17週齢において，PCB126投与群，対照群間で動物の体重また精巣重量に有意差は認められなかった。肝臓内PCB126含有量は7週齢では，対照群と比較して7.5ug群，250ng群で有意に高い値を示し，17週齢では7.5ug群で有意に高い値を示した。7週齢・17週齢において，PCB126投与群，対照群間で曲精細管内のセルトリ細胞数に有意差は認められなかった。7週齢・17週齢の7.5ug群，7週齢の250ng群ではVII-VIIIステージの曲精細管数は対照群と比較して有意に増加を示し，さらに，I-XIVステージのpreleptotene spermatocyte，spermatids数が有意に減少した。対照群と比較して7週齢・17週齢の250ng群では，VI-VIIステージのround spermatidsが有意に増加し，VIIIステージのelongating spermatidsの有意な減少が認められた。生後7週齢・17週齢において，PCB126投与群，対照群間でtestosterone値に有意差は認められなかった。

4. 考　察

PCB126胎生期曝露は用量相関的に次世代の精子形成能に影響を与えることが明らかとなった。高用量曝露群では，思春期から成獣期においてspermatogonia，spermatidsに障害が認められた。これに対し，低用量群では思春期ではspermatidsに障害が認められたが，成獣期では回復を示した。生後7週齢・17週齢において，PCB126投与群，対照群間でtestosterone値に有意差は認められなかったことから，これらの異常の原因には性ホルモンによる直接的変化以外の因子が関与することが考えられた。

5. 要　約

内分泌かく乱化学物質である3,3',4,4',5-pentachlorobipheny胎生期曝露後のラット精巣の変化に関して生後7週齢・17週齢に形態学的に検討した。高用量曝露群では思春期から成獣期においてspermatogonia，spermatidsに障害が認められた。また，低用量群では思春期ではspermatidsに障害が認められたが，成獣期では回復する可逆的障害であることが示唆された。

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